Tuberculosis: clinical diagnosis and management of tuberculosis, and measures for its prevention and control

NICE guideline

Second draft for consultation, September 2005

If you wish to comment on this version of the guideline, please be aware that all the supporting information and evidence is contained in the full version.
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Introduction

Where scientific evidence supports it, this guideline gives recommendations for aspects of service organisation as well as for individual teams of healthcare professionals. TB has widely varying incidence in different parts of the country, influenced by varying risk factors (exposure to, and susceptibility to, TB) and levels of deprivation (poverty, housing, nutrition and access to healthcare). The guideline attempts to focus NHS resources where they will effectively combat the spread of TB, and in some sections deals with high- and low-incidence areas separately.

Similarly, TB incidence is much higher in many other parts of the world, and readers outside England and Wales should exercise caution before applying these recommendations, which are designed for use within the National Health Service and English and Welsh epidemiology.

Patient-centred care

This guideline offers best practice advice on the care of people with, or at risk of contracting, tuberculosis.

Treatment and care should take into account patients' individual needs and preferences. People with, or at risk of contracting, tuberculosis should have the opportunity to make informed decisions about their care and treatment. Where patients do not have the capacity to make decisions, healthcare professionals should follow the Department of Health guidelines – Reference guide to consent for examination or treatment (2001) (available from www.dh.gov.uk).

Good communication between healthcare professionals and patients is essential. It should be supported by the provision of evidence-based information offered in a form that is tailored to the needs of the individual patient. The treatment, care and information provided should be culturally appropriate and in a form that is accessible to people who have additional needs, such as people with physical, cognitive or sensory disabilities, and people who do not speak or read English.
Unless specifically excluded by the patient, carers and relatives should have the opportunity to be involved in decisions about the patient's care and treatment.

Carers and relatives should also be provided with the information and support they need.
Key priorities for implementation

The following recommendations have been identified as priorities for implementation.

- The 6-month, four-drug initial regimen (6 months of isoniazid and rifampicin supplemented in the initial 2 months with pyrazinamide and ethambutol) should be used to treat:
  - adults with active respiratory tuberculosis, who are not known to be HIV-positive
  - adults with active respiratory tuberculosis, who are HIV-positive
  - children with active respiratory tuberculosis.

- Use of DOT is not usually necessary in the management of most cases of active tuberculosis. All patients should have a risk assessment for adherence with treatment, and DOT should be considered for patients who have adverse factors on their risk assessment, in particular:
  - street- or shelter-dwelling homeless people with active tuberculosis
  - patients with poor adherence rates, in particular those who have a history of non-adherence.

- Each person with TB should be informed by the TB service who their named key worker is, and how to contact them. This key worker should facilitate education and involvement of the person with TB in achieving adherence.

- Patients with active meningeal tuberculosis should be offered:
  - a treatment regimen, initially of 12 months’ duration, comprising an initial 2 months of isoniazid, pyrazinamide, rifampicin and a fourth drug (for example, ethambutol), then the remainder of the treatment period with isoniazid and rifampicin
  - a glucocorticoid at the normal dose range:
adults: equivalent to prednisolone 20–40mg if on rifampicin, 10–20 mg otherwise
children: equivalent to prednisolone 1–2 mg/kg, maximum 40 mg
with gradual withdrawal of the glucocorticoid considered within 2–3 weeks of initiation.

- New entrants should be identified for TB screening from the following information:
  - Port of Arrival reports
  - new registrations with primary care
  - entry to education or university
  - links with statutory and voluntary groups working with new entrants.

- Neonatal BCG vaccination for any newborn baby at increased risk of tuberculosis should be discussed with the parents or legal guardian. Neonates at increased risk are those:
  - born in a local authority with a notification rate \( \geq 40 \) per 100,000 population (as defined by the Health Protection Agency website www.hpa.org.uk), or
  - with one or more of the parents or grandparents born in a high-incidence country (as defined by the Health Protection Agency website www.hpa.org.uk), or
  - with a family history of TB in the previous 5 years.

- Primary care organisations with high notification rates (\( \geq 40 \) per 100,000 population, as defined by the Health Protection Agency website www.hpa.org.uk) should consider vaccinating all neonates soon after birth.
The following guidance is evidence based. Appendix A shows the grading scheme used for the recommendations: A, B, C, D or good practice point – D(GPP). Recommendations on diagnostic test are graded A(DS), B(DS), C(DS) or D(DS). A summary of the evidence on which the guidance is based is provided in the full guideline (see Section 5).

1 Guidance

1.1 Diagnosis

1.1.1 Diagnosing latent tuberculosis

1.1.1.1 To diagnose latent tuberculosis: [D]

- tuberculin skin testing should be performed
- those with positive results (or in whom tuberculin skin testing may not be reliable) should then be considered for interferon-gamma immunological testing, if available.

If latent tuberculosis has not been excluded by testing, the person should be referred to a TB specialist (see Section 1.4).

1.1.2 Diagnosing active tuberculosis

1.1.2.1 To diagnose active pulmonary tuberculosis:

- a chest X-ray should be taken, and chest X-ray appearances suggestive of TB should lead to further diagnostic investigation [C(DS)]
- multiple sputum samples (at least three, with one early morning sample) should be sent for TB microscopy and culture in suspected pulmonary TB before commencement of treatment if possible, or failing that, within 7 days of commencement [C(DS)]
- spontaneously produced sputum should be obtained if possible, otherwise induction of sputum or bronchoscopy and lavage should be used [B(DS)]
• in children unable to expectorate sputum, induction of sputum should be considered if it can be safely carried out, with gastric washings considered as third line [B(DS)]
• samples should be sent for TB culture from autopsy samples where pulmonary TB is a possibility [D(GPP)]
• clinical signs and symptoms consistent with a diagnosis of TB should lead to the commencement of TB treatment, without waiting for culture results (see Section 1.2.1 for details) [D(GPP)]
• the standard drug regimen should be continued in patients whose subsequent culture results are negative. [D(GPP)]

1.1.2.2 To diagnose active extra-pulmonary tuberculosis:

• advantages and disadvantages of both biopsy for culture and needle aspiration for cytology should be considered with the patient, with the aim of obtaining adequate material for diagnosis [B(DS)]
• part, or all, of any of the following samples should be placed in a dry pot (and not all placed in formalin) and sent for TB culture: [D(GPP)]
  - lymph node biopsy
  - pus aspirated from lymph nodes
  - pleural biopsy
  - any surgical sample sent for routine culture
  - any radiological sample sent for routine culture
  - histology sample where non-respiratory TB is a possibility
  - aspiration sample where non-respiratory TB is a possibility
  - autopsy sample
• microbiology staff should routinely perform TB culture on the above samples (even if it is not requested) [D(GPP)]
• histology consistent with a diagnosis of TB, in a patient with a clinical picture suggestive of TB, should lead to the
commencement of TB treatment, without waiting for culture results (see Sections 1.2 and 1.3) [C(DS)]

- all patients with non-respiratory TB should have a posterior-anterior chest X-ray to exclude or confirm co-existing respiratory TB and, in addition, tests as per Table 1 should be considered [D(GPP)]

- the appropriate drug regimen (see Sections 1.2 and 1.3) should be continued in patients whose subsequent culture results are negative. [D(GPP)]
Table 1: Suggested site-specific investigations in the diagnosis and assessment of non-respiratory TB

<table>
<thead>
<tr>
<th>Site</th>
<th>Imaging</th>
<th>Biopsy</th>
<th>Culture</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lymph node</td>
<td></td>
<td>Node</td>
<td>Node or aspirate</td>
</tr>
<tr>
<td>Bone/joint</td>
<td>Plain X-ray and CT MRI</td>
<td>Site of disease</td>
<td>Biopsy or para-spinal abscess Site or joint fluid</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>Ultrasound</td>
<td>Omentum</td>
<td>Biopsy</td>
</tr>
<tr>
<td></td>
<td>CT abdomen</td>
<td>Bowel</td>
<td>Ascites</td>
</tr>
<tr>
<td>Genitourinary</td>
<td>IVU</td>
<td>Site of disease</td>
<td>Early morning urine</td>
</tr>
<tr>
<td></td>
<td>Ultrasound</td>
<td></td>
<td>Site of disease</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Endometrial</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Curettings</td>
</tr>
<tr>
<td>Disseminated</td>
<td>HRCT thorax</td>
<td>Lung</td>
<td>Bronchial wash</td>
</tr>
<tr>
<td></td>
<td>Ultrasound abdomen</td>
<td>Liver</td>
<td>Liver</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Bone marrow</td>
<td>Bone marrow</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Blood</td>
</tr>
<tr>
<td>Central nervous system</td>
<td>CT brain MRI</td>
<td>Tuberculoma</td>
<td>CSF</td>
</tr>
<tr>
<td>Skin</td>
<td></td>
<td>Site of disease</td>
<td>Site of disease</td>
</tr>
<tr>
<td>Pericardium</td>
<td>Echocardiogram</td>
<td>Pericardium</td>
<td>Pericardial fluid</td>
</tr>
<tr>
<td>Cold/liver abscess</td>
<td>Ultrasound</td>
<td>Site of disease</td>
<td>Site of disease</td>
</tr>
</tbody>
</table>

