National Institute for Health and Clinical Excellence

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Tuberculosis

Clinical diagnosis and management of tuberculosis, and measures for its prevention and control

This updates and replaces NICE clinical guideline 33

NICE clinical guideline 117
Developed by the National Collaborating Centre for Chronic Conditions and the Centre for Clinical Practice at NICE

NICE clinical guideline 117
Tuberculosis: clinical diagnosis and management of tuberculosis, and measures for its prevention and control
Ordering information
You can download the following documents from
www.nice.org.uk/guidance/CG117

- The NICE guideline (this document) – all the recommendations.
- A quick reference guide – a summary of the recommendations for healthcare professionals.
- 'Understanding NICE guidance' – a summary for patients and carers.
- The full guideline – all the recommendations, details of how they were developed, and reviews of the evidence they were based on.

For printed copies of the quick reference guide or 'Understanding NICE guidance', phone NICE publications on 0845 003 7783 or email publications@nice.org.uk and quote:

- N2458 (quick reference guide)
- N2459 ('Understanding NICE guidance').

NICE clinical guidelines are recommendations about the treatment and care of people with specific diseases and conditions in the NHS in England and Wales.

This guidance represents the view of NICE, which was arrived at after careful consideration of the evidence available. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. However, the guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer, and informed by the summary of product characteristics of any drugs they are considering.

Implementation of this guidance is the responsibility of local commissioners and/or providers. Commissioners and providers are reminded that it is their responsibility to implement the guidance, in their local context, in light of their duties to avoid unlawful discrimination and to have regard to promoting equality of opportunity. Nothing in this guidance should be interpreted in a way that would be inconsistent with compliance with those duties.

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Contents

This guidance is an update of NICE clinical guideline 33 (published March 2006) and replaces it.

New recommendations on using interferon-gamma tests for the diagnosis of latent tuberculosis (TB) have been added.

Recommendations are marked as **[2006]**, **[2006, amended 2011]** or **[new 2011]**.

- **[2006]** indicates that the evidence has not been updated and reviewed since the original guideline.
- **[2006, amended 2011]** indicates that the evidence has not been updated and reviewed since 2006 but a small amendment has been made to the recommendation.
- **[new 2011]** indicates that the evidence has been reviewed and the recommendation has been updated or added.

Introduction

The incidence of TB is influenced by risk factors such as exposure to, and susceptibility to, TB and levels of deprivation (poverty, housing, nutrition and access to healthcare), and differs in different parts of England and Wales. Where scientific evidence supports it, this guideline makes recommendations on service organisation, as well as for individual teams of healthcare professionals. The guideline aims to focus NHS resources where they will combat the spread of TB, and some sections deal with high- and low-incidence areas separately.

The guideline is designed for use in the National Health Service in England and Wales. Readers in other countries, particularly where the incidence of TB is higher, should exercise caution before applying the recommendations.

Patient-centred care

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

Treatment and care should take into account patients' needs and preferences. People with, or at risk of contracting, TB should have the opportunity to make informed decisions about their care and treatment, in partnership with their healthcare professionals. If patients do not have the capacity to make decisions, healthcare professionals should follow the Department of Health's advice on consent (available from www.dh.gov.uk/consent) and the code of practice that accompanies the Mental Capacity Act (summary available from www.publicguardian.gov.uk). In Wales, healthcare professionals should follow advice on consent from the Welsh Assembly Government (available from www.wales.nhs.uk/consent).

Good communication between healthcare professionals and patients is essential. It should be supported by evidence-based written information tailored to the patient's needs. Treatment and care, and the information patients are given about it, should be culturally appropriate. It should also be accessible to people with additional needs such as physical, sensory or learning disabilities, and to people who do not speak or read English.

If the patient agrees, families and carers should have the opportunity to be involved in decisions about treatment and care.

Families and carers should also be given the information and support they need.

Key priorities for implementation

The following recommendations have been identified as priorities for implementation.

Management of active TB

- A 6-month, four-drug initial regimen (6 months of isoniazid and rifampicin supplemented in the first 2 months with pyrazinamide and ethambutol) should be used to treat active respiratory TB[1] in:
  - adults not known to be HIV positive
  - adults who are HIV positive
  - children.

  This regimen is referred to as 'standard recommended regimen' in this guideline. **[2006]**

- Patients with active meningeal TB should be offered:
  - a treatment regimen, initially lasting for 12 months, comprising isoniazid, pyrazinamide, rifampicin and a fourth drug (for example, ethambutol) for the first 2 months, followed by isoniazid and rifampicin for the rest of the treatment period
  - a glucocorticoid at the normal dose range
    - ◊ adults – equivalent to prednisolone 20–40 mg if on rifampicin, otherwise 10–20 mg
    - ◊ children – equivalent to prednisolone 1–2 mg/kg, maximum 40 mg

  with gradual withdrawal of the glucocorticoid considered, starting within 2–3 weeks of initiation. **[2006]**

Improving adherence

- Use of directly observed therapy (DOT) is not usually necessary in the management of most cases of active TB. All patients should have a risk assessment for adherence to 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 TB

[1] TB affecting the lungs, pleural cavity, mediastinal lymph nodes or larynx.

- patients with likely poor adherence, in particular those who have a history of non-adherence. **[2006]**

- The TB service should tell each person with TB 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. **[2006]**

New entrant screening

- New entrants[2] 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. **[2006]**

BCG vaccination

- Neonatal Bacille Calmette-Guèrin (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[3] should consider vaccinating all neonates soon after birth. **[2006]**

[2] New entrants are defined as people who have recently arrived in or returned to the UK from high-incidence countries, with an incidence of more than 40 per 100,000 per year, as listed by the Health Protection Agency (go to www.hpa.org.uk and search for 'WHO country data TB').
[3] Incidence of more than 40 per 100,000, as listed by the Health Protection Agency (go to www.hpa.org.uk and search for 'TB rate bands').

Definitions used in this guideline

Close contacts These can include a boyfriend or girlfriend and frequent visitors to the home of the index case, in addition to household contacts

Dual strategy A Mantoux test followed by an interferon-gamma test if the Mantoux is positive

Green Book The 2006 edition of 'Immunisation against infectious disease', published by the Department of Health (available from www.dh.gov.uk)

Hard-to-reach groups Children, young people and adults whose social circumstances or lifestyle, or those of their parents or carers, make it difficult to:

- recognise the clinical onset of tuberculosis
- access diagnostic and treatment services
- self-administer treatment (or, in the case of children, have treatment administered by a parent or carer)
- attend regular appointments for clinical follow-up

High-incidence country Country with more than 40 cases per 100,000 per year; these are listed by the Health Protection Agency – go to www.hpa.org.uk and search for 'WHO country data TB'

High-incidence primary care organisation A primary care organisation with more than 40 cases per 100,000 per year; these are listed by the Health Protection Agency – go to www.hpa.org.uk and search for 'TB rate bands'

Household contacts People sharing a bedroom, kitchen, bathroom or sitting room with the index case

'Inform and advise' information Advice on the risks and symptoms of TB, usually given in a standard letter

New entrants People who have recently arrived in or returned to the UK from high-incidence countries

Respiratory TB TB affecting the lungs, pleural cavity, mediastinal lymph nodes or larynx

Standard recommended regimen The ‘6-month, four-drug initial regimen’ of 2 months of isoniazid, rifampicin, pyrazinamide and ethambutol, followed by 4 months of isoniazid and rifampicin

Drug regimen abbreviations for TB treatment

Drug regimens are often abbreviated to the number of months a phase of treatment lasts, followed by letters for the drugs administered in that phase:

H is isoniazid, R rifampicin, Z pyrazinamide, E ethambutol, S streptomycin

For example:

2HRZE/4HR is the standard recommended regimen

2HRE/7HR is 2 months of isoniazid, rifampicin and ethambutol followed by 7 months of isoniazid and rifampicin

1 Guidance

The following guidance is based on the best available evidence. The full guideline (www.nice.org.uk/guidance/CG117) gives details of the methods and the evidence used to develop the guidance.

