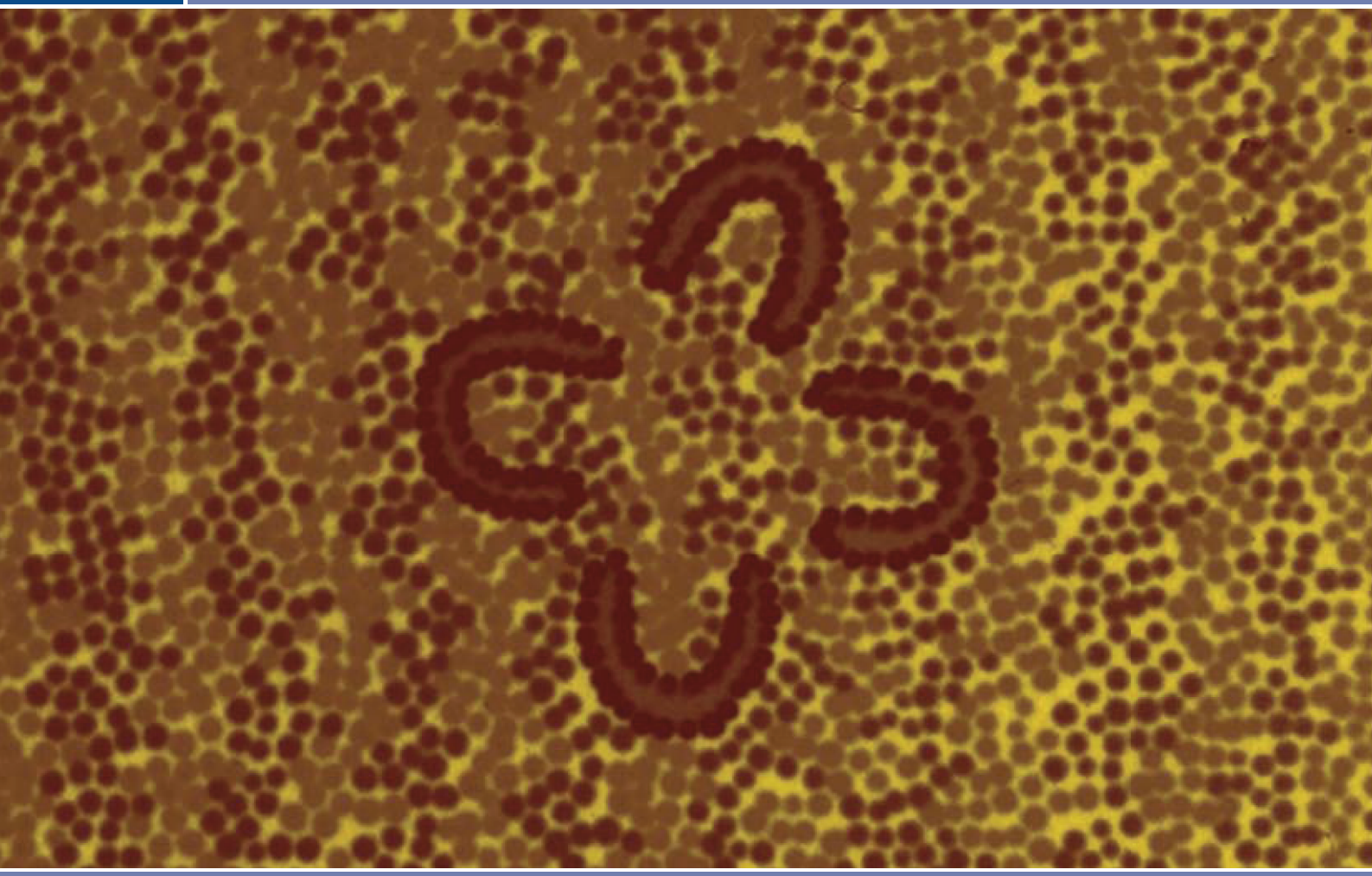
Northern Territory Government

DEPARTMENT OF **HEALTH AND COMMUNITY SERVICES**



CENTRE FOR DISEASE CONTROL

Guidelines for the control of Tuberculosis
in the Northern Territory

4th Edition
June 2008

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The graphic on the cover is taken from the
Australian Respiratory Council's flipchart "What is TB?".

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ABBREVIATIONS AND TERMS USED IN THESE GUIDELINES

ACS – Australian Customs Service
AEFI – Adverse event following immunisation
AFB – Acid fast bacillus
ASH – Alice Springs Hospital
ALT – Alanine aminotransferase
BCG – Bacille Calmette Guérin vaccine
CDC – Centre for Disease Control
CNS – Central Nervous System
CSF – Cerebrospinal fluid
CXR – Chest X-ray
DIAC – Department of Immigration and Citizenship
DMO – District medical officer
DOT – Directly observed therapy
DST – Drug susceptibility testing
FBE – Full blood examination
FNA – Fine needle aspirate
GFR – Glomerular-filtration rate
HIV – Human immunodeficiency virus
HRN – Hospital record number
ICU – Intensive care unit
IFF – Illegal foreign fisherpersons
IGRAs – Interferon gamma release assays
LFT – Liver function tests
LTBI – Latent tuberculosis infection
MAC or MAIC – *Mycobacterium avium – Mycobacterium intracellulare* complex,
MDR – Multi-drug resistant
MDR-TB – Multi-drug resistant tuberculosis
MOTT – Mycobacterium other than tuberculosis
MTB – Mycobacterium tuberculosis
NAAT – Nucleic acid amplification test
NGT – Nasogastric tube
NIDF – Northern Immigration Detention Facility
NMSS – National Mycobacterial Surveillance System
NNDSS – National Notifiable Disease Surveillance System
NTM – Non-tuberculous mycobacteria
NT – Northern Territory
PCR – Polymerase chain reaction
PPD – Purified protein derivative (also known as tuberculin)
RDH – Royal Darwin Hospital
RFLP – Restriction fragment linked polymorphism
RR – Relative risk,
Rx – Treatment
SA – South Australia
TB – Tuberculosis
TNF – Tumour necrosis factor
TST – Tuberculin skin test, also referred to as a Mantoux test
UEC – Urea, electrolytes and creatinine
WA – Western Australia
XDRTB – Extensively drug resistant TB
ZRE – Pyrazinamide/Rifampicin/Ethambutol.

WHAT'S NEW IN THIS VERSION OF THE GUIDELINES?

The last version of these guidelines was produced by the Northern Territory Centre for Disease Control in 2002. The 2008 edition has been updated to reflect more recent contributions to the field of TB control and also includes some changes to practice that have evolved through discussion among members of the NT TB Control Units and other interested parties. Major changes are summarised in this section and are explained in detail throughout the chapters.

The use of nucleic acid amplification tests (NAAT) in the diagnosis of tuberculosis (Chapter 2)

These tests can be used to rapidly determine whether a patient's specimen contains *Mycobacterium tuberculosis*. This should be considered a supplemental test and does not replace smear microscopy or culture. Its use should be a decision between the treating clinician and the pathologist.

The dosages of isoniazid for treatment in children and in 3 X weekly recommendations have increased as has the ripampicin 3 X weekly dose. The maximum doses of pyrazinamide and ethambutol in the 3 weekly dosage regimen have been increased (Chapter 4)

Drug doses take into account the *Therapeutic Guidelines: Antibiotic, Version 13, 2006* and the American Thoracic Society, CDC, Infectious Diseases Society of America, *Treatment of Tuberculosis Guidelines* 2003. The earlier Guidelines more closely followed the WHO recommendations.

Ethambutol can be discontinued once the organism is known to be sensitive to isoniazid and rifampicin even if this is prior to 2 months (Chapter 4)

Ethambutol is used in the intensive phase of treatment to prevent the emergence of drug resistance before sensitivities are known. In situations where isolates are fully sensitive this can then be stopped.

Multidrug-resistant TB (MDR-TB) (Chapter 4)

MDR-TB is defined as high level resistance to both rifampicin and isoniazid, with or without additional drug resistance. The general principles involved in treating MDR-TB are covered.

Management of relapse and treatment failure and smear negative/culture negative pulmonary TB (Chapter 4)

These 2 new sections have been added to the Treatment of Tuberculosis chapter.

Latent Tuberculosis Infection (LTBI) – Diagnosis (Chapter 6)

This chapter, previously titled Mantoux (Tuberculin) Testing, has been expanded to include information on Interferon-gamma Release Immunoassays (IGRAs). IGRAs are not currently recommended for use in Australian TB programs and further clinical and economic evaluation is required before further recommendations for their use can be made. An overview of the test, its indications and interpretation is provided.

An overview of Heaf testing has also been provided for reference and use in clients coming from the UK.

Dual skin testing is no longer available (Chapter 6)

Dual skin testing was used in an attempt to distinguish true tuberculosis infection from sensitisation due to non-tuberculous mycobacteria (NTM). The test involved testing with both PPD-human and PPD-avian at the same time in opposite arms. PPD-avian is no longer available.

Lifetime Risk of Reactivation Tuberculosis (Chapter 7)

The lifetime risk of reactivation table now included in this chapter, gives an estimation of the risk of developing tuberculosis on the basis of Mantoux test size, age, recent conversion of skin test and other risk factors. It can be used as a guide to decision making regarding treatment of LTBI.