1.1.2.3 Molecular tests for *M tuberculosis* complex on primary specimens should only be used where: [D(GPP)]

- rapid confirmation of a TB diagnosis in a sputum smear-positive individual would alter the patient’s care, or
- before conducting a large contact-tracing initiative.
1.1.2.4 Clinicians should still consider a diagnosis of non-respiratory tuberculosis in cases where nucleic acid amplification tests are negative, for example in pleural fluid, cerebro-spinal fluid and urine. [B(DS)]

1.1.2.5 Clinical signs and other laboratory findings consistent with TB meningitis should lead to treatment, regardless of a negative molecular test, as the potential consequences to the patient are severe (see Section 1.3.1). [D(GPP)]

1.1.2.6 Before conducting a large contact-tracing initiative (for example in a school or hospital), the species of mycobacterium should be confirmed to be *M tuberculosis* complex by molecular testing on microscopy- or culture-positive material. [D(GPP)]

1.1.2.7 Where a risk assessment suggests a patient has multi-drug resistant (MDR) TB (see Section 1.5.2): [D(GPP)]

   • rapid molecular tests should be conducted for rifampicin resistance
   • infection control measures and treatment as MDR TB should be started as per Section 1.5, pending the result of the tests.

1.1.2.8 Rapid molecular tests for *M tuberculosis* complex identification should only be conducted on biopsy material if: [D(GPP)]

   • all the sample has been inappropriately placed in formalin, and
   • acid-fast bacilli are visible on microscopy.

1.1.2.9 Clinical samples should be submitted for culture by automated liquid methods, bearing in mind the laboratory throughput required for quality control. [D(GPP)]
1.2 Management of respiratory tuberculosis

1.2.1 Drug treatment

1.2.1.1 Once a diagnosis of active TB is made, the clinician responsible for care should refer the person with TB to the care of a physician with full training in, and experience of, the specialised care of TB. The team to provide care should include specialised nurses and health visitors. Children should be managed either by a paediatrician with special experience and training, or by a general paediatrician with advice from a specialised physician. Where these arrangements are not possible, advice should be sought from more specialised colleagues throughout. [C]

1.2.1.2 The 6-month, four-drug initial regimen (6 months of isoniazid and rifampicin supplemented in the initial 2 months with pyrazinamide and ethambutol) should be used to treat:

- adults with active respiratory tuberculosis, who are not known to be HIV-positive [A]
- adults with active respiratory tuberculosis, who are HIV-positive [B]
- children with active respiratory tuberculosis. [B]

1.2.1.3 Fixed-dose combination tablets are strongly recommended for use as part of any tuberculosis treatment regimen. [C]

1.2.1.4 A thrice weekly dosing regimen should be considered for patients receiving directly observed therapy (DOT) (see Section 1.2.2). [D(GPP)]
Table 2: Advised dosages for thrice weekly treatment

<table>
<thead>
<tr>
<th>Drug</th>
<th>Children</th>
<th>Adults</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Weight</td>
<td>Dose</td>
</tr>
<tr>
<td>Isoniazid</td>
<td>15 mg/kg 3 times weekly</td>
<td>All</td>
</tr>
<tr>
<td></td>
<td>15 mg/kg thrice weekly</td>
<td></td>
</tr>
<tr>
<td>Rifampicin</td>
<td>15 mg/kg 3 times weekly</td>
<td>All</td>
</tr>
<tr>
<td></td>
<td>600–900 mg thrice weekly</td>
<td></td>
</tr>
<tr>
<td>Pyrazinamide</td>
<td>50 mg/kg 3 times weekly</td>
<td>&lt; 50 kg</td>
</tr>
<tr>
<td></td>
<td>2.0 g thrice weekly</td>
<td></td>
</tr>
<tr>
<td></td>
<td>&gt; 50 kg</td>
<td>2.5 g thrice weekly</td>
</tr>
<tr>
<td>Ethambutol</td>
<td>30 mg/kg 3 times weekly</td>
<td>All</td>
</tr>
<tr>
<td></td>
<td>30 mg/kg thrice weekly</td>
<td></td>
</tr>
</tbody>
</table>

1.2.1.5

1.2.1.6 A twice weekly dosing regimen should not be used for the treatment of active tuberculosis. [D(GPP)]

1.2.2 Improving adherence: directly observed therapy (DOT)

1.2.2.1 Use of DOT is not usually necessary in the management of most cases of active tuberculosis [A]. All patients should have a risk assessment for adherence with treatment, and DOT should be considered for patients who have adverse factors on their risk assessment, in particular:

- street- or shelter-dwelling homeless people with active tuberculosis [B]
- patients with poor adherence rates, in particular those who have a history of non-adherence. [D(GPP)]

1.2.2.2 Clinicians who are planning to start a patient on a course of DOT should consider ways to mitigate the environmental, financial and psychosocial factors that may reduce adherence, including stability of accommodation, prescription charges and transport. The setting, observer and frequency of treatment should be arranged to be most pragmatic for the individual with TB, on a patient-centred basis. DOT
should also be supported by frequent contact with a healthcare professional. [D(GPP)]

1.2.3 Improving adherence: non-pharmacological strategies

1.2.3.1 To promote adherence, patients should be involved in treatment decisions at the outset of TB treatment or chemoprophylaxis. The importance of adherence should be emphasised during discussion with the patient when agreeing the treatment or chemoprophylaxis regimen. [D(GPP)]

1.2.3.2 Each person with TB should be informed by the TB service who their named key worker is, and how to contact them. This key worker should facilitate education and involvement of the person with TB in achieving adherence. [D(GPP)]

1.2.3.3 TB teams should consider the following interventions for a strategy to improve adherence in either treatment or chemoprophylaxis if a patient defaults:

- reminder letters in appropriate languages [B]
- health education counselling [B]
- patient-centred interview and health education booklet [B]
- home visits [D(GPP)]
- patient diary [D(GPP)]
- random urine tests and other monitoring (for example, pill counts) [D(GPP)]
- information about help with paying for prescriptions [D(GPP)]
- assisting or advising patients regarding links to social security benefits and housing/social service. [D(GPP)]

1.2.3.4 Pharmacies should make liquid preparations of anti-tuberculosis drugs readily available to TB patients. [D(GPP)]

1.2.3.5 TB services should assess local language and other communication needs and, where there is a demonstrated need,
provide patient information accordingly. Such material should be drawn from national high-quality resources where available; for examples, see www.hpa.org.uk [D(GPP)]

1.2.3.6 The National Knowledge Service should maintain current patient and public information on tuberculosis. In most cases this should cover the topics in this guideline, and should be available in appropriate languages and also in audio/visual, Braille and British Sign Language. This information should be made readily available for local TB services, along with links to further translation should it be required. [D(GPP)]

1.2.4 Treatment completion and follow-up

1.2.4.1 Follow-up clinic visits should not routinely be conducted after treatment completion. [D]

1.2.4.2 Patients should be advised to be alert to symptoms of relapse and how to contact the TB service rapidly through primary care or a TB clinic. Key workers should ensure that patients at increased risk of relapse are well informed about symptoms. [D(GPP)]

1.2.4.3 Patients who have had drug-resistant tuberculosis should be considered for follow-up for 12 months after treatment completion. Patients who have had MDR TB should be considered for prolonged follow-up. [D(GPP)]

1.2.5 Infection control

The recommendations below deal with three levels of isolation for infection control in hospital settings:

- negative pressure rooms, which have air pressure continuously or automatically measured, and are defined by NHS Estatesª

1.2.5.1 Risk assessments for drug resistance (see Section 1.5) and for HIV should be made on all patients with TB. Where risk factors for MDR TB are present, see Section 1.5.3 for recommendations on infection control. [D(GPP)]

1.2.5.2 Unless there is a clear clinical or socio-economic need, such as homelessness, people with tuberculosis of any site of disease should not be admitted to hospital for diagnostic tests or for care. [D(GPP)]

1.2.5.3 Patients with suspected respiratory tuberculosis requiring admission should be admitted to a single room. [D(GPP)]

1.2.5.4 Patients with respiratory tuberculosis should be separated from immuno-compromised patients, either by admission to a single room on a separate ward, or to a negative pressure room on the same ward. [D(GPP)]

1.2.5.5 When a child is admitted to hospital with TB, any visitors should be screened as part of contact tracing, and kept separate from other patients until they have been excluded as the source of infection. [D(GPP)]
1.2.5.6 Smear-positive TB patients without risk factors for MDR TB (see Section 1.5.1), should be cared for in a single room, until: [D(GPP)]

- they have completed 2 weeks of the standard regimen (see Section 1.2.1), or
- they are discharged from hospital.