1.1 Diagnosis

1.1.1 Diagnosing latent TB

1.1.1.1 Offer Mantoux testing in line with the Green Book[4] to diagnose latent TB in people who are:

- household contacts (aged 5 years and older) of all people with active TB
- non-household contacts (other close contacts for example, in workplaces and schools). **[new 2011]**

1.1.1.2 Consider interferon-gamma testing for people whose Mantoux testing shows positive results, or in people for whom Mantoux testing may be less reliable, for example BCG-vaccinated people. **[new 2011]**

1.1.1.3 If Mantoux testing is inconclusive, refer the person to a TB specialist. **[new 2011]**

New entrants from high-incidence countries

1.1.1.4 Offer a Mantoux test to children aged 5–15 years. If positive, follow with an interferon-gamma test. **[new 2011]**

1.1.1.5 Offer either an interferon-gamma test alone or a dual strategy in people aged 16–35 years. For people aged 35 years or older, consider the individual risks and benefits of likely subsequent treatment, before offering testing. (Refer to other sections for other groups, for example, immunocompromised.) **[new 2011]**

[4] In this guideline the 'Green Book' is the 2006 edition of 'Immunisation against infectious disease', published by the Department of Health (available from www.dh.gov.uk). The Green Book contains details of people who may have suppressed responses to tuberculin skin testing.

1.1.1.6 Offer Mantoux testing as the initial diagnostic test for latent TB infection in children younger than 5 years who have recently arrived from a high-incidence country. If the initial test is positive (taking into account the BCG history):

- refer to a TB specialist to exclude active disease **and**
- consider treating latent TB. **[new 2011]**

Household contacts aged 2–5 years

For children younger than 2 years see recommendations 1.6.1.5–1.6.1.7.

1.1.1.7 Offer Mantoux testing as the initial diagnostic test for latent TB infection in child household contacts between the ages of 2 and 5 years. If the initial test is positive taking into account the BCG history:

- refer to a TB specialist to exclude active disease **and**
- consider treating latent TB. **[new 2011]**

1.1.1.8 If the initial Mantoux test is negative but the child is a contact of a person with sputum-smear-positive disease, offer an interferon-gamma test after 6 weeks and repeat the Mantoux test to increase the sensitivity (to reduce false negative results). **[new 2011]**

Contacts – outbreak situation

1.1.1.9 In an outbreak situation when large numbers of people may need to be screened, consider a single interferon-gamma test for people aged 5 years and older. **[new 2011]**

People who are immunocompromised

1.1.1.10 If latent TB is suspected in children who are immunocompromised, refer to a TB specialist. **[new 2011]**

1.1.1.11 For people with HIV and CD4 counts less than 200 cells/mm^3, offer an interferon-gamma test and a concurrent Mantoux test. If either test is positive:

- perform a clinical assessment to exclude active TB **and**
- consider treating latent TB infection. **[new 2011]**

1.1.1.12 For people with HIV and CD4 counts of 200–500 cells/mm^3, offer an interferon-gamma test alone or an interferon-gamma test with a concurrent Mantoux test. If either test is positive:

- perform a clinical assessment to exclude active TB **and**
- consider treating latent TB infection. **[new 2011]**

1.1.1.13 For other people who are immunocompromised, offer an interferon-gamma test alone or an interferon-gamma test with a concurrent Mantoux test. If either test is positive:

- perform a clinical assessment to exclude active TB **and**
- consider treating latent TB. **[new 2011]**

Healthcare workers

1.1.1.14 Offer a Mantoux test to new NHS employees who will be in contact with patients or clinical materials if the employees:

- are not new entrants from high-incidence countries **and**
- have not had BCG vaccination (for example, they are without scar, other documentation or reliable history).[5] **[new 2011]**

1.1.1.15 If the Mantoux test is negative, refer to the Green Book for BCG immunisation guidance. If the Mantoux test is positive, offer an interferon-gamma test. **[new 2011]**

1.1.1.16 Offer an interferon-gamma test to new NHS employees who have recently arrived from high-incidence countries or who have had

[5] If there is reliable evidence of BCG vaccination, refer to the Green Book.

contact with patients in settings where TB is highly prevalent. **[new 2011]**

1.1.1.17 Healthcare workers who are immunocompromised should be screened in the same way as other people who are immunocompromised. **[new 2011]**

Hard-to-reach groups

1.1.1.18 Offer people from hard-to-reach groups a single interferon-gamma test. **[new 2011]**

1.1.2 Diagnosing active TB

1.1.2.1 To diagnose active respiratory TB:

- a posterior–anterior chest X-ray should be taken; chest X-ray appearances suggestive of TB should lead to further diagnostic investigation
- multiple sputum samples (at least three, with one early morning sample) should be sent for TB microscopy and culture for suspected respiratory TB before starting treatment if possible or, failing that, within 7 days of starting
- spontaneously produced sputum should be obtained if possible; otherwise induction of sputum or bronchoscopy and lavage should be used
- in children unable to expectorate sputum, induction of sputum should be considered if it can be done safely, with gastric washings considered as third line
- if there are clinical signs and symptoms consistent with a diagnosis of TB, treatment should be started without waiting for culture results (see section 1.2.1 for details)
- the standard recommended regimen should be continued in patients whose subsequent culture results are negative
- samples should be sent for TB culture from autopsy samples if respiratory TB is a possibility. **[2006]**

1.1.2.2 To diagnose active non-respiratory TB:

- advantages and disadvantages of both biopsy and needle aspiration should be discussed with the patient, with the aim of obtaining adequate material for diagnosis
- if non-respiratory TB is a possibility, 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:
  - 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
  - aspiration sample
  - autopsy sample
- microbiology staff should routinely perform TB culture on the above samples (even if it is not requested)
- the appropriate treatment regimen should be started without waiting for culture results if the histology and clinical picture are consistent with a diagnosis of TB (see sections 1.2 and 1.3)
- all patients with non-respiratory TB should have a chest X-ray to exclude or confirm coexisting respiratory TB; in addition, tests as described in table 1 should be considered
- the appropriate drug regimen (see sections 1.2, 1.3 and 1.5) should be continued even if subsequent culture results are negative. **[2006]**

Table 1 Suggested site-specific investigations in the diagnosis and assessment of non-respiratory TB

Site	Imaging	Biopsy	Culture
Lymph node		• Node	• Node or aspirate
Bone/joint	• Plain X-ray and computed tomography (CT) • Magnetic resonance imaging (MRI)	• Site of disease	• Biopsy or paraspinal abscess • Site or joint fluid
Gastrointestinal	• Ultrasound • CT abdomen	• Omentum • Bowel	• Biopsy • Ascites
Genitourinary	• Intravenous urography • Ultrasound	• Site of disease	• Early morning urine • Site of disease • Endometrial curettings
Disseminated	• High-resolution CT thorax • Ultrasound abdomen	• Lung • Liver • Bone marrow	• Bronchial wash • Liver • Bone marrow • Blood
Central nervous system	• CT brain • MRI	• Tuberculoma	• Cerebrospinal fluid
Skin		• Site of disease	• Site of disease
Pericardium	• Echocardiogram	• Pericardium	• Pericardial fluid
Cold/liver abscess	• Ultrasound	• Site of disease	• Site of disease

1.1.2.3 Rapid diagnostic tests for *Mycobacterium tuberculosis* complex (*M tuberculosis*, *M bovis*, *M africanum*) on primary specimens should be used only if:

- rapid confirmation of a TB diagnosis in a sputum smear-positive person would alter their care, or
- before conducting a large contact-tracing initiative. **[2006]**

1.1.2.4 Clinicians should still consider a diagnosis of non-respiratory TB if rapid diagnostic tests are negative, for example in pleural fluid, cerebrospinal fluid and urine. **[2006]**