Treatment regimens and doses for LTBI (Chapter 7)

The dosage of isoniazid for treating children (defined as <12 years) for LTBI has increased to 10-15mg/kg daily and 15-20mg/kg when given thrice weekly - more in line with the *Therapeutic Guidelines: Antibiotic, Version 13, 2006* and American Thoracic Society and Centres for Disease Control and Prevention Guidelines, 2000.

Short-course rifampicin based regimens for the treatment of LTBI (Chapter 7)

Rifampicin alone, given daily for 4 months can be an alternative for the treatment of LTBI where isoniazid use is contraindicated or not appropriate. This regimen should only be prescribed and monitored by senior staff of TB Control Units.

Changes to School Screening (Chapter 10)

The recommendations for school screening have been changed and are based on data that shows primary outcome measures are best achieved in screening overseas-born students attending urban schools, Indigenous students in urban schools and students in communities where there has been a case of pulmonary TB in the previous 3 years (in certain communities in the previous 10 years). A CDC staff member should be involved in the school screening process.

Prisoners in Correctional Facilities and Detention Facilities (Chapter 10)

New flow charts have been added to this chapter and highlight the increasing workload of the Darwin TB Unit in relation to Illegal Foreign Fisherpersons (IFF). These figures set out clearly the procedures for health assessments of IFF and describe their ongoing management.

Updates or additions to the Appendices

Fine needle aspirate instructions have been made into an Appendix, the non-tubercuous mycobacteria (NTM) information has been updated as have the Fact Sheets. The Notification Form has been updated to incorporate current national and international enhanced data collection.

New Appendices include:

- Adverse events following immunisation (AEFI) form
- Emergency management of haemoptysis flowcharts
- Royal Darwin Hospital ICU protocol
- A list of Countries of High TB Prevalence.

1. INTRODUCTION

1.1. Transmission of infection

Tuberculosis (TB) is a communicable disease caused by bacteria of the 'tuberculosis complex group' (mainly *Mycobacterium tuberculosis* [MTB] and rarely *M bovis*, *M africanum* and *M microti*). The infection is transmitted from one person to another through invisible droplet nuclei which are generated when someone with active TB of the lungs or larynx coughs, sneezes, spits, laughs or talks. Active TB may also occur in sites outside the airways but transmission does not occur from these sites or is very uncommon (eg. discharging wounds or abscesses). Transmission is relatively inefficient (in comparison to highly contagious diseases such as measles and chickenpox) and depends on the infectivity of the source case, as well as the amount of time spent in contact with others and the environment in which contact occurs. Conditions such as overcrowding in poorly ventilated enclosed spaces that are not exposed to sunlight (which kills MTB bacilli) greatly enhance the risk of transmission.

M bovis (acquired directly or indirectly from cattle) has historically been a significant cause of TB. When ingested in milk containing large numbers of organisms, *M bovis* may penetrate the gastrointestinal mucosa or invade the lymphatic tissue of the oropharynx. Human infection with *M bovis* has been largely eliminated in developed countries as a result of milk pasteurisation and bovine TB control programs.

1.2. Latent TB infection (LTBI) and active disease

Following inhalation of a sufficient number of organisms, MTB bacilli can multiply in the lungs. Spread from the small airways of the lungs through local lymphatic channels to regional lymph nodes and then through the bloodstream to distant sites can also occur. In most people, MTB triggers an immune response that contains the infection at this stage without evidence of active disease though live but dormant bacilli may persist for many years known as latent TB infection (LTBI). This immune response can be detected by the Mantoux test (also referred to as a tuberculin skin test (TST) or Interferon-gamma Release Immunoassays (IGRAs). In some people, especially young children or those with underlying diseases that decrease immunity, the infection may overcome this initial immune response and progress immediately to active TB (progressive primary disease). The risk of reactivation of LTBI into active disease is highest in the first 2 years and averages about 10% over a lifetime (thus up to 90% of infected people may live with LTBI throughout their lives without symptoms and without risking transmission of MTB to others). The risk of reactivation is increased if other diseases or conditions develop which decrease immunity (such as diabetes, chronic renal failure, HIV infection, malnutrition or alcoholism).

1.3. Epidemiology

It is estimated that over one third of the world's 6 billion people are infected with MTB and that over 9 million new cases of active TB occur annually with 2-3 million deaths, making it the leading cause of death from a single infectious organism. In parts of the developed world, the steady decline in the incidence of TB over the past century has recently ceased or even reversed. This resurgence has been attributed to a combination of the deterioration of specific TB control programs, the HIV epidemic, immigration from countries where infection is highly prevalent, emergence of multi-drug resistant strains, rising poverty, and homelessness and overcrowding among urban populations. In 1993 the World Health Organization declared that TB was a global emergency and in 2006 a Global Plan to Stop TB 2006-2015 was introduced.

Australia has one of the lowest incidence rates of TB in the world with rates remaining stable at approximately 5-6 cases per 100,000 since the mid 1980's. In 2005, 86% of notifications were in overseas-born people with an overall notification rate of 20.6 per 100,000 in this group. The rate in Indigenous Australians was 5.9 per 100,000 and in non-Indigenous Australians, 0.8 per 100,000. The notification rate in the Northern Territory (NT) in 2005 was 13.3 per 100,000.

The level of acquired drug resistance in Australia remains low with 9.1% of isolates resistant to at least one first line anti-TB drug and 1.5% of isolates being multi drug resistant (MDR).

Each year there are between 20 and 30 new cases of active TB notified in the NT. Approximately 60% of these occur in Aboriginal persons, 30% in migrants and 10% in the remainder of the community. Rates over the past 12 years have been on average about 20 cases per 100,000 population. Notification rates are similar in overseas born and Aboriginal Territorians at approximately 40 per 100,000 population which is about 10 times the rate in other Territorians. About half of the NT cases occur in people aged 15-44 years. The spectrum of disease in the NT is similar to that in other populations, with approximately 70% of new cases due to pulmonary TB and the most common cause of extra-pulmonary disease being lymphadenitis.

1.4. TB control

There are a number of reasons to believe that TB can be controlled or even eliminated.

- While TB does occur in animals (eg. cattle and primates) essentially it is a disease that mainly affects humans and must be transmitted directly from person to person for new cases of disease to occur.
- Modern diagnostic methods enable accurate diagnosis, and infection control measures can reduce transmission of infection by people with active disease.
- People at highest risk of LTBI can be identified through epidemiological investigation and contact tracing followed by Mantoux testing (even allowing for the limitations of this test).
- Both LTBI and active TB are curable with current anti-TB drugs that are relatively cheap and readily available.

The cornerstones of TB control in developed countries are therefore the early detection of active TB followed by curative treatment and identification of those with LTBI for treatment and prevention of later progression to disease. This requires extensive cooperation between public health authorities and clinical medicine practitioners to detect those who will benefit from treatment and provide the support necessary to enable completion of the treatment courses. The infrastructure and methods required to achieve these aims in the NT will be outlined in the following chapters.

1.5. TB Control in the NT

In the NT, Centre for Disease Control (CDC) Units in regional areas are responsible for TB control activities. These units are situated in Darwin, Katherine, Alice Springs, Tennant Creek and Nhulunbuy. Each unit is responsible for all activities including screening, case management, contact tracing and disease notification.

1.5.1. Central Australian TB control strategy

Alice Springs, through a tristate initiative, is also responsible for the delivery of TB control activities to bordering areas of South Australia (SA) and Western Australia (WA). In the situation where a new case is detected the cases are notified in the state or territory where they are diagnosed but management is provided and coordinated by the Alice Springs TB Control Unit. Reporting of

outcomes is communicated regularly to the state or territory notifying the case and in the instances where community screens are required a collaborative approach will be negotiated.

1.5.1.1. The Central Australian TB Control Unit

The Central Australian TB Control unit is based in the CDC Alice Springs.

Its main roles are the:

- coordination of the Central Australian TB Strategy
- provision of clinical expertise (a central chest clinic) for TB diagnosis and disease management utilising Alice Springs Hospital (ASH) based physicians and TB Control CDC Darwin (Central Australian standard treatment protocols will be used for management of disease and infection)
- organisation and provision of TB medications.

The Central Australian TB Control Unit will assist community staff to ensure treatment compliance by:

- provision of resources and/or coordinating activities for contact tracing and community screening
- provision of resources and expertise for ongoing TB education and in-services (eg. procedural training such as Mantoux testing, Bacillus Calmette Guérin (BCG) administration, contact tracing protocol, etc)
- provision of health promotion resource materials (eg. videos, pamphlets, treatment cards, etc)
- provision of and/or collation of effective and meaningful recording and reporting of the following items mentioned under 1.5.1.2 below.

1.5.1.2. Notification aspects in the Tristate area

To prevent duplication of notifications at a national level the National Notifiable Disease Surveillance System (NNDSS) notification procedures are followed. Cases will be notified according to State or Territory where the diagnosis was made. This will extend to the National Mycobacterial Surveillance System (NMSS) via the NNDSS*.

A patient diagnosed in one State/Territory (eg. SA) but being treated in another State/Territory (eg. NT) will have the national notification remain as above, but the patient will be listed in a special field as a ‘Transfer in’ to the State/Territory of the treatment centre. This is to reflect the treatment centre as the place of TB Control work, ie., contact tracing, directly observed and recorded treatment, drug dispatching and overall responsibility. These cases can be identified in State/Territory notifications to reflect work, effort and cost but clarification should be made as to why the numbers differ from the NNDSS and NMSS.