1.2.5.7 For

- all patients on an HIV ward, regardless of whether a diagnosis of TB has been considered, and
- all patients in whom TB is considered a possible diagnosis, in any setting,

aerosol generating procedures such as bronchoscopy, sputum induction or nebuliser treatment should be carried out in an appropriately engineered and ventilated area. [D(GPP)]

1.2.5.8 Healthcare workers caring for people with tuberculosis should not use masks, gowns or barrier nursing techniques unless: [D(GPP)]

- MDR TB is suspected
- cough-inducing procedures are being performed.

When such equipment is used, the reason should be explained to the person with TB. Such equipment should meet the standards of the Health & Safety Executive. See Section 1.5.3 for further detail of MDR TB infection control.

1.2.5.9 TB patients admitted to a setting where care is provided for HIV-positive or other immuno-compromised patients should be considered non-infectious and leave a negative pressure room when: [D(GPP)]

For sputum smear positive cases:
1. the patient has had a minimum of 2 weeks of appropriate multiple drug therapy, and

2. if moving to accommodation (inpatient or home) with HIV positive or immuno-compromised patients, the patient has had a minimum of three negative microscopic smears on separate occasions over a 14-day period, and

3. the patient is showing tolerance to the prescribed treatment and an ability and agreement to adhere to treatment, and either

4. a complete resolution of cough, or

5. definite clinical improvement on treatment, for example remaining afebrile for a week.

For sputum smear negative cases (three negative samples taken on separate days, or, if no sputum sample has been possible and material has only been obtained by bronchoscopy or lavage): all of 1, 2, 3 and 5 above should apply.

1.2.5.10 Inpatients with smear positive pulmonary tuberculosis should be asked (with explanation) to wear a surgical mask whenever they leave their room if they have had less than 2 weeks’ drug treatment. [D(GPP)]

1.3 Management of non-respiratory tuberculosis

1.3.1 Meningeal tuberculosis

1.3.1.1 Patients with active meningeal tuberculosis should be offered:

• a treatment regimen, initially of 12 months’ duration, comprising an initial 2 months of isoniazid, pyrazinamide, rifampicin and a fourth drug (for example, ethambutol), then the remainder of the treatment period with isoniazid and rifampicin [D(GPP)]

• a glucocorticoid at the normal dose range:
1.3.1.2 Clinicians prescribing treatment for active meningeal tuberculosis should consider as first choice:

- a daily dosing schedule [B]
- using combination tablets. [D]

1.3.2 Peripheral lymph node tuberculosis

1.3.2.1 For patients with active peripheral lymph node tuberculosis, the first choice of treatment should:

- be the 6-month, four-drug initial regimen (6 months of isoniazid and rifampicin, supplemented in the initial 2 months with pyrazinamide and ethambutol) [B]
- use a daily dosing schedule [B]
- include combination tablets. [D]

See Section 1.2.1 for further details.

1.3.2.2 Patients with active peripheral lymph node tuberculosis where a gland has been surgically removed should still be treated with the 6-month, four-drug regimen. [D(GPP)]

1.3.2.3 Drug treatment of peripheral lymph node tuberculosis should normally be stopped after 6 months, regardless of the appearance of new nodes, residual nodes or sinuses draining during treatment. [D(GPP)]
1.3.3 Bone and joint tuberculosis: drug treatment

1.3.3.1 The standard 6-months’ four-drug initial regimen (6 months of rifampicin and isoniazid, supplemented in the initial 2 months with pyrazinamide and ethambutol) should be planned and started in people with:

- active spinal tuberculosis [B]
- active tuberculosis at other bone and joint sites. [C]

See Section 1.2.1 for details

1.3.3.2 Clinicians prescribing treatment for active bone and joint tuberculosis should consider as first choice:

- a daily dosing schedule [B]
- using combination tablets. [D(GPP)]

See Section 1.2.1 for details.

1.3.3.3 A CT or MR scan should be performed on patients with active spinal tuberculosis who have neurological signs/symptoms. If there is direct spinal cord involvement, for example spinal cord tuberculoma, then management should be as for meningeal tuberculosis under Section 1.3.1. [D(GPP)]

1.3.4 Bone and joint tuberculosis: routine therapeutic surgery

1.3.4.1 In patients with spinal tuberculosis, anterior spinal fusion should not be performed routinely. [B]

1.3.4.2 In patients with spinal tuberculosis, anterior spinal fusion should be considered if there is spinal instability or evidence of spinal cord compression. [D(GPP)]

1.3.5 Pericardial tuberculosis

1.3.5.1 For patients with active pericardial tuberculosis, the first choice of treatment should:
• be the 6-month, four-drug initial regimen (6 months of isoniazid and rifampicin, supplemented in the initial 2 months with pyrazinamide and ethambutol) [B]

• use a daily dosing schedule [B]

• include combination tablets. [D]

See Section 1.2.1 for further details.

1.3.5.2 In addition to anti-tuberculosis treatment, patients with active pericardial tuberculosis should be offered:

• for adults, a glucocorticoid equivalent to prednisolone at 60 mg/day tailing over 2–3 months [A]

• for children, a glucocorticoid equivalent to prednisolone 1mg/kg/day (maximum 40 mg/day) tailing over 2–3 months. [D(GPP)]

1.3.6 Disseminated (including miliary) tuberculosis

1.3.6.1 For patients with disseminated (including miliary) tuberculosis, the first choice of treatment should:

• be the 6-month, four-drug initial regimen (6 months of isoniazid and rifampicin, supplemented in the initial 2 months with pyrazinamide and ethambutol) [B]

• use a daily dosing schedule [B]

• include combination tablets. [D(GPP)]

See Section 1.2.1 for further details.

1.3.6.2 Treatment of disseminated (including miliary) tuberculosis should not be stopped if initial liver function tests are abnormal, unless the patient’s liver function is deteriorating significantly on drug treatment. If such deterioration is detected, advice on management options should be sought from clinical colleagues with specialist experience of these circumstances. [D(GPP)]
1.3.6.3 Patients with disseminated (including miliary) tuberculosis should be tested for CNS involvement by:

- brain scan (CT or MR) and/or lumbar puncture for those with CNS signs or symptoms
- lumbar puncture on those without CNS signs and symptoms.

When evidence of CNS involvement is detected, treatment should be the same as for meningeal tuberculosis (see Section 1.3.1).

[D(GPP)]

1.3.7 Other sites of infection

1.3.7.1 For patients with:

- active genitourinary tuberculosis, or
- active tuberculosis of any site other than:
  - respiratory system
  - central nervous system (typically meninges)
  - peripheral lymph nodes
  - bones and joints
  - pericardium
  - disseminated (including miliary) disease,

the first choice of treatment should:

- be the 6-month, four-drug initial regimen (6 months of isoniazid and rifampicin, supplemented in the initial 2 months with pyrazinamide and ethambutol) [B]
- use a daily dosing schedule [B]
- include combination tablets. [D(GPP)]

See Section 1.2.1 for further details.
1.4 Management of latent tuberculosis

1.4.1 Chemoprophylaxis

1.4.1.1 People with latent TB who have agreed to receive chemoprophylaxis should be started on one of the following regimens: [C]

- 3 months of rifampicin and isoniazid (3RH) or 6 months of isoniazid (6H) for adults aged 16–35 not known to have HIV [A], or
- 6 months of isoniazid (6H) for people aged 35 or younger with HIV [A], or
- 6 months of rifampicin (6R) for contacts, aged 35 or younger, of people with isoniazid resistant TB. [D(GPP)]

1.4.1.2 Neonates with a household member with sputum smear-positive tuberculosis, who has not received at least 2 weeks’ anti-tuberculosis drug treatment, should be treated as follows. [D(GPP)]

- The neonate should be commenced on isoniazid 5 mg/kg for 3 months and then a tuberculin skin test performed.
- If this is positive (Mantoux 6 mm or greater) the child should be assessed for tuberculosis. If this assessment is negative, then isoniazid should be continued to 6 months’ total treatment.
- If this tuberculin test is negative (Mantoux < 6mm), then isoniazid should be stopped and a BCG vaccination performed (see Section 1.6).

1.4.1.3 Children aged 4 weeks to 2 years without prior BCG vaccination, in close contact with people with sputum smear-positive tuberculosis, should be treated as follows. [D(GPP)]

- The child should be commenced on isoniazid 5 mg/kg and a tuberculin skin test performed.
• If the tuberculin skin test is positive (Mantoux 6 mm or greater), the child should be assessed for active TB (see Section 1.1.2). If active TB is ruled out, full chemoprophylaxis should be given as either 3 months of rifampicin and isoniazid (3RH) or 6 months of isoniazid (6H).