1.1.2.5 Clinical signs and other laboratory findings consistent with TB meningitis should lead to treatment (see section 1.3.1), even if a rapid diagnostic test is negative, because the potential consequences for the patient are severe. **[2006]**

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 rapid diagnostic tests on microscopy- or culture-positive material. Clinical judgement should be used if tests are inconclusive or delayed. **[2006]**

1.1.2.7 If a risk assessment suggests a patient has multidrug-resistant (MDR) TB (see section 1.5.1):

- rapid diagnostic tests should be conducted for rifampicin resistance
- infection control measures and treatment for MDR TB should be started as described in section 1.5, pending the result of the tests. **[2006]**

1.1.2.8 Rapid diagnostic tests for *M tuberculosis* complex identification should be conducted on biopsy material only if:

- all the sample has been inappropriately placed in formalin, **and**
- acid-fast bacilli are visible on microscopy. **[2006]**

1.1.2.9 Clinical samples should ideally be sent for culture by automated liquid methods, bearing in mind that laboratories need a certain level of throughput to maintain quality control. **[2006]**

1.2 Management of respiratory TB

Respiratory TB is defined as active TB that is affecting any of the following:

- lungs
- pleural cavity
- mediastinal lymph nodes
- larynx.

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 a physician with training in, and experience of, the specialised care of people with TB. The TB service should include specialised nurses and health visitors. TB in children should be managed either by a paediatrician with experience and training in the treatment of TB, or by a general paediatrician with advice from a specialised physician. If these arrangements are not possible, advice should be sought from more specialised colleagues throughout the treatment period. **[2006]**

1.2.1.2 A 6-month, four-drug initial regimen (6 months of isoniazid and rifampicin supplemented in the first 2 months with pyrazinamide and ethambutol) should be used to treat active respiratory TB[6] in:

- adults not known to be HIV positive
- adults who are HIV positive
- children.

This regimen is referred to as 'standard recommended regimen' in this guideline. **[2006]**

1.2.1.3 Fixed-dose combination tablets should be used as part of any TB treatment regimen. **[2006]**

[6] TB affecting the lungs, pleural cavity, mediastinal lymph nodes or larynx.

1.2.1.4 A thrice-weekly dosing regimen should be considered for patients receiving directly observed therapy (DOT) (see section 1.4.2). **[2006]**

1.2.1.5 A twice-weekly dosing regimen should not be used for the treatment of active TB. **[2006]**

1.2.2 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, as defined by NHS Estates[7]
- single rooms that are not negative pressure but are vented to the outside of the building
- beds on a ward, for which no particular engineering standards are required.

1.2.2.1 All patients with TB should have risk assessments for drug resistance (see section 1.5) and for HIV. If risk factors for MDR TB are present, see section 1.5.3 for recommendations on infection control. **[2006]**

1.2.2.2 Unless there is a clear clinical or socioeconomic need, such as homelessness, people with TB at any site of disease should not be admitted to hospital for diagnostic tests or for care. **[2006]**

1.2.2.3 If admitted to hospital, people with suspected respiratory TB should be given a single room. **[2006]**

1.2.2.4 Patients with respiratory TB should be separated from immunocompromised patients, either by admission to a single room on a separate ward, or in a negative-pressure room on the same ward. **[2006]**

[7] NHS Estates (2005) In patient accommodation: options for choice. Isolation facilities in acute settings HBN4 supplement 1. London: The Stationery Office. Available from www.dh.gov.uk

1.2.2.5 Any visitors to a child with TB in hospital should be screened as part of contact tracing, and kept separate from other patients until they have been excluded as the source of infection. **[2006]**

1.2.2.6 Smear-positive TB patients without risk factors for MDR TB (see section 1.5.1) should be cared for in a single room, until:

- they have completed 2 weeks of the standard treatment regimen (see section 1.2.1), **or**
- they are discharged from hospital. **[2006]**

1.2.2.7 Aerosol-generating procedures such as bronchoscopy, sputum induction or nebuliser treatment should be carried out in an appropriately engineered and ventilated area for:

- all patients on an HIV ward, regardless of whether a diagnosis of TB has been considered
- all patients in whom TB is considered a possible diagnosis, in any setting. **[2006]**

1.2.2.8 Healthcare workers caring for people with TB should not use masks, gowns or barrier nursing techniques unless:

- MDR TB is suspected
- aerosol-generating procedures are being performed.

When such equipment is used, the reason should be explained to the person with TB. The equipment should meet the standards of the Health and Safety Executive. See section 1.5.3 for further details of MDR TB infection control. **[2006]**

1.2.2.9 TB patients admitted to a setting where care is provided for people who are immunocompromised, including those who are HIV positive, should be considered infectious and, if sputum smear positive at admission, should stay in a negative-pressure room until:

1. the patient has had at least 2 weeks of appropriate multiple drug therapy, **and**
2. if moving to accommodation (inpatient or home) with people who are immunocompromised, including those who are HIV positive, the patient has had at least 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. any cough has resolved completely, **or**
5. there is definite clinical improvement on treatment, for example remaining afebrile for a week.

For people who were sputum smear negative at admission (that is, three negative samples were taken on separate days; samples were spontaneously produced sputum if possible, or obtained by bronchoscopy or lavage if sputum samples were not possible): **all** of 1, 2, 3 and 5 above should apply. **[2006, amended 2011]**

1.2.2.10 Inpatients with smear-positive respiratory TB should be asked (with explanation) to wear a surgical mask whenever they leave their room until they have had 2 weeks' drug treatment. **[2006]**

1.3 Management of non-respiratory TB

1.3.1 Meningeal TB

1.3.1.1 Patients with active meningeal TB should be offered:

- a treatment regimen, initially lasting for 12 months, comprising isoniazid, pyrazinamide, rifampicin and a fourth drug (for example, ethambutol) for the first 2 months, followed by isoniazid and rifampicin for the rest of the treatment period
- a glucocorticoid at the normal dose range
  - adults – equivalent to prednisolone 20–40 mg if on rifampicin, otherwise 10–20 mg
  - children – equivalent to prednisolone 1–2 mg/kg, maximum 40 mg

  with gradual withdrawal of the glucocorticoid considered, starting within 2–3 weeks of initiation. **[2006]**

1.3.1.2 Clinicians prescribing treatment for active meningeal TB should consider as first choice:

- a daily dosing schedule
- using combination tablets. **[2006]**

1.3.2 Peripheral lymph node TB

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

- be the standard recommended regimen (see section 1.2.1 for further details)
- use a daily dosing schedule
- include combination tablets. **[2006]**

1.3.2.2 Patients with active peripheral lymph node TB who have had an affected gland surgically removed should still be treated with the standard recommended regimen. **[2006]**

1.3.2.3 Drug treatment of peripheral lymph node TB should normally be stopped after 6 months, regardless of the appearance of new nodes, residual nodes or sinuses draining during treatment. **[2006]**

1.3.3 Bone and joint TB: drug treatment

1.3.3.1 The standard recommended regimen (see section 1.2.1 for details) should be planned and started in people with:

- active spinal TB
- active TB at other bone and joint sites. **[2006]**

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

- a daily dosing schedule
- using combination tablets.