A copy of the notification will be sent to the State or Territory of residence to provide or complete the epidemiological picture for each region and include:

- monthly compliance/treatment completion
- Mantoux test results
- contact tracing/community screening reports
- school screening results
- health care staff occupational screening results
- liaison with TB Control Units in SA and WA, providing a minimum of 3 monthly reporting of status of active cases and other summary reports.

* The NNDSS is reviewing the procedural process for national consistency and resident address may now be as considered as the basis for national notification with a decision forthcoming in 2009.

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2. DIAGNOSIS OF TB

2.1. Sites of presentation of TB

- ~70% of cases are pulmonary
- ~30% of cases are extra-pulmonary including
  - nodal
  - urogenital: ie. renal, bladder, genital tract
  - skeletal: commonly spine and hip
  - meningeal
  - miliary: ie. disseminated TB
  - serous membranes: pleurisy, pericarditis, peritoneal
  - almost any other site (eg. eye, breast)

2.2. Symptoms and signs

- cough with sputum for more than 2-3 weeks +/-haemoptysis
- fevers
- night sweat
- weight loss
- lethargy and tiredness
- chest pain
- localised chest signs in upper/mid zones
- enlarged matted lymph nodes, usually non-tender and most commonly around head and neck

2.3. Medical conditions which increase risk of TB activation

- diabetes
- alcohol abuse
- chronic renal disease
- immune compromising malignancies (lymphoma, leukaemias, etc) and head and neck cancers
- immune suppressive therapy, including prolonged corticosteroid therapy (equivalent to prednisolone 25mg daily for ≥2 weeks), tumour necrosis factor (TNF) antagonists eg. adalimumab (Humira) and infliximab (Remicade)
- HIV infection
- malnutrition
- silicosis

2.4. Differential diagnosis

- melioidosis
- lung cancer
- non-tuberculous mycobacterial (NTM) infection
- bronchiectasis
- aspiration pneumonia and lung abscess

- other pneumonias: *Staphylococcus aureus, Klebsiella*, Varicella-Zoster virus (chickenpox), *Pneumocystis jirovecci*
- fungal infections: cryptococcosis, aspergillosis, histoplasmosis
- allergic aspergillosis
- allergic bronchpulmonary aspergillosis
- pneumoconiosis
- actinomycosis/nocardiasis
- sarcoidosis

2.5. Diagnostic procedures

2.5.1. General principles

- TB is a notifiable disease and new or suspected cases must be notified to the NT CDC as soon as they are diagnosed to enable contact tracing to begin.
- Diagnostic specimens should be collected before starting treatment. Confirmation of the diagnosis is important as treatment for TB is long and drug side effects possible. Drug susceptibility testing of the patient's MTB isolate is essential for continuing the right treatment.
- Specimens should be transported to the laboratory without delay in leak-proof sterile containers. To prevent general bacterial overgrowth (as many specimens will contain normal bacterial flora), specimens should be refrigerated if transport to the laboratory is likely to take longer than 1 hour.
- Diagnosis of extra-pulmonary TB often requires biopsy or fine needle aspiration (FNA) of the infected site to obtain material for culture and for histopathological/cytological confirmation and should not be delayed. Biopsy specimens should be submitted to the laboratory in a dry container or with a maximum of 5 mL normal saline but **never in formalin** as this will kill viable MTB organisms.
- The use of specialised laboratory tests (including nucleic acid amplification testing (NAAT) techniques, such as PCR) for the diagnosis of TB should be discussed on a case by case basis with an expert in the management of TB. These tests are not routinely carried out currently in the NT and require approval by a specialist medical/clinical microbiologist.

2.5.2. Chest X-ray

- Should be ordered for all patients with suspected TB whether the primary site is pulmonary or extra-pulmonary (as the 2 forms of disease may coexist and there are infection control implications associated with pulmonary TB).
- Most common radiological features of pulmonary diseases in adults are fibro-nodular infiltrates with indistinct margins occurring in 1 or both upper lobes or the apices of the lower lobes. This may also be associated with volume loss and cavitation.

2.5.3. Sputum collection

- 50-80% of adults with symptomatic pulmonary TB will be smear-positive on microscopic examination of their sputum and >80% will be culture positive.
- A patient suspected of having pulmonary TB should have 3 sputum samples collected, including a spot sputum, and at least 1 early morning sample. These should be collected on 3 consecutive days.
- Care should be taken not to infect others when collecting sputum. Samples should be collected in a well ventilated place, either outside if in the community, or in negative pressure isolation rooms in hospital. Sputum MUST NOT be collected in bathroom or toilet areas.

- The specimens should be collected into sterile screw-top plastic containers (eg. yellow-lidded universal collection containers) for AFB (acid fast bacilli) smear and culture.
- Routine microscopy and culture for other bacterial pathogens need only be ordered on the first specimen in most cases. Culture for *Burkholderia pseudomallei* (melioidosis) should be considered in the Top End and other infections including those caused by cryptococcus, other fungi and nocardia should also be considered particularly if the patient has other co-morbidities or is immunosuppressed. Cytopathology should be requested if lung cancer is part of the differential diagnosis.
- The patient should be instructed to place their lips inside the edge of the collection container to avoid contaminating the outside of the container.
- A good sputum specimen is one which covers the bottom of the specimen container and contains very little saliva; eg. it should stick to the bottom of the container when tipped upside down. A volume of >5 mL is preferred.
- Sputum should be placed in a BioHazard Bag. The BioHazard Bag should form the secondary biological containment after the specimen container itself. The sample should be stored in the refrigerator until transport to the appropriate laboratory can occur.
- Patients, who are unable to cough, including children, may be able to produce an induced sputum or may require gastric aspirate or bronchoscopy for accurate diagnosis.
- Induced sputum involves aerolisation of hypertonic saline. This process should be carried out by qualified personnel using appropriate respiratory protection.
- Induced sputum has a sensitivity of 90%.
- Induced sputum and sputum collected at bronchoscopy must be clearly labelled as they are processed differently to spontaneously collected sputum by the laboratory.
- It is worthwhile collecting 2 more daily sputum specimens following bronchoscopy as the procedure itself may increase the yield of positive results.
- Please ensure request forms are correctly completed and relevant clinical information is included.

2.5.4. Fasting gastric aspirates

- May need to be collected from children and adults who can not produce sputum
  - Gastric aspirate has a sensitivity of 77%, similar to that of bronchoscopy.
  - Gastric aspirates contain sputum swallowed during the night.
  - Ideally collected in hospital early in the morning while the person is still in bed, as activity will promote peristalsis that empties the stomach contents.
  - 50 mL should be aspirated from a naso-gastric tube (NGT) by syringe and then emptied into a sterile container. If little or no aspirate is obtained and it is confirmed that the NGT is properly located, then small volumes (20-50 mL) of normal saline may be introduced through the NGT and re-aspirated.
  - Stomach acidity must be neutralised with 4% sodium hydroxide (NaOH) ideally **within 30 minutes of collection.**The lab should be notified of collection and specimens should be transported to the lab immediately.
  - A particulate filter mask must be worn by health workers carrying out this procedure (Chapter 3).

2.5.5. Fine needle aspiration of lymph nodes

Treatment of presumed tuberculous lymphadenitis should not be started until an adequate tissue specimen has been obtained for smear, histology and culture. NTM are another common cause of persistent lymphadenitis and require different treatment from TB. FNA (see Appendix 1) should only be performed by a doctor with procedural experience.

Hospital pathology departments and private pathology laboratories also provide this service.

Excisional biopsies of lymph nodes may also be carried out to confirm diagnosis. It is important that the specimen is not placed in formalin.

2.5.6. Body fluids

- The effusions and ascites of patients with pleural, pericardial and peritoneal TB should be examined but typically contain few organisms, are smear-negative and often culture negative. Biopsies are usually required to establish a diagnosis.
- At least 5-10mL of cerebrospinal fluid (CSF) should be collected from patients with suspected TB meningitis to increase the chance of a positive culture.
- Simultaneous collection of serum for protein and glucose determination is essential when submitting body fluids or CSF to the laboratory.
- The usual findings in body fluids and CSF are non-specific and include protein ≥50% of serum value, low glucose and lymphocytosis/monocytosis.
- **Urine** – Early morning first void urines are the best specimens. Large volumes (>40 mL) over 3 consecutive mornings are preferred to increase yields. Urine is not examined microspically but set up for culture.
- **Pus** – As much pus as possible should be aspirated from discharging wounds and abscesses and submitted to the laboratory in a sterile container. Appropriate infection control procedures must be followed to prevent aerosolisation and inhalation of infected material (Chapter 3). Swabs of pus have a much lower positive yield than directly aspirated specimens and will be often be rejected by pathology departments.
- **Faeces** – If TB of the bowel is suspected, stool specimens for AFB (typically 5-10 mL/sample) can be obtained. Culture only is performed on stool samples. It is advisable to liaise directly with the laboratory.

2.5.7. Mantoux test - also referred to as a tuberculin skin test (TST)

This may be an aid to the diagnosis of active TB especially in children. However, a negative Mantoux test does not exclude clinical disease. Up to 20-30% of patients with active TB will be Mantoux test negative and a positive Mantoux test may be indicative of asymptomatic infection without disease. If a definitive microbiological diagnosis has been made, a Mantoux test should not be done. Advanced HIV will also cause increased anergy, and a false negative result. Recent observations have suggested that kava abuse may be associated with Mantoux test anergy (false negativity).