• If the tuberculin skin test is negative (Mantoux 6 mm or greater), then isoniazid should be continued and the tuberculin test repeated after 6 weeks.

• If the repeat tuberculin skin test is negative, isoniazid may be stopped and BCG vaccination performed (see Section 1.6).

• If the repeat tuberculin skin test is positive (Mantoux 6 mm or greater), then an interferon-gamma test should be conducted, if available, and if this is positive, full chemoprophylaxis should be given.

Also see the algorithm on contact tracing for children under 2.

1.4.1.4 BCG vaccinated children aged 4 weeks to 2 years, in close contact with people with sputum smear-positive respiratory tuberculosis, should be treated as follows. [D(GPP)]

• The child should have a tuberculin skin test. If this is positive (Mantoux 15 mm or greater), the child should be assessed for active tuberculosis (see Section 1.1.2). If active tuberculosis is excluded, then chemoprophylaxis should be given as either 3 months of rifampicin and isoniazid (3RH) or 6 months of isoniazid (6H).

• If the result of the tuberculin skin test is as expected for prior BCG (Mantoux <15 mm), it should be repeated after 6 weeks.

• If the repeat test remains within these readings, no further action is needed.

• If the repeat test becomes more strongly positive (Mantoux 15 mm or greater and an increase of 5mm or more over the previous test), then an interferon-gamma test should be
conducted, if available, and if this is positive, the child should be assessed for active tuberculosis (see Section 1.1.2). If active tuberculosis is excluded, then chemoprophylaxis should be given.

1.4.1.5 For children requiring chemoprophylaxis, a regimen of either 3 months of rifampicin and isoniazid (3RH) or 6 months of isoniazid (6H) should be planned and started. [D(GPP)]

1.4.1.6 Chemoprophylaxis should be considered for: [D(GPP)]

- all people identified through screening aged under 36 years (because of increasing risk of hepatotoxicity with age), or people of all ages with HIV, or healthcare workers of all ages, who are:
  - tuberculin skin test (TST) positive (Mantoux 6 mm or greater), and without a prior BCG vaccination, or
  - strongly TST positive (Mantoux 15 mm or greater), interferon-gamma positive, and with prior BCG vaccination
- children aged 1–15 years identified through opportunistic screening, to be:
  - strongly TST positive (Mantoux 15 mm or greater), and
  - interferon-gamma positive, and
  - without prior BCG vaccination
- people of any age who demonstrate tuberculin conversion after contact with a person with sputum smear positive tuberculosis
- people with evidence of prior TB scars on chest X-ray, and without a history of adequate treatment.

1.4.1.7 People with HIV, in close contact with people with sputum smear positive respiratory tuberculosis, should have active disease excluded and then be given chemoprophylaxis. [D(GPP)]

1.4.1.8 Chemoprophylaxis should not be started in close contacts of sputum smear-positive MDR TB, who are strongly tuberculin test
positive (Mantoux 15 mm or greater), as no regimen is of proven benefit, and only a small proportion of infected persons will develop later disease. Ongoing monitoring should be undertaken for active disease. [D(GPP)]

1.4.1.9 Healthcare workers should be aware that certain groups have increased risk of developing active TB, including people who:

[D(GPP)]

- are HIV-positive
- are injecting drug users
- have had solid organ transplantation
- have a haematological malignancy
- have had a jejunole ileal bypass
- have chronic renal failure or receive haemodialysis
- have had a gastrectomy
- are receiving anti-TNF-alfa treatment
- have silicosis.

Patients in these groups should be advised of the risks and symptoms of TB on an individual risk assessment basis (by Inform and Advise information).

1.5 Management of drug-resistant tuberculosis

1.5.1 Risk factors

1.5.1.1 A risk assessment for drug resistance should be made for each patient with tuberculosis, based on the risk factors listed below, and on the geographical distribution of drug resistance within the UK: [C]

1. a history of prior TB drug treatment; prior TB treatment failure
2. contact with a known case of drug-resistant TB
3. birth in a foreign country, particularly high-incidence countries as defined by the Health Protection Agency website www.hpa.org.uk
4. HIV infection
5. residence in London
6. age profile, with highest rates between ages 25 and 44
7. male gender.

1.5.1.2 The TB team should consider the risk assessment for drug resistance, and if the risk is regarded as significant, then urgent molecular tests for rifampicin resistance on smear-positive material should be performed (or on positive cultures when they become available) (see Section 1.1.2). [D(GPP)]

1.5.1.3 Response to treatment should be closely monitored in any patient at increased risk of drug resistance. If there is no clinical improvement, or if cultures remain positive after the fourth month of treatment (‘treatment failure’), then drug resistance should be suspected and treatment options reviewed in conjunction with a clinician experienced in the treatment of MDR TB. [D(GPP)]

(See Section 1.2.1 for details of the standard, 6-months, four-drug initial treatment regimen.)

1.5.2 Referral

1.5.2.1 The options for organising care for people with MDR TB should be discussed with clinicians specialising in this area of management. The views of the patient should be sought and considered in the arrangement, and shared care between clinicians should be considered. [D(GPP)]

1.5.3 Infection control

1.5.3.1 All patients with suspected or known infectious MDR TB, if admitted to hospital, should be admitted to a negative pressure room. If none is available locally, the patient should be transferred to a hospital where the facilities, together with a clinician experienced in the management of complex drug-resistant cases, are available. Care should be carried out in the negative pressure room until the
patient is found to be non-infectious or non-resistant, and ideally until cultures are negative. [D(GPP)]

1.5.3.2 Staff and visitors should wear FFP3 masks meeting the standards of the Health & Safety Executive\(^b\) during contact with a patient with suspected or known MDR TB while the patient is considered infectious. [D(GPP)]

1.5.3.3 Before the decision to discharge a patient with suspected or known MDR TB from hospital is made, secure arrangements for the supervision and administration of all anti-tuberculosis therapy should have been made and agreed with the patient and carers. [D(GPP)]

1.5.3.4 The decision to discharge a patient with suspected or known MDR TB must be discussed with the infection control team, the local microbiologist, the local TB team, and the Consultant in Communicable Disease Control. [D(GPP)]

1.5.3.5 Hospital trusts using negative pressure rooms for infection control in MDR TB should clearly identify for all staff members those rooms that meet the standards of the Interdepartmental Working Group on Tuberculosis\(^c\), for instance by a standard sign. Such labelling should be kept up to date. [D(GPP)]

Also see the algorithm on admitting TB patients to hospital.

1.6 BCG vaccination

1.6.1.1 The benefits and risks of vaccination and remaining unvaccinated should be discussed with people to whom BCG vaccination is recommended, and with parents of neonates selected for


vaccination, so that they can make an informed decision about having the vaccination. This communication should be tailored to the individual, in an appropriate language, and should take into account cultural sensitivities and stigma. [D(GPP)]

1.6.1.2 If a person identified for BCG vaccination through occupational health, contact tracing or new entrant screening is considered to be at increased risk of being HIV positive, he/she should be offered HIV testing prior to BCG vaccination. (See Section 1.4.1.6 for details of further action in HIV-positive patients) [D(GPP)]

1.6.2 BCG vaccination for neonates

1.6.2.1 Neonatal BCG vaccination for any newborn baby at increased risk of tuberculosis should be discussed with the parents or legal guardian. Neonates at increased risk are those: [D(GPP)]

- born in a local authority with a notification rate ≥ 40 per 100,000 population (as defined by the Health Protection Agency website www.hpa.org.uk), or
- with one or more of the parents or grandparents born in a high-incidence country (as defined by the Health Protection Agency website www.hpa.org.uk), or
- with a family history of TB in the previous 5 years.

1.6.2.2 Primary care organisations with high notification rates (≥ 40 per 100,000 population, as defined by the Health Protection Agency website www.hpa.org.uk) should consider vaccinating all neonates soon after birth. [D(GPP)]

1.6.2.3 In communities with low notification rates (< 40 per 100,000 population, as defined by the Health Protection Agency website www.hpa.org.uk), Primary care organisations should offer BCG vaccination to selected neonates on the basis of one or more of the following criteria: [D(GPP)]
• born in a local authority with a notification rate $\geq 40$ per 100,000 population (as defined by the Health Protection Agency website www.hpa.org.uk), or
• with one or more of the parents or grandparents born in a high-incidence country (as defined by the Health Protection Agency website www.hpa.org.uk), or
• with a family history of TB in the previous 5 years.