See section 1.2.1 for details. **[2006]**

1.3.3.3 A computed tomography (CT) or magnetic resonance (MR) scan should be performed on patients with active spinal TB who have neurological signs or symptoms. If there is direct spinal cord involvement (for example, a spinal cord tuberculoma), management should be as for meningeal TB (see section 1.3.1). **[2006]**

1.3.4 Bone and joint TB: routine therapeutic surgery

1.3.4.1 In patients with spinal TB, anterior spinal fusion should not be performed routinely. **[2006]**

1.3.4.2 In patients with spinal TB, anterior spinal fusion should be considered if there is spinal instability or evidence of spinal cord compression. **[2006]**

1.3.5 Pericardial TB

1.3.5.1 For patients with active pericardial TB, the first choice of treatment should:

- be the standard recommended regimen (see section 1.2.1 for details)
- use a daily dosing schedule
- include combination tablets. **[2006]**

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

- for adults, a glucocorticoid equivalent to prednisolone at 60 mg/day
- for children, a glucocorticoid equivalent to prednisolone 1 mg/kg/day (maximum 40 mg/day)

with gradual withdrawal of the glucocorticoid considered, starting within 2–3 weeks of initiation. **[2006]**

1.3.6 Disseminated (including miliary) TB

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

- be the standard recommended regimen (see section 1.2.1 for details)
- use a daily dosing schedule
- include combination tablets. **[2006]**

1.3.6.2 Treatment of disseminated (including miliary) TB should be started even if initial liver function tests are abnormal. If the patient's liver function deteriorates significantly on drug treatment, advice on management options should be sought from clinicians with specialist experience of these circumstances. **[2006]**

1.3.6.3 Patients with disseminated (including miliary) TB should be tested for central nervous system (CNS) involvement by:

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

If evidence of CNS involvement is detected, treatment should be the same as for meningeal TB (see section 1.3.1). **[2006]**

1.3.7 Other sites of infection

1.3.7.1 For patients with:

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

the first choice of treatment should:

- be the standard recommended regimen (see section 1.2.1 for details)
- use a daily dosing schedule
- include combination tablets. **[2006]**

1.4 Monitoring, adherence and treatment completion

1.4.1 Treatment completion and follow-up

1.4.1.1 Follow-up clinic visits should not be conducted routinely after treatment completion. **[2006]**

1.4.1.2 Patients should be told to watch for 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 particularly well informed about symptoms. **[2006]**

1.4.1.3 Patients who have had drug-resistant TB should be considered for follow-up for 12 months after completing treatment. Patients who have had MDR TB should be considered for prolonged follow-up. **[2006]**

1.4.2 Improving adherence: directly observed therapy

1.4.2.1 Use of directly observed therapy (DOT) is not usually necessary in the management of most cases of active TB.

All patients should have a risk assessment for adherence to 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 TB
- patients with likely poor adherence, in particular those who have a history of non-adherence. **[2006]**

1.4.2.2 Clinicians who are planning to offer 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 practicable for the person with TB. The person with TB and his or her assigned key worker should be involved in deciding these arrangements. DOT should also be supported by frequent contact with the key worker (see section 1.4.3). **[2006, amended 2011]**

1.4.3 Other strategies to improve adherence

1.4.3.1 To promote adherence, patients should be involved in treatment decisions at the outset of treatment for active or latent TB. The

importance of adherence should be emphasised during discussion with the patient when agreeing the regimen. **[2006]**

1.4.3.2 The TB service should tell each person with TB 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. **[2006]**

1.4.3.3 TB services should consider the following interventions to improve adherence to treatment for active or latent TB if a patient defaults:

- reminder letters in appropriate languages
- health education counselling
- patient-centred interview and health education booklet
- home visits
- patient diary
- random urine tests and other monitoring (for example, pill counts)
- information about help with paying for prescriptions
- help or advice about where and how to get social security benefits, housing and social services. **[2006]**

1.4.3.4 Pharmacies should make liquid preparations of anti-TB drugs readily available to TB patients who may need them – for example, children and people with swallowing difficulties. **[2006]**

1.4.3.5 TB services should assess local language and other communication needs and, if there is a demonstrated need, provide patient information accordingly[8]. **[2006]**

[8] Patient information should be drawn from national high-quality resources if available; for examples, see www.hpa.org.uk

1.5 Risk assessment and infection control in drug-resistant TB

1.5.1 Risk factors

1.5.1.1 A risk assessment for drug resistance should be made for each patient with TB, based on the risk factors listed below:

- history of prior TB drug treatment; prior TB treatment failure
- contact with a known case of drug-resistant TB
- birth in a foreign country, particularly high-incidence countries as defined by the HPA on its website[9]
- HIV infection
- residence in London
- age profile, with highest rates between ages 25 and 44
- male gender. **[2006]**

1.5.1.2 The TB service should consider the risk assessment for drug resistance and, if the risk is regarded as significant, urgent molecular tests for rifampicin resistance should be performed on smear-positive material or on positive cultures when they become available (see section 1.1.2). **[2006]**

1.5.1.3 Response to treatment should be closely monitored in patients 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'), drug resistance should be suspected and treatment reviewed with a clinician experienced in the treatment of MDR TB. **[2006]**

(See section 1.2.1 for details of the standard recommended regimen.)

[9] Countries with more than 40 cases per 100,000 per year, as listed by the Health Protection Agency (go to www.hpa.org.uk and search for 'WHO country data TB').

1.5.2 Referral

1.5.2.1 The options for organising care for people with MDR TB should be discussed with clinicians who specialise in this. The views of the patient should be sought and taken into account, and shared care should be considered. **[2006]**

1.5.3 Infection control

1.5.3.1 Patients with suspected or known infectious MDR TB who are admitted to hospital should be admitted to a negative-pressure room. If none is available locally, the patient should be transferred to a hospital that has these facilities and a clinician experienced in managing complex drug-resistant cases. 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. **[2006]**

1.5.3.2 Staff and visitors should wear FFP3 masks[10] during contact with a patient with suspected or known MDR TB while the patient is considered infectious. **[2006]**

1.5.3.3 Before the decision is made to discharge a patient with suspected or known MDR TB from hospital, secure arrangements for the supervision and administration of all anti-TB therapy should have been agreed with the patient and carers. **[2006]**

1.5.3.4 The decision to discharge a patient with suspected or known MDR TB should be discussed with the infection control team, the local microbiologist, the local TB service, and the consultant in communicable disease control. **[2006]**

1.5.3.5 Negative-pressure rooms used for infection control in MDR TB should meet the standards of the Interdepartmental Working Group

[10] European standard EN149:2001; masks should meet the standards in 'Respiratory protective equipment at work: a practical guide HSG53' published by the Health and Safety Executive (2005). Available from www.hse.gov.uk

on Tuberculosis[11], and should be clearly identified for staff, for example by a standard sign. Such labelling should be kept up to date. **[2006]**

For a summary of recommendations on infection control, see the algorithm on isolation decisions for patients with suspected respiratory TB (appendix C).

1.5.4 Treatment of non-MDR drug-resistant TB

1.5.4.1 Patients with drug-resistant TB, other than MDR, should be under the care of a specialist physician with appropriate experience in managing such cases. First-choice drug treatment is set out in table 2. **[2006]**

Table 2 Recommended drug regimens for non-MDR drug-resistant TB

Drug resistance	Initial phase	Continuation phase
S	2RHZE	4RH
H known before treatment	2RZSE	7RE
found after starting treatment	2RZE	10RE
Z	2RHE	7RH
E	2RHZ	4RH
R (only if confirmed isolated resistance)	2HZE	16HE
S+H	2RZE	10RE
Other	individualised	
See page 9 for details of the system of drug regimen abbreviations		

[11] The Interdepartmental Working Group on Tuberculosis (1998) The prevention and control of tuberculosis in the United Kingdom: UK guidance on the prevention and control of transmission of 1. HIV-related tuberculosis 2. drug-resistant, including multiple drug-resistant, tuberculosis. London: Department of Health. Available from www.dh.gov.uk

1.6 Management of latent TB

1.6.1 Treatment of latent TB infection

1.6.1.1 Treatment of latent TB infection should be considered for people in the following groups, once active TB has been excluded by chest X-ray and examination.