2.5.8. Rapid Diagnostic Tests

Nucleic acid amplification tests (NAAT) can be used to rapidly determine whether a patient's specimen contains *Mycobacterium tuberculosis*.

- False positive and false negative result do occur and depend on the quality of the specimen submitted as well as the nucleic acid copy numbers present in the specimen.
- NAAT is a supplemental test and does not replace smear microscopy or culture.
- The decision to perform a NAAT is a decision between the treating clinician and the pathologist.
- NAAT can be considered in smear (AFB) positive specimens when it is likely to influence clinical and/or public health decisions and in smear negative specimens with a high probability of TB when a prompt management decision is necessary.
- NAAT can be used in selected non-respiratory specimens (eg. CSF, tissue biopsies) also when a prompt management decision is required. It needs to be recognised that testing in these instances has not been fully validated.

2.6. Diagnosis of TB in children

- Active TB in children is usually a result of progression of initial infection within weeks to months of contact with an infectious adult rather than reactivation of latent infection. Extra-pulmonary disease is more common than in adults.
- The most common **chest X-ray** findings are hilar and mediastinal lymph node enlargement (often best seen on a lateral chest X-ray). These may obstruct air passages resulting in segmental hyperinflation or collapse. Parenchymal changes may occur but cavitation is rare prior to adolescence.
- **CT scanning** of the chest may be useful in children to assess hilar lymphadenopathy.
- The rates of positive cultures for MTB are reduced compared to adults as the bacterial burden is much lower in children and production of sputum may be difficult in childhood.
- In children with suspected pulmonary TB, 3 properly collected gastric aspirates (which contain sputum swallowed overnight) can produce culture-positive rates of 30-50% (up to 70% in children <2 years of age). Bronchoscopy adds little to the yield from well collected gastric aspirates.
- A highly positive Mantoux test or interferon-gamma release assay (IGRA) blood test may provide useful information in children when diagnostic specimens are difficult to obtain. This may provide enough evidence to start treatment in a child with a compatible clinical picture and a history of contact with an infectious adult. In this case obtaining the adult case's drug susceptibility results is essential to guide treatment.

2.7. Diagnosis of TB in HIV-positive patients

- Patients with HIV may present with early progression of primary infection after a recent contact or with reactivation of LTBI - in which case the risk of disease may be as high as 10% per year rather than the 10% per lifetime commonly quoted in healthy adults.
- The clinical spectrum is vast and is primarily dependent on the level of immunosuppression. HIV patients without advanced immunosuppression are more likely to present with the typical features described for adults (above).
- Advanced immunosuppression is associated with an increased likelihood of extra-pulmonary (and disseminated) disease and pulmonary disease is more likely to have either a florid (eg. pneumonic) or subtle (eg. normal chest X-ray, negative sputum smear) presentation. Cavitation depends on a robust immune response so is rare in advanced HIV.
- Blood cultures (3 in total from 3 separate days) should be collected from HIV patients with suspected TB into specialised mycobacterial culture media (MycoF®) and incubated at 37°C as soon as possible after collection and not refrigerated.

2.8. Non-tuberculous mycobacteria (NTM)

These are mycobacteria other than those belonging to the "tuberculosis complex group" and are sometimes referred to as "atypical mycobacteria" or "mycobacteria other than TB (MOTT)". There are a number of species of NTM, *Mycobacterium avium-M intracellulare complex* (MAIC) and *Mycobacterium kansasii* are more likely to cause pathological disease in humans, although infection with the latter is infrequent in the NT. Other NTM include *M scrofulaceum*, *M xenopei*, and *M fortuitum/chelonei* complex. Some NTM tend to cause disease more in lungs, and others more in nodes. Presently there are a large number of atypical mycobacteria identified (see Appendix 2). For further information refer to the NT CDC *Guidelines for the Control of Nontuberculous Mycobacteria in the Northern Territory*.

Points to note

- NTM are environmental organisms, usually found in the soil or water.
- NTM, are sometimes grown in sputum cultures, but they usually have no pathological significance in immune competent people.
- NTM are more likely to cause clinical disease in people over the age of fifty years, people with chronic lung disease, or in people whose immunity is compromised, eg. HIV positive patients. Therefore, HIV testing should be considered for all people presenting with clinical disease due to NTM.
- Exposure to high levels of NTM will result in some response to a Mantoux test as a result of cross reaction with tuberculin antigen. This can make interpretation of Mantoux tests difficult in some cases and may justify the use of IGRA blood tests if risk factors for *M tuberculosis* are low.
- NTM can colonise within other inflammatory pulmonary lesions. Therefore in a patient who has a clinical picture of TB, initial growth of NTM does not exclude coexisting TB.
- The radiological features of NTM can be the same as those of TB.
- Diagnosis of pulmonary disease due to NTM requires isolation of the same species of NTM at least 2 times (3 preferable) over a period of time (2 to 3 weeks), and evidence of clinical or chest X-ray progression of disease.
- Diagnosis and treatment of patients with pathological infection with NTM is complex and difficult and requires referral to a specialist.
- Pathological infection with NTM is a notifiable disease in the NT (refer to the *Guidelines for the Control of Nontuberculous Mycobacteria in the Northern Territory*).

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3. INFECTION CONTROL

TB is transmitted via invisible airborne droplet nuclei generated when a patient with infectious pulmonary or laryngeal TB coughs, sneezes, spits, laughs or talks. Infectivity is increased in patients who are smear-positive on sputum examination and/this often occurs when cavitation is seen on chest X-ray. Spread can be dependent on the length of exposure. Normal air currents can keep infectious particles suspended for prolonged periods of time (eg. up to 4 hours) and spread them throughout a room or building. TB is usually transmitted only through air, not by surface contact.

Following basic infection control procedures when a case of pulmonary TB is suspected reduces the spread of MTB to others. Extra-pulmonary TB is not associated with transmission of infection provided that measures are taken to prevent aerosolisation of infected material, such as pus from discharging wounds or abscesses.

3.1. Infection control in a community setting

- Patients with pulmonary TB are potentially infectious and special care must be taken to prevent transmission of infection to contacts and health personnel.
- Because TB is uncommon and the symptoms vary, health care workers in a primary care setting need a high index of suspicion for TB. An important clue is persistent symptoms, especially a cough for longer than 2-3 weeks or that persists after antibiotic therapy.
- From the time that pulmonary or laryngeal TB is first suspected, the patient should be educated about the mechanisms of TB transmission and taught to cover their mouth and nose with tissues when coughing or sneezing.
- Patients with suspected TB should be given a specimen container and asked to go outside into the fresh air away from other people to produce sputum specimens (Chapter 2).

3.2. Transport of patients with known or suspected TB

- Advice on transport of patients with known or suspected TB from their home to hospital can be obtained from the district medical officer on call for the region (through the local hospital switchboard) or by calling the regional TB Control Unit. Appendix 3 contains the NT Aerial Medical Service policy on transporting suspected TB patients.
- People with suspected active TB should only travel by air on commercial aircraft if known to be smear negative on 3 adequately collected sputum smears (Chapter 2).
- Patients who are smear-positive or whose sputum smears have not yet been examined should wear a mask during transport and only travel by air with an air medical service, preferably without other patients on board.
- Road travel should be undertaken with masks on and windows down to promote maximum ventilation.

3.3. Infection control in hospital

All patients with suspected or confirmed infectious TB who are admitted to hospital should immediately have appropriate isolation precautions initiated. They should be managed in an area of the hospital separate from patients with HIV or other forms of immunosuppression. Immune-compromised staff should not work on wards where there are cases of TB. Respiratory isolation procedures, as outlined in the hospital's infection control policy, should be strictly followed and any

breaches immediately reported to infection control personnel. Patients with non pulmonary disease who require admission do not require isolation as long as pulmonary infection has already been ruled out.

3.3.1. Emergency department management

The key to limiting transmission of MTB to other patients and staff in the emergency department is the rapid recognition of clinical features that are associated with active pulmonary TB. Pulmonary TB should be suspected when a patient from a high risk group presents with signs and symptoms consistent with the diagnosis (Chapter 2) or when someone from a lower risk group presents with typical features of TB. A chest X-ray is the most important test in deciding the likelihood that the clinical picture represents active TB and sputum for AFBs should always be collected to confirm the diagnosis. The flow chart "Suspected Pulmonary Tuberculosis Emergency Department Protocol" should be followed (p 13). If in doubt, the advice of experts in the management of TB and/or infection control staff should be sought.