1.6.2.4 Tuberculin skin testing prior to BCG should not routinely be conducted in children under 6 years of age. [D(GPP)]

1.6.3 BCG vaccination for children of school-going age

1.6.3.1 Routine BCG vaccination of children aged 10–14 is not recommended. Healthcare professionals should identify unvaccinated children at increased risk of TB (see Section 1.5.1) and provide tuberculin skin testing and BCG (if tuberculin negative). [C]

1.6.4 BCG vaccination for new entrants from high-incidence areas

1.6.4.1 BCG vaccination should be offered to tuberculin-negative new entrants:

• from high-incidence countries (as defined by the Health Protection Agency website www.hpa.org.uk) [B], and
• who have not had prior BCG vaccination (supported by adequate documentation or a characteristic scar) [B], and
• are aged up to 35 years. [D(GPP)]

1.6.5 BCG vaccination for healthcare workers

1.6.5.1 BCG vaccination should be offered to healthcare workers, irrespective of age, who: [D(GPP)]

• are previously unvaccinated (supported by adequate documentation or a characteristic scar), and
• will have contact with patients or clinical materials, and
• are tuberculin skin test (or interferon-gamma) negative.

The aim of this vaccination should be to protect healthcare workers, who are at continuing risk of exposure to TB, and therefore the patients they care for. See Sections 1.8.1 and 1.8.2 for details of occupational health screening.

1.6.6 BCG vaccination for contacts of people with active tuberculosis

1.6.6.1 BCG vaccination should be offered to previously unvaccinated (supported by adequate documentation or a characteristic scar), tuberculin negative contacts of cases of respiratory tuberculosis: [D(GPP)]

• aged up to 35 years (see Section 1.7.1 for details of contact tracing)
• over 35 years, if there are special occupational or travel risks of exposure, as detailed in the Department of Health’s ‘Green Book’.

1.6.7 BCG vaccination for other groups

1.6.7.1 BCG vaccination should be offered to people in groups at increased risk of exposure to tuberculosis, according to the ‘Green Book’: [D(GPP)]

• veterinary and other staff who handle animal species known to be susceptible to tuberculosis
• prison staff
• staff of homes for care of older people
• staff of hostels for refugees
• staff of hostels for homeless people
• people intending to stay in high-incidence countries (see Section 1.6.2) for longer than 1 month.
1.7 Active case finding

1.7.1 Contact tracing: human to human transmission

1.7.1.1 Once a patient has been diagnosed with active tuberculosis, the diagnosing physician should inform relevant colleagues so that need for contact tracing can be assessed without delay. Contact tracing should not be delayed until notification. [D(GPP)]

1.7.1.2 The TB team should assess the household contacts of any person with active tuberculosis, irrespective of the site of infection. Household contacts are defined as those who are sharing a bedroom, kitchen, bathroom or sitting room. [D(GPP)]

1.7.1.3 For people with sputum smear positive tuberculosis, other close contacts should be assessed. These may include boyfriend/girlfriend and frequent visitors to the home of the index case. Occasionally, a workplace associate may be judged to have had contact equivalent to that of household contacts, and should be assessed in the same way. [D(GPP)]

1.7.1.4 Casual contacts of people with tuberculosis, who will include the great majority of workplace contacts, should not normally be assessed. [C]

1.7.1.5 The need for tracing casual contacts of people with tuberculosis should be assessed if: [D(GPP)]

- the index case is judged to be particularly infectious (for example, evidenced by transmission to close contacts), or
- a casual contact is known to possess features that put them at special risk of infection (see Section 1.5.1).

1.7.1.6 Inform and Advise information should be offered to all contacts of people with smear positive tuberculosis. [D(GPP)]
1.7.2 Contact tracing: cattle–human transmission

1.7.2.1 Inform and Advise information should be provided to any people in contact with TB-diseased animals. Diagnostic tests for latent TB should only be considered in children (age < 16 years) without prior BCG, who have regularly drunk unpasteurised milk from animals with TB udder lesions. [D(GPP)]

1.7.2.2 Inform and Advise information should be offered to all people in contact with TB-diseased animals. [D(GPP)]

1.7.3 Contact tracing: cases on aircraft

1.7.3.1 Following diagnosis of tuberculosis in an aircraft traveller, contact tracing of fellow passengers should not routinely be undertaken [D(GPP)]. However, the notifying clinician should inform the relevant Consultant in Communicable Disease Control (CCDC) if:

- less than 3 months has elapsed since the flight and the flight was over 8 hours’ duration [D(GPP)], and
- the index case is sputum smear-positive [D(GPP)], and
- the index case has MDR TB [C], or
- the index case coughed frequently during the flight. [D(GPP)]

The CCDC should provide the airline with Inform and Advise information to send to passengers seated in the same part of the aircraft as the index case. [D(GPP)]

1.7.3.2 Where the TB index case is an aircraft crew member, contact tracing of passengers should not routinely take place. [D(GPP)]

1.7.3.3 Where the TB index case is an aircraft crew member, contact tracing of other members of staff is appropriate in accordance with

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*Published evidence does not allow for a precise definition, but such contact tracing on aircraft has often only included people within three rows on either side of the index case.
the usual principles of screening workplace colleagues (see Section 1.8.2). [B]

1.7.4 Contact tracing: cases in schools

1.7.4.1 Following diagnosis of tuberculosis in a schoolchild or member of staff, the relevant Consultant in Communicable Disease Control should be prepared to address the staff, parents and the press to explain the prevention and control procedures. Advice on managing these incidents and their public relations is available from the local or regional Health Protection Unit. [D(GPP)]

1.7.4.2 When a school pupil is diagnosed with sputum smear-positive tuberculosis, the rest of his/her class (if there is a single class group), or the rest of the year group who share classes, should be assessed as part of contact tracing. [B]

1.7.4.3 If a teacher has sputum smear-positive tuberculosis, the pupils in his/her classes during the preceding 3 months should be assessed as part of contact tracing. [C]

1.7.4.4 Clinicians conducting contact tracing in a school setting should consider extending contact tracing, based on:

- degree of infectivity of the index case
- length of time the index case was in contact with others
- whether contacts are unusually susceptible to infection
- proximity of contact

...to include those involved in extra-curricular activities (both children and teachers), and non-teaching staff. [D(GPP)]

1.7.4.5 Secondary cases of sputum smear positive tuberculosis should be treated as an index case in respect of contact tracing. [Grade of recommendation same as for the recommendations on the index case.]
1.7.4.6 Where the index case of a school pupil’s tuberculosis infection is not found, and the child is not in a high-risk group for TB, contact tracing and screening by either symptom enquiry or chest X-ray should be considered for all relevant members of staff at the school. [D(GPP)]

1.7.5 Contact tracing: cases in hospital inpatients

1.7.5.1 Following diagnosis of tuberculosis in a hospital inpatient, a risk assessment should be undertaken. This should take into account:

- degree of infectivity of the index case
- length of time before the infectious patient was isolated
- whether other patients are unusually susceptible to infection
- proximity of contact.

Contact tracing and testing should only be carried out in patients where the risk is regarded as significant. [D(GPP)]

1.7.5.2 Patients should be regarded as at risk of infection if they were in the same bay, for more than 8 hours, as an inpatient with sputum smear-positive tuberculosis who had a cough. The risk should be documented in the contact’s clinical notes, for the attention of the contact’s consultant, with Inform and Advise information given to the contact and information to their general practitioner and the contact’s hospital consultant. [D(GPP)]

1.7.5.3 If patients were exposed to a patient with sputum smear positive TB for long enough to be equivalent to household contacts (as determined by the risk assessment), or the exposed patient is known to be particularly susceptible to infection, they should be managed as equivalent to household contacts (see Section 1.7.1). [D(GPP)]

1.7.5.4 If an inpatient with sputum smear-positive TB is found to have MDR TB, or if exposed patients are HIV-positive, contact tracing
should be in line with The Interdepartmental Working Group on Tuberculosis guidelines. [D(GPP)]

1.7.5.5 In cases of doubt when planning contact tracing following a diagnosis of sputum smear-positive TB in an inpatient, further advice should be sought from the regional or national HPA and/or individuals experienced in the field. [D(GPP)]

1.7.6 New entrants (people recently arriving in or returning to the UK from high-incidence countries)

1.7.6.1 Healthcare professionals responsible for new entrant screening, which will include primary care, should maintain a coordinated programme to:

- detect active tuberculosis and initiate treatment [B]
- detect latent tuberculosis and initiate chemoprophylaxis [B]
- provide BCG vaccination to those not infected and previously un-vaccinated in high-risk groups [D(GPP)]
- provide Inform and Advise information to all new entrants. [D(GPP)]

1.7.6.2 Assessment for, and management of, tuberculosis in new entrants from high-incidence countries (as defined by the Health Protection Agency website www.hpa.org.uk) should consist of: [D(GPP)]

- clinical assessment for those with an abnormal pre-entry chest X-ray
- risk assessment for HIV, including HIV prevalence rates in the country of origin, which is then taken into account for tuberculin skin testing and BCG vaccination

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• tuberculin skin test, and interferon-gamma test if positive, for those with normal pre-entry chest X-ray who are:
  – aged under 16, or
  – aged 16–36, from sub-Saharan Africa or a country with incidence over 500 per 100,000, or
  – known to be HIV-positive
• tuberculin skin test, and interferon-gamma test if positive, for those with no pre-entry chest X-ray
• chest X-ray if there are no contra-indications, to rule out active TB in those who have not had a pre-entry chest X-ray and in whom either tuberculin skin testing is contra-indicated, or who have a positive tuberculin skin test inappropriate to their BCG history, and a positive interferon-gamma test
• chemoprophylaxis for people aged under 35 with a positive tuberculin skin test inappropriate to their BCG history, and a positive interferon-gamma test
• Inform and Advise information for asymptomatic individuals aged over 35 years
• consideration of BCG vaccination (see Section 1.6.4).