- People identified through screening who are:
  - 35 years or younger (because of increasing risk of hepatotoxicity with age)[12]
  - any age with HIV
  - any age and a healthcare worker

  and are either:
  - Mantoux positive (6 mm or greater), and without prior BCG vaccination, **or**
  - strongly Mantoux positive (15 mm or greater), interferon-gamma positive, and with prior BCG vaccination.
- Children aged 1–15 years identified through opportunistic screening to be:
  - strongly Mantoux positive (15 mm or greater), **and**
  - interferon-gamma positive (if this test has been performed), **and**
  - without prior BCG vaccination.
- People with evidence of TB scars on chest X-ray, and without a history of adequate treatment. **[2006, amended 2011]**

1.6.1.2 People with HIV who are in close contact[13] with people with sputum-smear-positive respiratory TB should have active disease excluded and then be given treatment for latent TB infection (see recommendations 1.1.1.10–1.1.1.13). **[2006, amended 2011]**

[12] For people aged 36 or older, consider risks and benefits for the individual before offering treatment.
[13] Close contacts may include a boyfriend or girlfriend and frequent visitors to the home of the index case, in addition to household contacts.

1.6.1.3 Treatment for latent TB infection should not be started in close contacts of people with sputum-smear-positive MDR TB who are strongly Mantoux positive (15 mm or greater), as no regimen is of proven benefit, and only a small proportion of people infected will develop the disease. Long-term monitoring should be undertaken for active disease. **[2006]**

1.6.1.4 People who have agreed to receive treatment for latent TB infection should be started on one of the following regimens:

- either 6 months of isoniazid (6H) or 3 months of rifampicin and isoniazid (3RH) for people aged 16–35 not known to have HIV
- either 6 months of isoniazid (6H) or 3 months of rifampicin and isoniazid (3RH) for people older than 35 in whom treatment for latent TB infection is recommended (see recommendation 1.6.1.1), and who are not known to have HIV
- 6 months of isoniazid (6H) for people of any age who have HIV
- 6 months of rifampicin (6R) for contacts, aged 35 or younger, of people with isoniazid-resistant TB.

People eligible for treatment of latent TB infection, but who decline to take this treatment, should be given 'Inform and advise' information about TB and have chest X-rays 3 and 12 months later. **[2006]**

1.6.1.5 Neonates who have been in close contact with people with sputum-smear-positive TB who have not received at least 2 weeks' anti-tuberculosis drug treatment should be treated as follows.

- The baby should be started on isoniazid (according to the current 'British national formulary for children' for 3 months and then a Mantoux test performed after 3 months' treatment.
- If the Mantoux test is positive (6 mm or greater) the baby should be assessed for active TB (see section 1.1.2). If this assessment

is negative, then isoniazid should be continued for a total of 6 months.

- If the Mantoux test is negative (less than 6 mm), it should be repeated together with an interferon-gamma test. If both are negative then isoniazid should be stopped and a BCG vaccination performed (see section 1.7). **[2006, amended 2011]**

1.6.1.6 Children older than 4 weeks but younger than 2 years who have not had BCG vaccination and are in close contact with people with sputum-smear-positive TB should be treated as follows.

- The child should be started on isoniazid (according to the current 'British national formulary for children') and a Mantoux test performed.
- If the Mantoux test is positive (6 mm or greater), the child should be assessed for active TB (see section 1.1.2). If active TB is ruled out, full treatment for latent TB infection should be given (see recommendation 1.6.1.8).
- If the Mantoux test is negative (less than 6 mm), then isoniazid should be continued for 6 weeks, and then a repeat Mantoux test together with an interferon-gamma test should be carried out.
- If the repeat tests are negative, isoniazid may be stopped and BCG vaccination performed (see section 1.7).
- If either repeat test is positive (6 mm or greater), then the child should be assessed for active TB (see section 1.1.2) and consider treating for latent TB. Contact tracing for children younger than 2 years when the index case is sputum smear positive is summarised in an algorithm (see appendix C). **[2006, amended 2011]**

1.6.1.7 BCG-vaccinated children older than 4 weeks but younger than 2 years, in close contact with people with sputum-smear-positive respiratory TB, should be treated as follows.

- The child should have a Mantoux test. If this is positive (15 mm or greater), the child should be assessed for active TB (see section 1.1.2). If active TB is excluded, then treatment for latent TB infection should be given (see recommendation 1.6.1.8).
- If the result of the test is as expected for prior BCG (less than 15 mm), it should be repeated after 6 weeks together with an interferon-gamma test.
- If the repeat Mantoux test is also less than 15 mm, and the interferon-gamma test is also negative, no further action is needed.
- If the repeat Mantoux test becomes more strongly positive (15 mm or greater and an increase of 5 mm or more over the previous test), or the interferon-gamma test is positive the child should be assessed for active TB (see section 1.1.2). If active TB is excluded, treatment for latent TB infection should be given. **[2006, amended 2011]**

1.6.1.8 For children requiring treatment for latent TB infection, a regimen of either 3 months of rifampicin and isoniazid (3RH) or 6 months of isoniazid (6H) should be planned and started, unless the child is known to be HIV positive, when 6H should be given (see recommendation 1.6.1.4). **[2006]**

1.6.1.9 Healthcare workers should be aware that certain groups of people with latent TB are at increased risk of going on to develop active TB, including people who:

- are HIV positive
- are injecting drug users
- have had solid organ transplantation
- have a haematological malignancy

- have had a jejunoileal bypass
- have chronic renal failure or receive haemodialysis
- have had a gastrectomy
- are receiving anti-tumour necrosis factor-alpha treatment
- have silicosis.

Patients in these groups should be advised of the risks and symptoms of TB, on the basis of an individual risk assessment, usually in a standard letter of the type referred to as 'Inform and advise' information. **[2006]**

1.7 BCG vaccination

1.7.1.1 When BCG is being recommended, the benefits and risks of vaccination and remaining unvaccinated should be discussed with the person (or, if a child, with the parents), so that they can make an informed decision. This discussion should be tailored to the person, be in an appropriate language, and take into account cultural sensitivities and stigma. **[2006]**

1.7.1.2 People identified for BCG vaccination through occupational health, contact tracing or new entrant screening who are also considered to be at increased risk of being HIV positive, should be offered HIV testing before BCG vaccination[14]. **[2006]**

1.7.2 BCG vaccination for neonates

1.7.2.1 Neonatal BCG vaccination for any baby at increased risk of TB should be discussed with the parents or legal guardian. **[2006]**

1.7.2.2 Primary care organisations with a high incidence of TB[15] should consider vaccinating all neonates soon after birth. **[2006]**

[14] See the British HIV Association guideline for details of further action in HIV-positive patients. Available from www.bhiva.org.
[15] As defined by the HPA; go to www.hpa.org.uk and search for 'tuberculosis rate bands'.

1.7.2.3 In areas with a low incidence of TB[16], primary care organisations should offer BCG vaccination to selected neonates who:

- were born in an area with a high incidence of TB[16], or
- have one or more parents or grandparents who were born in a high-incidence country, or
- have a family history of TB in the past 5 years. **[2006]**

1.7.3 BCG vaccination for infants and older children

1.7.3.1 Routine BCG vaccination is not recommended for children aged 10–14.

- Healthcare professionals should opportunistically identify unvaccinated children older than 4 weeks and younger than 16 years at increased risk of TB (see section 1.6.1) who would have qualified for neonatal BCG and provide Mantoux testing and BCG (if Mantoux negative).
- This opportunistic vaccination should be in line with the Chief Medical Officer's advice on vaccinating this age group following the end of the school-based programme[17]. **[2006]**

1.7.3.2 Mantoux testing should not be done routinely before BCG vaccination in children younger than 6 years unless they have a history of residence or prolonged stay (more than 1 month) in a country with a high incidence of TB[18]. **[2006]**

[16] As defined by the HPA; go to www.hpa.org.uk and search for 'tuberculosis rate bands'.
[17] Available from www.dh.gov.uk
[18] More than 40 cases per 100,000 per year, as listed by the Health Protection Agency (go to www.hpa.org.uk and search for 'TB WHO country data').