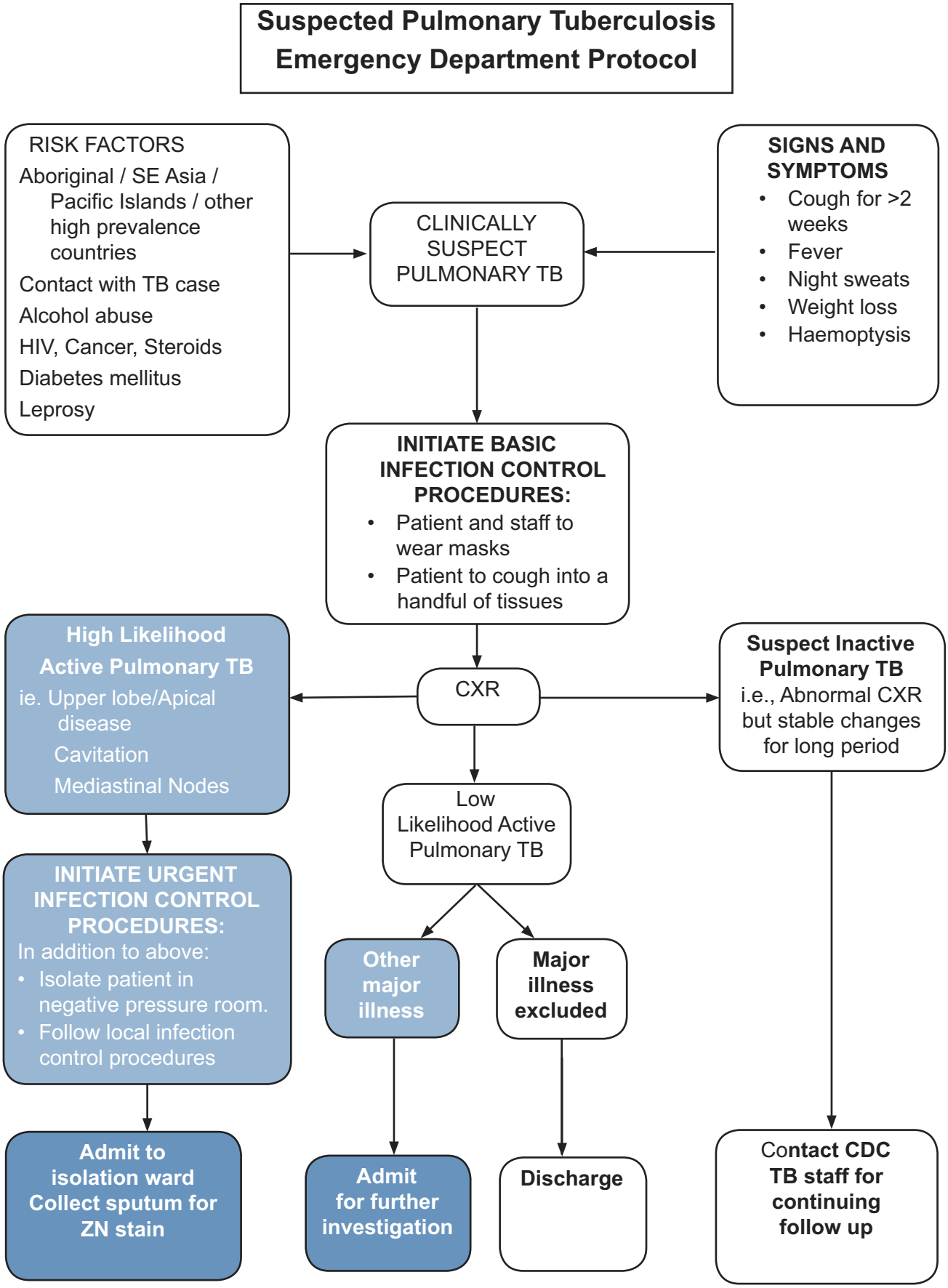
3.3.2. Patient isolation

- Suspected or confirmed pulmonary or laryngeal TB cases should be accommodated in a purpose-built, negative pressure isolation room which provides a minimum of 6 complete air exchanges per hour.
- Patients presenting to a hospital without such a facility may require transfer to a hospital where one exists (discuss with TB Control Unit; see Transport of Patients, above).
- Isolation may sometimes be required for patients with extra-pulmonary TB in whom aerosol generating procedures such as wound irrigation are required or until pulmonary TB has been reliably excluded.
- Patients in isolation should remain in their rooms with the door closed unless in transit, at which times they should wear surgical masks to cover their mouths and noses. Investigative procedures should be scheduled for times when they can be performed rapidly so that patients are not kept waiting out of negative pressure areas for long periods.
- Arrangements to spend time outdoors may be made on a case by case basis after discussion with nursing and medical staff, ensuring that staff, other patients or members of the public are not placed at risk.
- Children (other than the patient's own children or children living within the same household who have likely already been exposed) and immunosuppressed friends should be discouraged from visiting the patient until infectious TB has been excluded or treated.
- Visitors and staff entering the isolation room should wear particulate filter respirator masks ((N95) "duck bill" masks).
- Patients with confirmed or suspected active TB in Intensive Care Units should be treated the same as patients in non-critical care settings, ie. in a single negative pressure room. A suitable particulate filter should be placed in the expiratory circuit of mechanical ventilators.

3.3.3. Discontinuation of isolation

Isolation can be discontinued once the diagnosis of TB is excluded **or:**

- Where the diagnosis is confirmed **and** 3 consecutive clearance sputum smears (of adequate quality) collected over 3 separate days have been smear-negative for AFBs.
  - If initial diagnostic sputum is trace, 1+ or 2+ smear-positive for AFBs, then repeat sputum samples are collected a minimum of 2 weeks after commencement of treatment.


Suspected Pulmonary Tuberculosis
Emergency Department Protocol
RISK FACTORS
Aboriginal / SE Asia / Pacific Islands / other high prevalence countries
Contact with TB case
Alcohol abuse
HIV, Cancer, Steroids
Diabetes mellitus
Leprosy
CLINICALLY SUSPECT PULMONARY TB
SIGNS AND SYMPTOMS
Cough for >2 weeks
Fever
Night sweats
Weight loss
Haemoptysis
INITIATE BASIC INFECTION CONTROL PROCEDURES:
Patient and staff to wear masks
Patient to cough into a handful of tissues
High Likelihood Active Pulmonary TB
ie. Upper lobe/Apical disease
Cavitation
Mediastinal Nodes
CXR
Suspect Inactive Pulmonary TB
i.e., Abnormal CXR but stable changes for long period
Low Likelihood Active Pulmonary TB
INITIATE URGENT INFECTION CONTROL PROCEDURES:
In addition to above:
Isolate patient in negative pressure room.
Follow local infection control procedures
Other major illness
Major illness excluded
Admit to isolation ward Collect sputum for ZN stain
Admit for further investigation
Discharge
Contact CDC TB staff for continuing follow up

  - If initial diagnostic sputum is ≥3+ smear-positive for AFBs, then repeat sputum samples are collected after a minimum of 3 weeks after commencement of treatment.
  - When a patient says they are unable to produce sputum, at least 1 early morning specimen should still be attempted. If the patient is clearly not coughing and it is not possible to collect 3 specimens, then this should be clearly documented and specifically discussed with TB control unit.
- If the initial clearance sputum is still AFB smear-positive then repeat weekly until a negative smear is obtained, followed by 2 more smears over separate days.
- Induced sputums are not indicated to establish AFB clearance, regardless of whether or not this technique was used to make the diagnosis.

3.3.4. Recommended equipment for isolation rooms

- Outside the room – Particulate filter masks. If exposure to bodily secretions (eg. discharging wounds or abscesses) is expected, then other clean supplies, such as plastic aprons, gowns and disposable gloves may also be required.
- Inside the room – Dedicated thermometer, blood pressure cuff etc., garbage bag holder for infectious waste, linen trolley with lid.
- Routine use of crockery, cutlery and bed linen is acceptable as MTB is killed by normal machine dishwashing and laundering procedures.
- Although items contaminated with respiratory secretions are not normally associated with transmission of infection, linen and waste (other than crockery and cutlery) should be handled carefully and generally disposed of into an infectious waste bag or linen trolley within the room.
- Isolation rooms can be cleaned daily using the same procedures used elsewhere in the hospital with disposable cloths that are discarded as infectious waste. Cleaning staff should observe the same respiratory precautions as other staff when entering the room.

3.3.5. Cough and aerosol generating procedures

Aerosol-inducing procedures include:

- endotracheal intubation and suction
- diagnostic sputum induction
- bronchoscopy
- diagnostic aspiration or irrigation of tuberculous abscesses and wounds
- certain laboratory and autopsy procedures.

These procedures should only be performed by trained staff in appropriate isolation areas.

Following sputum induction, patients should remain in the isolation area until they have ceased coughing and should be instructed to cover their mouth and nose with a handful of tissues when coughing or sneezing.

3.3.6. Use of masks for infection control

Masks should be seen as an adjunct to the more important measures of prompt identification, isolation, treatment, and environmental controls.

Appropriately designed “duck-bill” masks incorporate a particulate filter material which has 99.5% efficiency against particles in the 0.3-0.5 micron range – these are also known as “sub-micron” or “particulate filter” masks. They are designed to effectively seal around the face and must be adjusted carefully to ensure this occurs.

"Duck-bill" style masks should be worn by those who are at risk of inhaling infectious droplet nuclei, ie. staff and visitors sharing the same air space as patients with infectious pulmonary TB, whether in isolation rooms, during specimen collection or during transport.

Patients with suspected or known infectious pulmonary TB must wear a mask when not in negative pressure TB isolation rooms. Standard surgical masks are equally as effective as "duck-bill" masks for preventing aerosolisation of infectious droplet nuclei and may be preferred by patients. Either type of mask is suitable for this purpose

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4. TREATMENT OF TUBERCULOSIS (TB)

4.1. Overview

The overall goals of treatment for TB are to:

- cure the individual patient
- minimize the transmission of *M tuberculosis* to other people.