See the algorithm in Appendix E for further detail.

1.7.6.3 New entrants should be identified for TB screening from the following information:

• Port of Arrival reports [D(GPP)]
• new registrations with primary care [B]
• entry to education or university [D(GPP)]
• links with statutory and voluntary groups working with new entrants. [D(GPP)]

1.7.6.4 Any healthcare professional working with new entrants should encourage them to register with a GP. [D(GPP)]
1.7.6.5 New entrant screening for tuberculosis should be incorporated within larger health screening programmes for new entrants, linked to local services. [D(GPP)]

1.7.7 Street homeless

1.7.7.1 Active case finding should be carried out among street homeless people, by chest X-ray screening, on an opportunistic and/or symptomatic basis. Simple incentives for attending, such as hot drinks and snacks, should be made available. [D(GPP)]

1.7.7.2 Healthcare professionals working with those with tuberculosis should reinforce and update education about TB, and referral pathways, to primary care colleagues, social workers and voluntary workers who work with homeless people. [D(GPP)]

1.8 Preventing infection in specific settings

1.8.1 Healthcare environments: new NHS employees

1.8.1.1 Employees new to the NHS, who: [D(GPP)]

- will be working with patients or clinical specimens should not commence work until a tuberculosis screen or health check has been completed, or documentary evidence is provided of such screening having taken place within the preceding 12 months
- will not have patient or clinical specimen contact should not commence work if they have signs or symptoms of tuberculosis.

1.8.1.2 Health checks for employees new to the NHS should include: [D(GPP)]

- assessment of personal or family history of TB
- symptom and signs enquiry, possibly by questionnaire
- documentary evidence of TB and/or BCG scar check by Occupational Health professional, not relying on the applicant’s personal assessment
• tuberculin skin test result within the last 5 years, if available.

1.8.1.3 If an employee new to the NHS has no (or inconclusive) evidence of a BCG scar, a tuberculin skin test should be performed. [D(GPP)]

1.8.1.4 NHS employees who are tuberculin negative (<6mm) should have an individual risk assessment for HIV infection made before BCG vaccination is given. [D(GPP)]

1.8.1.5 Employees new to the NHS, of any age, who will have contact with patients and/or clinical specimens, and who are tuberculin negative (<6mm) and without prior BCG vaccination, should be offered BCG vaccination. [D(GPP)]

1.8.1.6 Employees new to the NHS, of any age, from countries of high tuberculosis incidence (see Section 1.6.2), or with previous patient contact in high TB prevalence settings, should have a tuberculin test. If negative (<6mm), proceed as in Recommendations 1.8.1.4 and 1.8.1.5. If positive (6mm or greater), refer for clinical assessment for diagnosis and possible treatment of latent infection or active disease. [D(GPP)]

1.8.1.7 If a prospective or current healthcare worker, who is tuberculin negative (<6mm), declines BCG vaccination, the risks should be explained and the oral explanation supplemented by written advice. If the individual still declines BCG vaccination, he or she should not carry out any work in settings with a risk of exposure to TB. The employing organisation will need to consider each such case on an individual basis with reference to employment and health & safety obligations. [D(GPP)]

1.8.1.8 Clinical students, agency/locum staff and contract ancillary workers who have contact with patients or clinical materials should be screened for tuberculosis to the same standard as new NHS employees, according to the recommendations set out above. Documentary evidence of screening to this standard should be
sought from locum agencies and contractors who carry out their own screening. [D(GPP)]

1.8.1.9 NHS Trusts arranging care for NHS patients in non-NHS settings should ensure that healthcare workers employed in these settings, who have contact with patients or clinical materials, have been screened for tuberculosis to the same standard as new NHS employees would be (see Recommendations 1.8.1.1–8). [D(GPP)]

1.8.2 Healthcare environments: occupational health

1.8.2.1 Reminders of the symptoms of tuberculosis, and of the need for prompt reporting of such symptoms, should be included with annual reminders about occupational health matters for staff who: [D(GPP)]

- are in regular contact with TB patients or clinical materials, or
- have worked in a high-risk clinical setting for 4 weeks or longer.

One-off reminders should be carried out following a tuberculosis incident on a ward.

1.8.2.2 If no documentary evidence of prior screening is available, staff in contact with patients or clinical material, who are transferring jobs within the NHS, should be screened as for new NHS employees (see Section 1.8.1). [D(GPP)]

1.8.2.3 The risk of tuberculosis for a new healthcare worker who knows he/she is HIV-positive at the time of recruitment should be assessed as part of the occupational health checks. [D(GPP)]

1.8.2.4 The employer, through the Occupational Health department, should be aware of the settings with increased risk of exposure to TB, and that these pose increased risks to HIV-positive healthcare workers. [D(GPP)]
1.8.2.5 Healthcare workers who are found to be HIV-positive during employment will also require medical and occupational assessments of TB risk, and may need work exposure modifications. [D(GPP)]

**1.8.3 Community childcare**

1.8.3.1 In the event of an adult worker in a childcare setting being diagnosed as suffering from smear-positive tuberculosis, management is as for contact tracing (see Section 1.7.1). [D(GPP)]

**1.8.4 Prisons and remand centres**

1.8.4.1 Healthcare workers providing care for prisoners and remand centre detainees should be aware of the signs and symptoms of active tuberculosis (see Section 1.1.2). TB services should ensure that awareness of these signs and symptoms is also promoted among prisoners and prison staff. [D(GPP)]

1.8.4.2 Prisoners should be screened for tuberculosis by:

- a health questionnaire on each entry to the prison system [D(GPP)], then
- a chest X-ray for those with signs and symptoms of active tuberculosis (see Section 1.1.2) [(C)], and
- three sputum samples taken in 24 hours for TB microscopy, including a morning sputum sample. [D(GPP)]

1.8.4.3 All prisoners receiving treatment for active or latent tuberculosis should receive DOT. [D(GPP)]

1.8.4.4 Prison medical services should carry out liaison and handover arrangements to ensure continuity of care before any prisoner on TB treatment is transferred between prisons. [D(GPP)]

1.8.4.5 As early as possible prison medical services should draw up, for each prisoner being treated for active or latent TB, a contingency plan for early discharge, potentially directly from a court appearance.
This should include firm arrangements for clinical follow-up and treatment monitoring in the intended district of residence. A named key worker, whose contact details are given to the prisoner and who visits and monitors the prisoner, should be available to provide liaison. [D(GPP)]

1.8.4.6 Prison Service staff and others with regular prisoner contact (for example, probation officers and education and social workers) should have pre- and on-employment screening at the same level as for healthcare workers with patient contact (see Sections 1.8.1 and 1.8.2). [D(GPP)]

2 Notes on the scope of the guidance

All NICE guidelines are developed in accordance with a scope document that defines what the guideline will and will not cover. The scope of this guideline was established, after a period of consultation, at the start of the guideline development process; it is available from www.nice.org.uk/page.aspx?o=224051

This guideline sets out best practice guidance for the diagnosis, treatment, prevention and control of tuberculosis (TB) in the NHS in England and Wales. It covers latent TB infection and active TB of the following sites:

- respiratory (lung, bronchus, pleura, thoracic lymph nodes)
- meningeal
- pericardial
- bone and joint
- peripheral lymph nodes
- genitourinary
- disseminated (including miliary).

The guideline does not extend to co-morbidities such as HIV, drug dependencies, diabetes, hepatic disease, renal disease, or mental illness, nor does it give guidance on highly specialised and individualised activities such
as treatment of multi-drug resistant (MDR) TB. It does not include special
guidance for patients who are pregnant, planning pregnancy or unconscious,
or for older people in long-term care. It considers only the *M tuberculosis*
complex of bacteria, and therefore does not provide guidance on other
mycobacterial infections.

3 Implementation in the NHS

3.1 Resource implications

Local health communities should review their existing practice for tuberculosis
against this guideline. The review should consider the resources required to
implement the recommendations set out in Section 1, the people and
processes involved, and the timeline over which full implementation is
envisaged. It is in the interests of people with latent or active tuberculosis, and
those at risk, that the implementation is as rapid as possible.