1.7.4 BCG vaccination for new entrants from high-incidence areas

1.7.4.1 BCG vaccination should be offered to Mantoux-negative new entrants[19] who:

- are from high-incidence countries, **and**
- are previously unvaccinated (that is, without ad**equate** documentation or a characteristic scar), **and**
- are aged:
  - younger than 16 years, **or**
  - 16 to 35 years[20] from sub-Saharan Africa or a country with a TB incidence of 500 per 100,000. **[2006]**

1.7.5 BCG vaccination for healthcare workers

1.7.5.1 BCG vaccination should be offered to healthcare workers, irrespective of age[21], who:

- are previously unvaccinated (that is, without adequate documentation or a characteristic scar), **and**
- will have contact with patients or clinical materials, **and**
- are Mantoux (or interferon-gamma) negative.

See sections 1.9.1 and 1.9.2 for details of occupational health screening. **[2006]**

1.7.6 BCG vaccination for contacts of people with active TB

1.7.6.1 BCG vaccination should be offered to Mantoux-negative contacts of people with respiratory TB (see section 1.8.1 for details of contact

[19] People who have recently arrived in or returned to the UK from high-incidence countries.
[20] The Green Book recommends BCG for new entrants only up to the age of 16 years. However, in this guideline BCG is recommended for those up to 35 years who come from the countries with the very highest rates of TB because there is some evidence of cost effectiveness.
[21] As outlined in the Green Book, there is not sufficient age-specific evidence to make recommendations on BCG vaccination for people older than 35 (see full guideline for details). However, in this guideline BCG vaccination is recommended for healthcare workers of all ages because of the increased risk to them – and consequently the patients they care for – if they remain unvaccinated.

tracing) if they are previously unvaccinated (that is, without adequate documentation or a characteristic scar) and are:

- aged 35 or younger
- aged 36 and older and a healthcare or laboratory worker who has contact with patients or clinical materials (see section 1.7.5). **[2006]**

1.7.7 BCG vaccination for other groups

1.7.7.1 BCG vaccination should be offered to previously unvaccinated, Mantoux-negative people aged 35 or younger in the following groups at increased risk of exposure to TB, in accordance with the Green Book:

- veterinary and other staff such as abattoir workers who handle animal species known to be susceptible to TB, such as simians
- prison staff working directly with prisoners
- staff of care homes for elderly people
- staff of hostels for homeless people and facilities accommodating refugees and asylum seekers
- people going to live or work with local people for more than 1 month in a high-incidence country.

See section 1.7.5 for advice on healthcare workers. **[2006]**

1.8 Active case finding

1.8.1 Contact tracing: human to human transmission

1.8.1.1 Once a person has been diagnosed with active TB, the diagnosing physician should inform relevant colleagues so that the need for contact tracing can be assessed without delay. Contact tracing should not be delayed until notification. **[2006]**

1.8.1.2 Screening should be offered to the household contacts of any person with active TB, irrespective of the site of infection. Household contacts are defined as those who share a bedroom,

kitchen, bathroom or sitting room with the index case. Screening should comprise:

- standard testing for latent TB for those aged 35 or younger, and consideration of BCG or treatment for latent TB infection once active TB has been ruled out
- interferon-gamma test 6 weeks after the Mantoux test, and consideration of BCG or treatment for latent TB infection once active TB has been ruled out, for those who:
  - are previously unvaccinated **and**
  - are household contacts of a person with sputum-smear-positive TB **and**
  - are Mantoux negative (less than 6 mm)
- chest X-ray (if there are no contraindications) for those older than 35, possibly leading to further investigation for active TB. **[2006]**

1.8.1.3 For people with sputum-smear-positive TB, other close contacts should be assessed. These may include boyfriends or girlfriends 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. **[2006]**

1.8.1.4 Casual contacts of people with TB, who will include the great majority of workplace contacts, should not normally be assessed. **[2006]**

1.8.1.5 The need for tracing casual contacts of people with TB should be assessed if:

- the index case is judged to be particularly infectious (for example, evidenced by transmission to close contacts), **or**
- any casual contacts are known to possess features that put them at special risk of infection (see section 1.6.1). **[2006]**

1.8.1.6 'Inform and advise' information should be offered to all contacts of people with smear-positive TB. **[2006]**

1.8.2 Contact tracing: cattle to human transmission

1.8.2.1 'Inform and advise' information should be given to people in contact with TB-diseased animals. Diagnostic tests for latent TB should be considered only for children younger than 16 who have not had BCG vaccination and have regularly drunk unpasteurised milk from animals with TB udder lesions. **[2006]**

1.8.3 Contact tracing: cases on aircraft

1.8.3.1 Following diagnosis of TB in an aircraft traveller, contact tracing of fellow passengers should not routinely be undertaken. **[2006]**

1.8.3.2 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 longer than 8 hours, **and**
- the index case is sputum smear positive, **and either**
  - the index case has MDR TB, **or**
  - the index case coughed frequently during the flight.

The CCDC should provide the airline with 'Inform and advise' information to send to passengers seated in the same part[22] of the aircraft as the index case. **[2006]**

1.8.3.3 If the TB index case is an aircraft crew member, contact tracing of passengers should not routinely take place. **[2006]**

1.8.3.4 If the TB index case is an aircraft crew member, contact tracing of other members of staff is appropriate, in accordance with the usual principles for screening workplace colleagues (see section 1.8.1). **[2006]**

[22] Published evidence does not allow for a precise definition, but such contact tracing on aircraft has often included only people within three rows on either side of the index case.

1.8.4 Contact tracing: cases in schools

1.8.4.1 Following diagnosis of TB in a school pupil or member of staff, the consultant in communicable disease control should be prepared to explain the prevention and control procedures to staff, parents and the press. Advice on managing these incidents and their public relations is available from the Health Protection Unit. **[2006]**

1.8.4.2 If a school pupil is diagnosed with sputum-smear-positive TB, the rest of his or 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. **[2006]**

1.8.4.3 If a teacher has sputum-smear-positive TB, the pupils in his or her classes during the preceding 3 months should be assessed as part of contact tracing. **[2006]**

1.8.4.4 Clinicians conducting contact tracing in a school should consider extending it to include children and teachers involved in extracurricular activities, and non-teaching staff, on the basis of:

- the degree of infectivity of the index case
- the length of time the index case was in contact with others
- whether contacts are unusually susceptible to infection
- the proximity of contact. **[2006]**

1.8.4.5 Secondary cases of sputum-smear-positive TB should be treated as index cases for contact tracing. **[2006]**

1.8.4.6 If the index case of a school pupil's TB 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. **[2006]**

1.8.5 Contact tracing: community childcare

1.8.5.1 When an adult who works in childcare (including people who provide childcare informally) is diagnosed with sputum-smear-

positive TB, management is as for contact tracing (see section 1.8.1). **[2006]**

1.8.6 Contact tracing: cases in hospital inpatients

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

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

Contact tracing and testing should be carried out only for patients for whom the risk is regarded as significant. **[2006]**

1.8.6.2 Patients should be regarded as at risk of infection if they spent more than 8 hours in the same bay as an inpatient with sputum-smear-positive TB who had a cough. The risk should be documented in the contact's clinical notes, for the attention of the contact's consultant. The contact should be given 'Inform and advise' information, and their GP should be informed. **[2006]**

1.8.6.3 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 an exposed patient is known to be particularly susceptible to infection, they should be managed as equivalent to household contacts (see section 1.8.1). **[2006]**

1.8.6.4 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[23]. **[2006]**

[23] The Interdepartmental Working Group on Tuberculosis (1998) The prevention and control of tuberculosis in the United Kingdom: UK guidance on the prevention and control of transmission of 1.