Short-course treatment of TB with multiple active drugs results in cure rates exceeding 98% at 6 months, provided that the MTB isolate is susceptible to all first line drugs and the patient completes the treatment. Rifampicin and isoniazid are given for the entire 6 months. Pyrazinamide (which promotes rapid sterilisation) and ethambutol (to prevent the emergence of drug resistance) are given for the first 2 months. Because ethambutol may affect vision, its use is restricted to adults and children ≥6 years who are able to report early visual symptoms (ie. detect colours in an Ishihara chart and perform acuity testing). Treatment of patients with TB is most successful within a comprehensive framework that addresses both clinical and social issues.

4.2. Aims of TB treatment

- decrease infectivity of TB as quickly as possible
- ensure a complete cure without relapse
- prevent the emergence of drug resistance
- minimise the adverse effects of treatment

4.3. Principles

The NT CDC coordinates the clinical and public health management of all cases of TB infection and disease in partnership with other health providers. TB is a notifiable disease which must be reported to the NT CDC as soon as the diagnosis is confirmed.

Patients with suspected or confirmed smear-positive pulmonary or laryngeal TB need to be placed in respiratory isolation until non-infectious (Chapter 3).

Every effort should be made to obtain adequate laboratory specimens (Chapter 2) to ensure the correct diagnosis is made and to perform drug susceptibility testing, as the treatment for drug-resistant strains is substantially different from that of fully sensitive strains.

An attempt to document bacteriological conversion of sputum smear and culture to negative should always be made. All patients should be monitored on a monthly basis during treatment (or more frequently if required) and reviewed following treatment.

Contact tracing should be performed on all smear (AFB) positive cases and consideration given to contact tracing of close contacts of culture postitive only cases (Chapter 8).

4.4. Initiation of treatment

A history of current medication use should be obtained prior to treatment starting and patients should be advised to tell other doctors they are taking anti-TB medication prior to taking any new drugs due to the possibility of drug interactions.

A history should also be taken looking for risk factors for hepatotoxicity including alcohol use, IV drug use, being a blood product recipient and being from high risk areas/countries for hepatitis.

Patients and their carers should be given the following advice prior to initiating anti-TB treatment.

- Education about TB disease, the benefits of treatment and importance of adhering to treatment. Translators should be used, when necessary, to maximise understanding and written material should also be offered (Appendix 4).
- Possible adverse effects of medications (p20 and Appendix 5).
- Not to drink alcohol at all while on treatment to minimise their risk of drug-related liver toxicity.
- For women, to avoid becoming pregnant until treatment is completed. Although anti-TB drugs are generally safe in pregnancy, the risks to the foetus from some drugs are less certain in the first trimester and there is an increased risk of drug-related liver toxicity in pregnant women.

4.4.1. Pre-treatment investigations

- diagnostic specimens for smear and culture
- chest X-ray
- LFTs, UEC, FBE, (also blood sugar and uric acid in adults)
- visual acuity (Snellen test) and an Ishihara test for colour blindness (if ethambutol used)
- baseline weight
- examination for leprosy in at risk patients (Aboriginal, or migrants from countries with high rates)
- screen for viral hepatitis if risk factors are present
- anti-HIV antibodies (after obtaining informed consent)
- HTLV-1* in Aboriginal patients (see Marinho J, et al and Verdonck K, et al, bibliography p28)

4.4.2. Directly observed treatment (DOT)

DOT administered by a trained health worker is the preferred method for administration of TB treatment in the NT and is defined as watching the patient swallow each dose of medicine. DOT enables adherence to be regularly monitored and allows treatment defaulters to be quickly identified. Administration of TB treatment by DOT is associated with reduced rates of drug-resistance and relapse following treatment. DOT is mandatory when TB treatment is given on an intermittent basis (ie. 3 times weekly) and for the treatment of drug-resistant TB.†

4.4.3. Drug regimens and doses

Anti-TB drugs are just as effective and have comparable toxicity profiles if given daily or in higher doses 3 times a week. The preferred regimen in the NT for treatment of TB disease is to give the medicines three times a week by DOT which is recorded on the treatment card (p 102) Dosages are calculated in mg/kg up to a maximum daily dose and may need to be recalculated for weight gain (especially in children) or weight loss during treatment. To maximise adherence and drug levels, all medication should ideally be given together in a single dose 30 minutes before breakfast. Pyridoxine (Vitamin B6) 25 mg is given, with the anti-TB drugs, to minimise neurological side effects that isoniazid may cause. The likelihood of drug-resistance (see below) should always be considered prior to initiating treatment for TB.

*HTLV-1 is a retrovirus endemic in some populations, including some indigenous Australian populations. There is a suggested association of HTLV-1 with TB disease. Standard TB treatment is adequate for clients co-infected with HTLV-1 and TB however the risk of HTLV-1 and treatment outcomes continue to be evaluated.

† A risk assessment performed on an individual can be used to assess whether a patient may be suitable for self administered treatment but they would still require regular, close contact with the treatment provider. Any one with a history of previous non adherence, homelessness, drug resistance, relapse, previous treatment for TB, alcohol or substance abuse, memory impairment of psychiatric illness would not be suitable for self-administered treatment.

Drug*	**Mon/Wed/Fri 3 x weekly dose**		**Daily Dose**		**Tablet formulation**
	dose mg/kg (range)	dose mg (maximum)	dose mg/kg (range)	dose mg (maximum)	mg
Isoniazid†	15	600	5 (adults 10 (children)	300	100
Rifampicin‡	10 (8-12)	600	10 (8-12)	600	150 300 600
Pyrazinamide	35 (30-40)	3000	25 (20-30)	2000	500
Ethambutol§	30 (25-35)	2400	15 (15-20)	1600	100 400
Pyridoxine Vit B6 **Adults** **(children 5-11yrs)** **(children <5yrs)**		1 tab ½ tab 5mg‖ - 6.25mg (¼ tab)		1 tab ½ tab 5mg‖ - 6.25mg (¼ tab)	25

* Drug doses have taken into account the *Therapeutic Guidelines: Antibiotic*, Version 13, 2006 and American Thoracic Society, CDC, Infectious Diseases Society of America, *Treatment of Tuberculosis* and to a lesser extent WHO/IUATLD guidelines.

† Isoniazid can be made into a suspension by crushing the tablets.

‡ Rifampicin is also available in intravenous (IV) formulation and as a suspension.

§ Ethambutol should be avoided if visual acuity cannot be accurately assessed (see below).

‖ For each 5mg pyridoxine dose, crush a 25mg tablet, makeup to 5ml with water, give 1 ml (see p159 *Therapeutic Guidelines: Antibiotic*).

Points to note

Standard short course treatment (assuming fully sensitive MTB isolate) is for 6 months with:

- rifampicin, isoniazid, pyrazinamide and ethambutol (in adults and children ≥6 yr) for the initial 2 months of intensive treatment
- rifampicin plus isoniazid for a subsequent 4 months continuation treatment
- ethambutol can be discontinued once the organism is known to be sensitive to isoniazid and rifampicin even if this is prior to 2 months
- pyridoxine (vitamin B6) is given for the full duration of treatment with isoniazid.

In certain situations prolongation of treatment is required. The first 2 months (intensive phase) remain unchanged, but the continuation phase treatment is given for longer eg.:

- In HIV negative patients who have both cavitation on initial CXR and are still culture positive at 2 months with a fully drug susceptible organism it is recommended to extend the continuation phase to 7 months. This is based on demonstration of relapse in this setting of almost 21% in patients receiving standard 6 month treatment.
- Extending the continuation phase in HIV positive patients and in some forms of extra-pulmonary TB (especially TB meningitis) may also be considered. Decisions should be made on an individual basis and under specialist guidance.
- If pyrazinamide cannot be used because of drug intolerance or contraindication (see section 4.5), then the minimum treatment duration is 9 months that includes rifampicin plus isoniazid, ie. 2 months with 3 drugs (including ethambutol initially until susceptibility results are known) and a

further 7 months of isoniazid and rifampicin. *M bovis* is naturally resistant to pyrazinamide, so is treated in this way for a minimum of 9 months.

The choice of drugs for the treatment of relapse must be individualised after considering the time that has elapsed from the initial diagnosis as well as the likelihood of resistance from previous incomplete or inadequate treatment regimens.

As rifampicin increases the metabolism of corticosteroids, TB patients taking corticosteroids for diseases other than TB should, in consultation with their treating doctor, double their dose of corticosteroids while on rifampicin.

4.4.4. Treatment of extra-pulmonary TB

Because there are usually fewer organisms present at extra-pulmonary sites than with pulmonary TB, and standard TB treatment has excellent tissue penetration, **6 months** of standard short-course treatment is adequate for most cases. Exceptions include TB meningitis which requires 12 months of treatment and for patients with TB at any site that is slow to respond to treatment.

In the early stages of treatment for **tuberculous lymphadenitis,** new nodes may appear or existing ones enlarge. This is relatively common and may be associated with the discharge of pus through a sinus to the skin, but this does not usually indicate treatment failure.

Corticosteroids are used as adjunctive treatment in certain situations provided the patient is on full dose anti-TB medications at the same time. The data is strongest for meningitis and pericarditis. Corticosteroids may also be used for selected cases with extra-pulmonary disease, including for large pleural effusions (to reduce acute manifestations and possibly reduce scarring and loss of lung volume); extensive mediastinal lymphadenopathy in children (to reduce obstructive manifestations); genito-urinary disease (to reduce ureteric strictures) and in some patients with severe, or disseminated, disease. Because the decision whether or not to use corticosteroids, for other than meningitis and pericarditis, is often a complicated one and the regimens used may be complex and differ in each setting, such treatment should only be prescribed and monitored by specialists in TB management.