Relevant local clinical guidelines, care pathways and protocols should be
reviewed in the light of this guidance and revised accordingly.

Information on the cost impact of this guideline in England is available on the
NICE website and includes a template that local communities can use
(www.nice.org.uk/CGXXXcosttemplate). [Note: the costing information will
be available when the guideline is published.]

3.2 General

The implementation of this guideline should form part of the service
development plans for each local health community in England and Wales.

3.3 Audit

Suggested audit criteria based on the key priorities for implementation are
listed in Appendix D, and can be used to audit practice locally.

4 Research recommendations

The Guideline Development Group has made the following recommendations
for research, on the basis of its review of the evidence. The Group regards
these recommendations as the most important research areas to improve NICE guidance and patient care in the future. The Guideline Development Group’s full set of research recommendations is detailed in the full guideline (see Section 5).

4.1 Research is needed to determine whether interferon-gamma tests are acceptable to patients and more effective than tuberculin skin tests for predicting subsequent development of active TB when undertaking TB screening in:
   - new immigrants from high TB incidence countries
   - healthcare workers
   - children in high-risk areas who missed neonatal BCG
   - contacts of sputum smear positive TB
   - HIV positive patients.

4.2 A cluster RCT of directly observed therapy (DOT) compared with self-administered treatment for latent and/or active TB should be conducted in a UK population. This should be targeted at homeless people, and those with a history of non-adherence, alcoholism, drug abuse, or mental illness.

4.3 A cohort study of people found by new entrant screening to be tuberculin skin test positive and interferon-gamma positive with follow-up for the development of active TB, to establish better estimates of the cost-effectiveness of screening and chemoprophylaxis in this population, and to identify factors predisposing people to developing active TB so that more effective targeted chemoprophylaxis programmes can be developed.

4.4 A case-control study is needed, comparing people who developed active or latent TB with those who did not, and comparing the proportion vaccinated and the time since vaccination. The aim will be to derive improved estimates of protective efficacy and duration of protection of the BCG vaccine.
4.5 A study is needed to ascertain quality of life score estimates from those with TB disease and latent infection including adverse treatment effects, using an appropriate quality of life instrument. This will improve economic decision-making throughout TB.

4.6 Is contact tracing more effective (in terms of identifying cases of latent infection and active TB disease) among household contacts, than among homeless contacts, of patients with confirmed TB disease?

4.7 Research is needed to determine whether Port of Arrival scheme referrals with incentives for attendance of screening identify more cases of latent TB infection and active TB disease in comparison with Port of Arrival scheme referrals with no incentives for screening attendance in the new immigrant population.

4.8 Research is needed to determine whether incentives for attending chest X-ray screening in the homeless population achieve better coverage, or identify more cases of latent TB infection and active TB disease, than no incentives.

5 Other versions of this guideline

The National Institute for Clinical Excellence commissioned the development of this guidance from the National Collaborating Centre for Chronic Conditions. The Centre established a Guideline Development Group, which reviewed the evidence and developed the recommendations. The members of the Guideline Development Group are listed in Appendix B. Information about the independent Guideline Review Panel is given in Appendix C.

The booklet The guideline development process – an overview for stakeholders, the public and the NHS has more information about the Institute’s guideline development process. It is available from the Institute’s website and copies can also be ordered by telephoning 0870 1555 455 (quote reference N0472).
5.1 Full guideline

The full guideline, *Tuberculosis: National clinical guideline for diagnosis, management, prevention and control*, is published by the Royal College of Physicians of London; it is available from [website details to be added], the NICE website (www.nice.org.uk/CGXXXfullguideline) and the website of the National Library for Health (www.nlh.nhs.uk). [Note: these details will apply to the published full guideline.]

5.2 Quick reference guide

A quick reference guide for health professionals is also available from the NICE website (www.nice.org/CGXXXquickrefguide) or from the NHS Response Line (telephone 0870 1555 455; quote reference number N0XXX). [Note: these details will apply when the guideline is published.]

5.3 Information for the public

A version of this guideline for people with latent or active tuberculosis and their carers, and for the public, is available from the NICE website (www.nice.org.uk/CGXXXpublicinfo) or from the NHS Response Line (0870 1555 455); quote reference number N0xxx. [Note: these details will apply when the guideline is published.]

6 Related NICE guidance

There is no related NICE guidance.

7 Review date

The process of reviewing the evidence is expected to begin 4 years after the date of issue of this guideline. Reviewing may begin before this if significant evidence that affects the guideline recommendations is identified. The updated guideline will be available within 2 years of the start of the review process.
Appendix A: Grading scheme

The classification of recommendations and the levels of evidence for intervention studies used in this guideline are adapted from the Scottish Intercollegiate Guidelines Network (SIGN 50: a guideline developers’ handbook), and summarised in the tables on page 48). The classification of recommendations and levels of evidence for the accuracy of diagnostic tests are adapted from The Oxford Centre for Evidence-Based Medicine levels of evidence (2001) and the Centre for Reviews and Dissemination report No. 4 (2001). They are summarised in the tables on page 49 and are being used on a pilot basis.
### Classification of recommendations on interventions

<table>
<thead>
<tr>
<th>Recommendation grade</th>
<th>Evidence</th>
</tr>
</thead>
</table>
| A                    | • At least one meta-analysis, systematic review, or randomised controlled trial (RCT) that is rated as 1**, and is directly applicable to the target population, or  
  • A systematic review of RCTs or a body of evidence that consists principally of studies rated as 1+, is directly applicable to the target population and demonstrates overall consistency of results, or  
  • Evidence drawn from a NICE technology appraisal |
| B                    | • A body of evidence that includes studies rated as 2**, is directly applicable to the target population and demonstrates overall consistency of results, or  
  • Extrapolated evidence from studies rated as 1** or 1+ |
| C                    | • A body of evidence that includes studies rated as 2+, is directly applicable to the target population and demonstrates overall consistency of results, or  
  • Extrapolated evidence from studies rated as 2** |
| D                    | • Evidence level 3 or 4, or  
  • Extrapolated evidence from studies rated as 2+, or  
  • Formal consensus |
| D(GPP)               | • A good practice point (GPP) is a recommendation for best practice based on the experience of the Guideline Development Group |

### Levels of evidence for intervention studies

<table>
<thead>
<tr>
<th>Level of evidence</th>
<th>Type of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>1**</td>
<td>• High-quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias</td>
</tr>
<tr>
<td>1+</td>
<td>• Well-conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias</td>
</tr>
<tr>
<td>1</td>
<td>• Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias</td>
</tr>
</tbody>
</table>
| 2**               | • High-quality systematic reviews of case–control or cohort studies  
  • High-quality case–control or cohort studies with a very low risk of confounding, bias or chance and a high probability that the relationship is causal |
| 2+                | • Well-conducted case–control or cohort studies with a low risk of confounding, bias or chance and a moderate probability that the relationship is causal |
| 2                | • Case–control or cohort studies with a high risk of confounding, bias, or chance and a significant risk that the relationship is not causal                                                                  |
| 3                 | • Non-analytical studies (for example, case reports, case series)                                                                                                                                          |
| 4                 | • Expert opinion, formal consensus                                                                                                                                                                          |
### Classification of recommendations on diagnostic tests

<table>
<thead>
<tr>
<th>Grade</th>
<th>Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>A(DS)</td>
<td>• Studies with level of evidence Ia or Ib</td>
</tr>
<tr>
<td>B(DS)</td>
<td>• Studies with level of evidence II</td>
</tr>
<tr>
<td>C(DS)</td>
<td>• Studies with level of evidence III</td>
</tr>
<tr>
<td>D(DS)</td>
<td>• Studies with level of evidence IV</td>
</tr>
</tbody>
</table>

DS, diagnostic studies.

### Levels of evidence for studies of the accuracy of diagnostic tests

<table>
<thead>
<tr>
<th>Levels of evidence</th>
<th>Type of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ia</td>
<td>• Systematic review (with no or minor variations in the directions and degrees of results between studies) of level-1 studies, which are studies that use: – a blind comparison of the test with a validated reference standard (gold standard) – a sample of patients that reflects the population to whom the test would apply</td>
</tr>
<tr>
<td>Ib</td>
<td>• Level-1 studies</td>
</tr>
<tr>
<td>II</td>
<td>• Level-2 studies, which are studies that have only one of the following: – the population is narrow (the sample does not reflect the population to whom the test would apply) – a poor reference standard is used (defined as that where the ‘test’ is included in the ‘reference’, or where the ‘testing’ affects the ‘reference’) – the comparison between the test and reference standard is not blind – the study is a case–control study • Systematic reviews of level-2 studies</td>
</tr>
<tr>
<td>III</td>
<td>• Level-3 studies, which are studies that have at least two of the features listed for level-2 studies • Systematic reviews of level-3 studies</td>
</tr>
<tr>
<td>IV</td>
<td>• Expert committee reports, opinions and/or clinical experience without explicit critical appraisal; or based on physiology, bench research or ‘first principles’</td>
</tr>
</tbody>
</table>
Appendix B: The Guideline Development Group

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Appendix C: The Guideline Review Panel

The Guideline Review Panel is an independent panel that oversees the development of the guideline and takes responsibility for monitoring its quality. The Panel includes experts on guideline methodology, health professionals and people with experience of the issues affecting patients and carers. The members of the Guideline Review Panel were as follows.