1.8.6.5 In cases of doubt when planning contact tracing after diagnosing sputum-smear-positive TB in an inpatient, further advice should be sought from the regional or national Health Protection Agency or people experienced in the field. **[2006]**

1.8.7 Screening new entrants

1.8.7.1 Healthcare professionals, including primary care staff, responsible for screening new entrants[24] should maintain a coordinated programme to:

- detect active TB and start treatment
- detect latent TB and start treatment
- provide BCG vaccination to those in high-risk groups who are not infected and who are previously unvaccinated
- provide relevant information to all new entrants. **[2006]**

1.8.7.2 New entrant screening for TB should be incorporated within larger health screening programmes for new entrants, linked to local services. **[2006]**

1.8.7.3 Assessment for, and management of TB in new entrants should consist of the following.

- Risk assessment for HIV, including HIV prevalence rates in the country of origin, which is then taken into account for Mantoux testing and BCG vaccination.
- Assessment for active TB if interferon-gamma test is positive; which would include a chest X-ray.
- Treatment for latent TB infection for people aged 35 years or younger in whom active TB has been excluded, with a positive Mantoux test inconsistent with their BCG history, and a positive interferon-gamma test.

HIV-related tuberculosis 2. drug-resistant, including multiple drug-resistant, tuberculosis. London: Department of Health. Available from www.dh.gov.uk

[24] In this guideline, new entrants are defined as people who have recently arrived in or returned to the UK from high-incidence countries, as defined by the HPA; go to www.hpa.org.uk and search for 'WHO country data TB'.

- Consideration of BCG for unvaccinated people who are Mantoux negative (see section 1.7.4).
- 'Inform and advise' information for people who do not have active TB and are not being offered BCG or treatment for latent TB infection. **[2006, amended 2011]**

1.8.7.4 New entrants[25] 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. **[2006]**

1.8.7.5 Any healthcare professional working with new entrants should encourage them to register with a GP. **[2006]**

1.8.8 Street homeless

1.8.8.1 Active case finding should be carried out among street homeless people (including those using direct access hostels for the homeless) by chest X-ray screening on an opportunistic and/or symptomatic basis. Simple incentives for attending, such as hot drinks and snacks, should be considered. **[2006]**

1.8.8.2 Healthcare professionals working with people with TB should reinforce and update education about TB, and referral pathways, to primary care colleagues, social workers and voluntary workers who work with homeless people. **[2006]**

[25] In this guideline, new entrants are defined as people who have recently arrived in or returned to the UK from high-incidence countries, as defined by the HPA; go to www.hpa.org.uk and search for 'WHO country data TB'.

1.9 Preventing infection in specific settings

1.9.1 Healthcare environments: new NHS employees

1.9.1.1 Employees new to the NHS who will be working with patients or clinical specimens should not start work until they have completed a TB screen or health check, or documentary evidence is provided of such screening having taken place within the preceding 12 months. **[2006]**

1.9.1.2 Employees new to the NHS who will not have contact with patients or clinical specimens should not start work if they have signs or symptoms of TB. **[2006]**

1.9.1.3 Health checks for employees new to the NHS who will have contact with patients or clinical materials should include:

- assessment of personal or family history of TB
- symptom and signs enquiry, possibly by questionnaire
- documentary evidence of TB skin testing (or interferon-gamma testing) and/or BCG scar check by an occupational health professional, not relying on the applicant's personal assessment
- Mantoux result within the last 5 years, if available. **[2006]**

1.9.1.4 See recommendations 1.1.1.14–1.1.1.17 for screening new NHS employees for latent TB. **[2006, amended 2011]**

1.9.1.5 Employees who will be working with patients or clinical specimens and who are Mantoux negative (less than 6 mm) should have an individual risk assessment for HIV infection before BCG vaccination is given. **[2006]**

1.9.1.6 Employees new to the NHS should be offered BCG vaccination, whatever their age, if they will have contact with patients and/or clinical specimens, are Mantoux negative (less than 6 mm) and have not been previously vaccinated. **[2006]**

1.9.1.7 Employees of any age who are new to the NHS and are from countries of high TB incidence, or who have had contact with patients in settings with a high TB prevalence should have an interferon-gamma test. If negative, offer BCG vaccination as with a negative Mantoux result (see recommendations 1.9.1.5 and 1.9.1.6). If positive, the person should be referred for clinical assessment for diagnosis and possible treatment of latent infection or active disease. **[2006, amended 2011]**

1.9.1.8 If a new employee from the UK or other low-incidence setting, without prior BCG vaccination, has a positive Mantoux and a positive interferon-gamma test, they should have a medical assessment and a chest X-ray. They should be referred to a TB clinic for consideration of TB treatment if the chest X-ray is abnormal, or for consideration of treatment of latent TB infection if the chest X-ray is normal. **[2006, amended 2011]**

1.9.1.9 If a prospective or current healthcare worker who is Mantoux negative (less than 6 mm) declines BCG vaccination, the risks should be explained and the oral explanation supplemented by written advice. If the person still declines BCG vaccination, he or she should not work where there is a risk of exposure to TB. The employer will need to consider each case individually, taking account of employment and health and safety obligations. **[2006]**

1.9.1.10 Clinical students, agency and locum staff and contract ancillary workers who have contact with patients or clinical materials should be screened for TB to the same standard as new employees in healthcare environments, 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. **[2006]**

1.9.1.11 NHS trusts arranging care for NHS patients in non-NHS settings should ensure that healthcare workers who have contact with

patients or clinical materials in these settings have been screened for TB to the same standard as new employees in healthcare environments (see recommendations 1.9.1.1–1.9.1.10).

See the algorithm on screening new NHS employees (appendix C) for a summary. **[2006]**

1.9.2 Healthcare environments: occupational health

These recommendations set the standard for NHS organisations and therefore should apply in any setting in England and Wales where NHS patients are treated.

1.9.2.1 Reminders of the symptoms of TB, and the need for prompt reporting of such symptoms, should be included with annual reminders about occupational health for staff who:

- 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 given after a TB incident on a ward. **[2006]**

1.9.2.2 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 employees (see section 1.9.1). **[2006]**

1.9.2.3 The risk of TB for a new healthcare worker who knows he or she is HIV positive at the time of recruitment should be assessed as part of the occupational health checks. **[2006]**

1.9.2.4 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. **[2006]**

1.9.2.5 Healthcare workers who are found to be HIV positive during employment should have medical and occupational assessments of TB risk, and may need to modify their work to reduce exposure. **[2006]**

1.9.3 Prisons and remand centres

1.9.3.1 Healthcare workers providing care for prisoners and remand centre detainees should be aware of the signs and symptoms of active TB. TB services should ensure that awareness of these signs and symptoms is also promoted among prisoners and prison staff. **[2006]**

1.9.3.2 Prisoners should be screened for TB by:

- a health questionnaire on each entry to the prison system, **then**
- for those with signs and symptoms of active TB, a chest X-ray, and three sputum samples taken in 24 hours for TB microscopy, including a morning sputum sample (see section 1.1.2). **[2006]**

1.9.3.3 All prisoners receiving treatment for active or latent TB should receive DOT. **[2006]**

1.9.3.4 Prison medical services should have liaison and handover arrangements to ensure continuity of care before any prisoner on TB treatment is transferred between prisons. **[2006]**

1.9.3.5 If a prisoner is being treated for active or latent TB, the prison medical services should draw up as early as possible a contingency plan for early discharge, which could happen directly from a court appearance. This plan should include firm arrangements for clinical follow-up and treatment monitoring in the intended district of residence, and should take into account that there may not be a fixed residence arranged for the prisoner after release. The prisoner should be given contact details for a named key worker, who will visit and monitor the prisoner after release and liaise between services involved. **[2006]**

1.9.3.6 Prison service staff and others who have regular contact with prisoners (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 1.9.1 and 1.9.2). **[2006]**

2 Notes on the scope of the guidance

NICE guidelines are developed in accordance with a scope that defines what the guideline will and will not cover. The scopes of the original guideline and of this update are available from www.nice.org.uk/guidance/CG117.

This guideline sets out best practice guidance for the diagnosis, treatment, prevention and control of 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 comorbidities 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 multidrug-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.

This update looked at the diagnosis of latent TB using *M tuberculosis*-specific antigens (ESAT-6, CFP-10, and TB7.7) interferon gamma release assays (IGTs).