4.4.5. Treatment of drug-resistant TB

Drug-resistance (ie. resistance to 1 or more of the first line drugs) may be present prior to initiating treatment or may emerge while on treatment if not on DOT or prior to drug susceptibility testing guidance. The likelihood of pre-existing drug-resistance can be difficult to predict but is increased in the setting of previous, often incomplete, treatment for TB; ie. in migrant groups from high prevalence countries where access to TB treatment is interrupted; and in contacts of a drug-resistant case. It is usually detected through routine drug susceptibility testing (DST), but may also be suspected on clinical grounds because of treatment failure in patients known to be adherent (eg. no improvement after 2 weeks of treatment or ongoing positive cultures after 2 months).

Stopping 1 or more drugs, especially early in treatment when AFB loads are highest, may in some instances also lead to the emergence of drug resistance. Other causes may include improperly prescribed drug regimens (eg. under dosing), malabsorption or rarely, reinfection with a drug-resistant strain while on treatment. Multidrug-resistant TB (MDR-TB) is defined as combined resistance to isoniazid and rifampicin and often involves other first line drugs. The incidence of MDR-TB is increasing worldwide, with the median prevalence being 1.2% and some countries recording levels as high as 23.4%.

Extensively drug resistant TB (XDR-TB) is now described in some parts of the world and is defined as MDR-TB with resistance to second line drugs including all fluroquinalones and 1 of the injectable agents.

The general principles for management of drug-resistant TB are:

- Patients with drug resistance should be under the care of a specialist physician.
- Patients should receive either hospital based or domiciliary DOT.
- A single drug should never be added to a failing regimen. At least 2, and preferably, 3 drugs to which the organism is likely to be susceptible should be added in this situation.
- Intermittent therapy should not be used in treating TB caused by drug resistant organisms.
- I**solated isoniazid resistance**, rifampicin plus pyrazinamide plus ethambutol for 9 months is usually adequate. A fluroquinolone may be added if disease is extensive. If isoniazid resistance is of an intermediate level, then there may be some benefit in continuing the drug.
- **Rifampicin resistance** is frequently combined with resistance to other drugs and treatment options vary - specialist advice should be sought. If isolated rifampicin resistance, isoniazid, ethambutol and a fluroquinalone should be used for 12-18 months with pyrazinamide used during the first 2 months.
- **Pyrazinamide resistance** is usually associated with *M bovis.* Isoniazid, and rifampicin should be used for the first 2 months (supplemented with ethambutol until susceptibility is known) then a further 7 months of rifampicin and isoniazid given.

4.4.5.1. Multidrug-resistant TB (MDR-TB)

MDR-TB is defined as high level resistance to both rifampicin and isoniazid, with or without additional drug resistances. The general principles involved in treating MDR-TB are:

- The initial regimen should include at least 4 new agents based on DST.
- The treatment should be given for at least 18 months beyond conversion and up to 24 months beyond conversion if disease is extensive.
- Drug administration should be for at least 6 days of the week and dosage should be determined by weight.
- An injectable agent should be used for at least 6 months with this being 4 months beyond sputum conversion.
- DOT should be used for all patients with MDR-TB.
- Sputum smears and cultures should be monitored closely throughout treatment. Conversion is defined as 2 consecutive negative smears and cultures taken 30 days apart. Cultures should be continued every 2 months after conversion.
- Second line drugs have more adverse affects then first line drugs and patients should be evaluated and managed promptly to increase adherence to drug regimens.

4.5. Drug side effects and interactions

Patients must be thoroughly educated about the possible side effects of anti-TB medications prior to initiating treatment and this should be reinforced at each follow up visit. The most essential piece of advice is that **patients must stop all medications and seek review immediately if they experience any adverse events while on treatment.**

4.5.1. Individual drug toxicities

- **Isoniazid.** Hepatitis is the most severe toxic effect. Alcohol consumption, liver disease and increasing age are associated with increased toxicity. Other side effects include nausea and vomiting, rash, peripheral neuropathy, CNS effects (eg. fatigue, drowsiness, headache, neuropsychiatric symptoms including depression) and a commonly recognised drug interaction with phenytoin which increases levels of **both** drugs. May cause acne (especially in SE Asian people).

- **Rifampicin.** Causes pink-orange discolouration of bodily secretions (ie. urine, sweat and tears) which may stain contact lenses but is otherwise harmless. Also causes gastrointestinal upset, hepatitis and drug-induced fever. Prolonged or unscheduled breaks in treatment can be associated with shock, acute-renal failure, thrombocytopenic purpura and haemolytic anaemia which are all contraindications to its reintroduction. Flu-like syndrome with myalgia, arthralgia, fever, malaise and mild haemolysis is also more common with intermittent use. Any reintroduction should be done in consultation with TB specialists. It decreases the level of many drugs, especially methadone, warfarin, corticosteroids, oral hypoglycaemics, anticonvulsants, dapsone, ketoconazole cyclosporin and drugs used for treatment of HIV infection. It should be used with caution in HIV-positive patients (expert advice is essential). Rifampicin can decrease the effectiveness of oral and injectable contraceptives (including implants), therefore other birth control methods should be used.
- **Pyrazinamide.** Arthralgias are common and can often be relieved with aspirin. Acute gout may also occur as pyrazinamide blocks the terminal excretion of uric acid. Therefore pyrazinamide should be avoided when there is a history of gout. It may be poorly tolerated because of gastrointestinal side effects, especially in older people. Like isoniazid, pyrazinamide is a relatively common cause of anti-TB drug related hepatitis especially in the elderly. The lowest drug dose in the range for weight should be used for the elderly. Other side effects include flushing, rash, photosensitivity and difficulty in diabetes control.
- **Ethambutol.** The most serious toxicity is optic neuropathy which may result in decreased visual acuity, red-green colour blindness or visual field losses. If it occurs, it is usually after a number of months and is dose-related, but may be reversible weeks to months after the drug is stopped. Patients on ethambutol should have their visual acuity and colour vision reviewed at each visit. Ethambutol causes cutaneous reactions more commonly than other first line anti-TB drugs and may cause anorexia.

Second line drugs used in the treatment of MDR-TB are associated with an increasing amount of adverse effects. Patients should be encouraged to report any abnormalities and direct questioning regarding adverse effects should occur on each review. Special monitoring may need to be implemented for those patients on MDR treatment depending on their drug regimens. Consultation with a specialist is required.

4.5.2. Management of common minor adverse events

- **Drowsiness** – give the drugs at bedtime rather than in the morning.
- **Mild skin itches** – anti-histamines.
- **Gastrointestinal intolerance** – treatment should be stopped until LFTs have been checked as this may be a sign of hepatotoxicity. In patients on standard, first line, multi-drug treatment, the most common cause of gastric irritation is rifampicin, followed by pyrazinamide, therefore.
  - Gastrointestinal symptoms should settle within 4 or 5 days of stopping the drugs. If not then another cause of the symptoms (eg. peptic ulcer) should be sought.
  - Initially changing the timing of the medication or administering the drug with food may settle the complaint. If not settling and the patient is on rifampicin, isoniazid, pyrazinamide and ethambutol, then the latter 3 drugs should be restarted first without rifampicin. If symptoms recur, then the likely cause is pyrazinamide, which may need to be omitted from a longer, modified regimen.
  - If these 3 drugs (isoniazid, pyrazinamide and ethambutol), are tolerated, then rifampicin should be re-introduced with a modified dosing schedule – such as starting at half dose and building up over 1-2 weeks, giving the rifampicin with a small meal and/or at bedtime. This approach is often successful but if symptoms of gastritis recur, then antacids may be trialled provided that they are given at least 1-2 hr after isoniazid (as they interfere with isoniazid absorption).

4.5.3. Management of abnormal liver function

- If the ALT rises to less than 3 times the upper limit of normal, then LFTs should be monitored weekly for 2 weeks, then 2 weekly until normal. Thereafter, they need only be repeated in the event of symptoms or if monthly testing was previously indicated (see section 4.6.2.).
- If the patient has symptoms of hepatotoxicity or the ALT rises to ≥3-4 times normal or the bilirubin rises, all medications should be ceased immediately. Consider testing for other causes of hepatitis such as hepatitis B and C or other viral causes of hepatitis.
- If the patient is not clinically unwell from TB, then wait until the LFTs return to baseline (pre-treatment) levels and then reintroduce medications as outlined below. If the patient's form of TB is infectious, then strict respiratory isolation will need to be maintained during this period.
- If the patient remains clinically unwell from TB then another form of drug treatment will need to be given as an inpatient. This will usually result in ethambutol being continued and streptomycin added at a dose of 15 mg/kg (to a maximum of 1 g) unless contraindicated or drug resistance known/suspected. This regimen should be continued until the ALT drops to below 3 times normal, and the bilirubin drops to below 2 times normal; then medications reintroduced as outlined below. The streptomycin can be ceased following the successful reintroduction of treatment.
- In patients with cirrhosis rifampicin and ethambutol, with moxifloxicin, gatifloxicin, or cycloserine, for 12-18 months can be considered.

4.5.4. Reintroduction schedule

The schedule below is based on the fact that ethambutol is very rarely hepatotoxic. Of the remaining drugs, the one least likely to cause hepatotoxicity, and also very important for early sterilisation of sputum and cure is rifampicin. LFTs should be checked daily during the reintroduction of medication, and second daily in the week following successful reintroduction.