**Dr Peter Rutherford (Chair)**
Senior Lecturer in Nephrology, University of Wales College of Medicine

**Dame Helena Shovelton**
Chief Executive, British Lung Foundation

**Dr Rob Higgins**
Consultant in Renal and General Medicine, University Hospitals Coventry and Warwickshire NHS Trust, Coventry

**Mrs Fiona Wise**
Chief Executive, Ealing Hospital NHS Trust

**Dr John Young**
Medical Director, Merck Sharp & Dohme (MSD)
Appendix D: Technical detail on the criteria for audit

Data collection

Criteria 1, 2 and 4 can be collected from patient notes or prescribing software. Given the small number of patients receiving directly observed therapy (DOT), a retrospective data collection across a year will be needed to provide an accurate proportion.

Criterion 3 will only be useful for local or national comparative audit and discussion; it is not possible to determine a target. These data probably need to be collected from patients at clinic visit (at a consistent point in their treatment for comparability), which also provides an opportunity to collect qualitative data on interaction with, or understanding of the roles of, key workers.

Criterion 5 can be collected in PCTs where the sources of names (Port of Arrival, GP registration, educational institutions, etc.) are all compiled at one point, and where it is possible to remove duplicated names.

Criterion 6 should be assessed retrospectively on a population-wide basis by the primary care trust.

<table>
<thead>
<tr>
<th>Criterion</th>
<th>Exception</th>
<th>Definition of terms</th>
</tr>
</thead>
</table>
| 1. a) Process measure: percentage of patients with active TB receiving rifampicin, isoniazid, pyrazinamide and ethambutol (or other 4th drug) for the first 2 months of treatment  
  b) Outcome measure: percent cure and completion rate | Contra-indications, meningeal TB, CNS involvement, drug resistance | |
<p>| 2. Process measure: percentage of patients with active TB who are treated with DOT | A ‘patient on DOT’ is any patient who has been prescribed anti-tuberculosis drugs as directly observed therapy (regardless of observer) for part or all of their treatment. | |
| 3. Process measure: percentage of TB patients in possession of Hospital inpatients | Key worker will have been named as | |</p>
<table>
<thead>
<tr>
<th>Process measure: percentage of patients with meningeal TB receiving rifampicin, isoniazid, pyrazinamide and ethambutol (or other 4th drug) for the first 2 months of treatment</th>
<th>b) Any patient who received glucocorticoids for at least 2 weeks.</th>
</tr>
</thead>
<tbody>
<tr>
<td>b) Process measure: percent receiving/having received glucocorticoids</td>
<td></td>
</tr>
<tr>
<td>c) Outcome measure: percent cure and completion rate (12 months)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Process measure: percentage of new entrants referred or recorded who are contacted for screening</th>
<th>b) Any person who completes the screening process according to the algorithm is counted.</th>
</tr>
</thead>
<tbody>
<tr>
<td>b) Process measure: percent of new entrants contacted for screening, who complete the screening</td>
<td></td>
</tr>
<tr>
<td>c) Process measure: percent of new entrants contacted for screening, who are referred to secondary care TB teams</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Process measure: percentage of neonates vaccinated with BCG</th>
<th>Informed refusal, HIV</th>
</tr>
</thead>
</table>

current correct key worker’s details specified in recommendations.
Appendix E: The algorithms

Management of people with suspected respiratory TB who are admitted to hospital

Known or suspected MDR TB, based on risk assessment?

- Yes
  - Admit to negative pressure room
  - Sputum smear positive (1 or more from 3 samples)?
    - Yes
      - Conduct Molecular probe for rifampicin resistance
    - No
      - Single room on ward
- No
  - Admit to single room
  - Risk for MDR TB?
    - Yes
      - Does ward have immunocompromised patients?
        - Yes
          - Negative pressure room
        - No
          - Standard ward
    - No
      - Admit to negative pressure room
Algorithm for testing and treating children under 2 years old who are contacts of people with sputum smear-positive TB

Prior BCG?

Yes

Perform initial Mantoux test

-ve < 6mm

Assess for TB clinical disease

+ve ≥ 6mm

Continue isoniazid; repeat Mantoux test in 6 weeks

-ve < 6mm

Commence isoniazid 5mg/kg and perform initial Mantoux test

Mantoux ≥ 6mm and increase on initial test ≥ 5mm

No

Assess for TB clinical disease

Chemoprophylaxis: 3RH or completion of 6H (see 1.4.1.3)

No action

Chemoprophylaxis; commence 6H or 3RH

Treat and notify

No

Repeat Mantoux after 6 weeks

Mantoux ≥ 15mm and increase on initial test ≥ 5mm

Stop isoniazid; advise BCG

No

Assess for TB clinical disease

Treat and notify

Interferon-gamma test

+ve

Interferon-gamma test

-ve

+ve

Stop isoniazid; advise BCG

No

Assess for TB clinical disease

Chemoprophylaxis; commence 6H or 3RH

Treat and notify

-ve

Stop isoniazid; advise BCG

No

Assess for TB clinical disease

Treat and notify

Interferon-gamma test

+ve

Interferon-gamma test

-ve

+ve

Stop isoniazid; advise BCG

No

Assess for TB clinical disease

Chemoprophylaxis; commence 6H or 3RH

Treat and notify

-ve

Stop isoniazid; advise BCG
Algorithm for household contacts of all cases of TB, and other close contacts not covered by Algorithm X.

1. **Had BCG?**
   - Yes
     - **Age <35?**
       - Yes
         - Chemoprophylaxis
         - Discharge
       - No
         - CXR & clinical exam
       - No
         - Interferon-γ test
           - +ve
             - Discharge
           - -ve
             - Inform and Advise***
2. No
   - Mantoux test **
     - ≥15mm?
       - Yes
         - CXR
         - Interferon-γ test
           - +ve
             - Index case sputum smear-negative?
               - Yes
                 - Discharge
               - No
                 - Investigate
           - -ve
             - Investigate
     - No
       - Inform and Advise***
       - Discharge

---

* - Previous BCG vaccination cannot be accepted as evidence of immunity in HIV-infected subjects.
** - A negative test in immuno-compromised people does not exclude TB infection.
*** - People advised to have chemoprophylaxis, but who decline, should have Inform & Advise information reinforced and (7 CXR FU at 3 and 12 months)
This algorithm sets out the actions for screening new entrants (or people returning after a prolonged stay) to England or Wales from a country with a high incidence of TB (as defined by the Health Protection Agency website www.hpa.org.uk). It applies to dedicated new entrant screening services, and therefore does not detail the systems for detecting new entrants, nor the clinic activities that follow. Service providers with a different service model may need to adapt this to their individual processes.

* - Select new entrants for further screening if they are any one of the following:
  - Age < 16
  - Age 16-35 from sub-Saharan Africa or a country with incidence > 500 per 100,000 known to be HIV+

** - Timing of chest X-ray and/or BCG may depend on pregnancy

\[\text{Algorithm for new entrant screening}\]
Algorithm for screening new NHS employees

Pre-employment questionnaire

New entrant?

Yes

Risk assessment

CXR normal?

No

Prior BCG (scar or documented)?

Yes

Mantoux or Interferon-γ test positive?

Yes

Medical assessment

No

TB clinic

No action

Inform & Advise

? Consider Chemoprophylaxis

Yes

Working with patients or clinical materials?

Yes

Medical assessment, CXR

No

Normal?

Yes

TB clinic

No action

Inform & Advise

? Consider Chemoprophylaxis

No

Aged 35 or over?

Yes

See new entrants algorithm

No

Suspicous symptoms or circumstances?

Yes

Medical assessment

No

CXR normal?

Yes

TB clinic

No action

Inform & Advise

? Consider Chemoprophylaxis

No

TB clinic

No action

Inform & Advise

? Consider Chemoprophylaxis

Yes

TB clinic

No action

Inform & Advise

? Consider Chemoprophylaxis

No

TST / interferon-γ test. Or TST / int-γ in previous 5 years

No

Mantoux or Interferon-γ test positive?

Yes

Risk assessment

No

Record refusals. Notify OH.

Offer BCG