It covers the following population groups:

- Adults and children at increased risk of infection by *M tuberculosis* complex (*M tuberculosis, M africanum, M bovis*), specifically if they:
- have arrived or returned from high-prevalence countries within the past 5 years
- were born in high prevalence countries
- live with people diagnosed with active TB
- have close contact with people diagnosed with active TB, for example at school or work
- are homeless and/or problem drug users
- are, or have a recently been, a prisoner
- are immunocompromised.

How this guideline was developed

The original guideline was developed by the National Collaborating Centre for Chronic Conditions (now the National Clinical Guideline Centre). This update was developed by the Centre for Clinical Practice at NICE. Both Centres established a Guideline Development Group (see appendix A), which reviewed the evidence and developed the recommendations. Independent Guideline Review Panels oversaw the development of the guidelines (see appendix B).

There is more information about how NICE clinical guidelines are developed on the NICE website (www.nice.org.uk/HowWeWork). A booklet, 'How NICE clinical guidelines are developed: an overview for stakeholders, the public and the NHS' (fourth edition, published 2009), is available from NICE publications (phone 0845 003 7783 or email publications@nice.org.uk and quote reference N1739).

3 Implementation

NICE has developed tools to help organisations implement this guidance (see www.nice.org.uk/guidance/CG117).

4 Research recommendations

The Guideline Development Group has made the following recommendations for research, based on its review of evidence, 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 Interferon-gamma tests

A diagnostic and qualitative study is needed to assess whether interferon-gamma tests are acceptable to patients and are more effective than tuberculin skin tests for:

- predicting subsequent development of active TB, or
- diagnosing or ruling out current active TB

when undertaking TB screening in:

- new entrants from high TB prevalence countries
- healthcare workers
- children in high-risk areas who missed neonatal BCG
- contacts of people with sputum smear-positive TB
- HIV positive patients.

This study should compare the strategies of Mantoux test only, Mantoux test then interferon gamma test if positive, and interferon gamma test only.

Why this is important

These are new diagnostic tests and there is not yet evidence to show increased effectiveness in predicting subsequent development of active TB, which could enable better targeting of preventive treatment. Also, the acceptability of the tests to various screening groups has not been investigated.

4.2 Directly observed therapy

A cluster randomised controlled trial 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.

Why this is important

There is currently no evidence from controlled studies on the use of DOT in the UK. If a UK programme of DOT is found to promote adherence to treatment in these populations, then patients would be less likely to experience future relapse or drug resistance, or to transmit TB to other patients.

4.3 New entrant screening and treatment for latent TB infection

A study is needed of people found by new entrant screening (as set out in section 1.8.7) to be Mantoux positive and interferon-gamma positive, to establish better estimates of the cost effectiveness of screening and treatment for latent TB infection in this population. This could identify factors predisposing people to developing active TB so that more effective targeted treatment programmes can be developed for latent TB infection.

Why this is important

The current guideline recommendations are based on a health economic model, which attempts to target effort on those people at highest risk. This would be more useful if more accurate cost-effectiveness estimates were available.

4.4 Protective effects of BCG

A case-control study is needed, comparing people who developed active or latent TB with those who did not, and comparing the proportions of people in each group who had been 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.

Why this is important

There is little up-to-date evidence on the duration of BCG protection in England and Wales across various age ranges and population groups. This information would aid the development of future BCG vaccination policies in these groups.

4.5 Quality of life

A study is needed to ascertain quality-of-life score estimates from those with TB (both active disease and latent infection), including adverse treatment effects, using an appropriate quality-of-life instrument. This will improve economic decision-making throughout TB care.

Why this is important

Patients' views on their quality of life would be more accurately reflected in future work. There are currently no quality-of-life estimates in the guideline models based on data drawn directly from patients. Cost-effectiveness estimates in the form of QALYs would increase the accuracy of health economic models.

4.6 Contact tracing in household contacts and homeless people

Research is needed to determine whether contact tracing is more effective (in terms of identifying cases of latent infection and active disease) among household contacts than among street homeless contacts of patients with confirmed TB (including those using direct-access hostels for the homeless).

Why this is important

Evidence from one non-analytic study suggests that contact tracing identifies fewer cases of TB in the homeless than in contacts who were housed. Depending on the outcome, the research findings could have implications for modifying conventional contact tracing so that it is tailored to the needs of the homeless population.

4.7 Incentives for attending new entrant screening

Research is needed to determine whether Port of Arrival scheme referrals with incentives for attending screening identify more cases of latent TB infection and active TB disease in new entrants than Port of Arrival scheme referrals with no incentives.

Why this is important

Currently there is no evidence from controlled studies in this area. If incentives were found to improve attendance for TB screening among this population, then this method would be a more effective way of reaching and treating this population.

4.8 Incentives for homeless people attending chest X-ray screening

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

Why this is important

Currently there is no evidence from controlled studies in this area. If incentives were found by the research evidence to improve attendance for chest X-ray screening among this population, then this method would be a more effective way of reaching and treating this group.

5 Other versions of this guideline

5.1 Full guideline

The full guideline, 'Tuberculosis: clinical diagnosis and management of tuberculosis, and measures for its prevention and control' contains details of the methods and evidence used to develop the guideline. It is available from our website (www.nice.org.uk/guidance/CG117/FullGuidance).

5.2 Quick reference guide

A quick reference guide for healthcare professionals is available from www.nice.org.uk/guidance/CG117/QuickRefGuide

For printed copies, phone NICE publications on 0845 003 7783 or email publications@nice.org.uk (quote reference number N2458).

5.3 'Understanding NICE guidance'

A summary for patients and carers ('Understanding NICE guidance') is available from www.nice.org.uk/guidance/CG117/PublicInfo

For printed copies, phone NICE publications on 0845 003 7783 or email publications@nice.org.uk (quote reference number N2459).

We encourage NHS and voluntary sector organisations to use text from this booklet in their own information about tuberculosis.

6 Related NICE guidance

Published

- Medicines adherence NICE clinical guideline 76 (2009). Available from www.nice.org.uk/guidance/CG76

Under development

NICE is developing the following guidance (details available from www.nice.org.uk):

- Tuberculosis: hard-to-reach groups. NICE public health guidance. Publication expected March 2012.

7 Updating the guideline

NICE clinical guidelines are updated so that recommendations take into account important new information. New evidence is checked 3 years after publication, and healthcare professionals and patients are asked for their views; we use this information to decide whether all or part of a guideline needs updating. If important new evidence is published at other times, we

may decide to do a more rapid update of some recommendations. Please see our website for information about updating the guideline.

Appendix A: The 2006 and 2011 Guideline Development Groups and the 2011 NICE project team

2011 Guideline Development Group

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2011 NICE project team

A short clinical guidelines technical team was responsible for this guideline update. It prepared information for the Guideline Development Group, drafted the guideline and responded to consultation comments. The following NICE employees made up the technical team:

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Stefanie Reken
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Appendix B: The 2006 and 2011Guideline Review Panels

The Guideline Review Panel is an independent panel that oversees the development of the guideline and takes responsibility for monitoring adherence to NICE guideline development processes. In particular, the panel ensures that stakeholder comments have been adequately considered and responded to. The panel includes members from the following perspectives: primary care, secondary care, lay, public health and industry.

2011 Guideline Review Panel

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Ms Catherine Arkley
Patient and carer member

Dr David Gillen
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Mrs Fiona Wise

Chief Executive, Ealing Hospital NHS Trust

Dr John Young

Medical Director, Merck Sharp & Dohme

Appendix C: The algorithms

The quick reference guide (available from www.nice.org.uk/guidance/CG117/QuickRefGuide) contains algorithms on:

- infection control
- testing and treating asymptomatic children aged 4 weeks–2 years who are close contacts of people with sputum-smear-positive TB
- testing and treating asymptomatic household and other close contacts of all cases of active TB
- screening new NHS employees.