	Ethambutol	Rifampicin	Isoniazid	Pyrazinamide
Day 1	Full dose*	75mg		
Day 2	”	150mg		
Day 3	”	300mg		
Day 4	”	Full dose*		
Day 5	”	”	50mg	
Day 6	”	”	100mg	
Day 7	”	”	Full dose*	
Day 8	”	”	”	250mg
Day 9	”	”	”	500mg
Day 10	”	”	”	Full dose*

* Full doses as per section 4.4.3.

If there is a further reaction during reintroduction of drugs, the offending drug should be stopped in favour of an alternative regimen. Pyrazinamide can be safely omitted from the regimen used for fully sensitive organisms provided that treatment is prolonged (refer section 4.4.3). If other drug(s) require exclusion, then an alternative regimen should be prescribed by a specialist in the management of TB.

4.5.5. Management of hypersensitivity to medication

Reactions usually occur within the first 2 months of treatment and most commonly involve rash (typically maculopapular, erythematous and itchy) and/or fever. Generalised reactions

may also include fever, rigors, headache, myalgia, peri-orbital oedema, lymphadenopathy, hepatosplenomegaly and transient jaundice.

4.5.5.1. Principles of management of drug hypersensitivity

All drugs should be stopped until the reaction has subsided.

No attempt should be made to reintroduce a drug that has been associated with exfoliative dermatitis, Stevens-Johnson syndrome or a severe systemic reaction such as hypotension, renal failure, thrombocytopenic purpura or severe haemolytic anaemia.

If the reaction was not severe, then a regimen for challenge dosing can be followed as below. This regimen starts with those drugs least likely to cause hypersensitivity reactions. If there is no reaction to the challenge doses, the full dose of the drug should be continued.

	Isoniazid	**Rifampicin**	**Pyrazinamide**	**Ethambutol**
Day 1	50mg			
Day 2	100mg			
Day 3	Full dose			
Day 4	”	75mg		
Day 5	”	300mg		
Day 6	”	Full dose*		
Day 7	”	”	250mg	
Day 8	”	”	1000mg	
Day 9	”	”	Full dose*	
Day 10	”	”	”	100mg
Day 11	”	”	”	500mg
Day 12	”	”	”	Full dose*

Adapted from the Oxford Textbook of Medicine, 3rd Ed. See references.

*Full doses as per section 4.4.3.

If a reaction occurs during challenge dosing and the drug is essential for the patient’s management, then a more formal drug sensitisation regimen may be required (below).

4.5.5.2. General principles of formal desensitisation (always done in hospital)

The decision to attempt desensitisation should only be made after deciding that the requirement for the particular drug outweighs the disadvantages of an alternative regimen.

Desensitisation is a potentially lengthy process, therefore should be done under the cover of at least two drugs to which the patient is not hypersensitive to prevent the emergence of drug resistance.

If the initial reaction was moderately severe or a reaction occurred to the first challenge dose (above), then start with a daily dose of 1/10 the first day’s challenge dose and gradually build up the dose by equal amounts to reach the full dose in approximately 7 days.

If a reaction occurred to the second challenge dose (above), then start with a dose equivalent to that of the first challenge dose and increase by this same amount each day. If a patient has a mild reaction to a dose, the same (or lower) dose is given the next day and then increased more gradually.

Patients who have developed hypersensitivity reactions should be continued on a daily regimen for the duration of treatment. If drugs need to be discontinued or changed, then the overall duration for the new regimen may need to be adjusted accordingly.

4.6. Hospital discharge, follow up and review

4.6.1. Hospital discharge

All TB cases should have a nominated case manager.

With impending discharge from hospital the case manager from the TB unit will ensure that all education and discharge planning has occurred. The TB case manager will liase with health care providers ensuring that any special needs are communicated and arrangements for DOT are in place. A TB discharge sheet (available from CDC, TB Clinic) and Tuberculosis Treatment card (Appendix 6) should accompany the patient back to the urban or remote community health centre or service taking responsibility for the patient. A visit to the community by the TB case manager should be arranged at this time to enable timely education of family and health care providers and a smooth transition of case management. Assistance with and evaluation of contact tracing can be provided if required.

4.6.2. Monthly reviews by medical officer while on anti-TB treatment

Every visit	2 months	3 months	6 months or end
Review adherence to treatment	Check initial drug sensitivities	Repeat chest X-ray (for pulmonary TB)	Review overall treatment duration
Review symptoms of drug toxicity + LFTs* (check vision if on EMB)	Discontinue ethambutol and pyrazinamide if isolate fully sensitive	Check sputum culture from last visit if collected **	Chest X-ray as end of treatment baseline
Weigh patient & clinical examination for signs of treatment failure	Ensure sputum conversion has occurred (that there are 3 consecutive smear and culture negative specimens)		Check if contact tracing complete
Ask about health of contacts	Repeat sputum smear and culture if necessary		Advise patient to report early if symptoms of relapse occur and organise follow up visits***

* **Monthly LFTs** are not routinely required unless **any** of the following circumstances are present: pre-treatment LFTs abnormal; pregnancy; underlying liver disease; HIV infection; continuing alcohol consumption; or age ≥50 yrs. In the case of **drug intolerance** or **drug-resistance**, changes to the treatment regimen may be needed - consultation with an expert in the management of TB is mandatory.

** **Culture negativity** should occur in >90% of patients by 2-3 months. If this does not occur then adherence to treatment should be carefully reviewed and earlier drug susceptibility results re-checked. If the patient is progressing well, then treatment will not need to be changed until repeat drug susceptibility tests are available. If there has been a lack of clinical response, then drug-resistance should be assumed and treatment altered in consultation with a specialist. Sputum cultures should continue to be performed at monthly intervals until conversion occurs.

*** **Reviews following treatment** completion should be a clinical review and chest X-ray at 6 months, 1½ years and 2½ years to detect relapse and to check health of family members/contacts. If adherence to treatment was questionable or drug-resistance was present, then it is recommended the patient be followed up more regularly, eg. at 6 months and then yearly for at least the next 5 yrs.

4.6.3. Duration and completion of treatment/Defaulter action

- If a treatment dose is missed, then the patient should be immediately visited and located. Optimal short-course treatment for TB requires taking 100% of the intended doses within 6 months.
- In practice, acceptable cure rates are obtained as long as ≥80% of the intended doses are taken within 8 months **and** no more than 1 month of treatment is missed in a row.
  - For **3 times weekly** treatment, this means taking 63 of the 78 intended doses within 8 months. If <63 doses are taken within 8 months **or** 12 doses are missed in a row, the patient must **restart** a full course of treatment **from the beginning** after reassessment for smear/culture positivity and drug resistance.
  - For daily treatment, this means taking 146 of the 182 intended doses within 8 months. If <146 doses are taken within 8 months or 28 doses are missed in a row, the patient must restart a full course of treatment from the beginning after reassessment for smear/culture positivity and drug resistance.
- Provided that the patient has taken ≥80% of the intended doses within 8 months **and** has missed no more than 1 month of treatment in a row, then every attempt should be made to continue treatment beyond 8 months so that all of the initially intended doses are given (above).
- As a last resort, the patient can be detained under the Notifiable Disease Act for treatment if this is necessary to safeguard the public.

4.7. Special clinical situations

4.7.1. Children

- Treatment of children <5 yrs of age should be prompt to decrease the risk of dissemination of disease.
- In general, dosages should be rounded up in children and may need to be recalculated with weight gain. Children should be weighed monthly for this reason.
- Ethambutol is omitted from the drug regimen in children <6 yrs of age who are too young to report visual symptoms or in older children unable to comply with visual testing methods.
- If diagnostic specimens (including gastric aspirates) are culture negative, then drug susceptibility results from an identified adult contact should be used to guide treatment.

4.7.2. Pregnancy and breast-feeding

- Rifampicin, isoniazid, pyrazinamide and ethambutol are not contraindicated in pregnancy as the risks to the mother and unborn child from untreated TB almost always exceed those of treatment.
- Aminoglycosides (including the alternative first line drug, streptomycin and second line drugs such as amikacin) can cause deafness in the baby and should not be used.
- Pyridoxine (vitamin B6) should be given to all pregnant and breast-feeding women.
- LFTs should be monitored monthly as the risk of drug-associated liver toxicity is increased.
- In some cases (eg. isolated tuberculous lymphadenitis), it may be possible to defer treatment until late pregnancy or post-delivery, but in these instances, the pregnant woman should be monitored closely for signs of pulmonary disease and/or dissemination.
- Breast-feeding should be encouraged as the small concentrations of the drugs in breast milk are not associated with toxicity to the baby.
- Infants born to mothers with infectious TB should receive primary prophylaxis with isoniazid (Chapter 7).

4.7.3. Elderly people

- Elderly people are more likely to experience drug intolerance, especially if malnourished (eg. low serum albumin). Pyrazinamide is particularly poorly tolerated in this age group.
- LFTs should be checked monthly if age ≥50 yrs.
- Consideration should be given to starting drugs sequentially at lower doses. For example, ethambutol (at full dose) and isoniazid (at reduced dose) are started together initially and built up to full dose over a week, at which time LFTs are checked; rifampicin is introduced next at reduced dose and built up over the next week, LFTs are again checked; pyrazinamide (low dose) is started last and cautiously increased over the next week with LFT monitoring.

4.7.4. Kidney failure

- Medications should be given on a 3 times weekly dosing regimen rather than daily.
- If the GFR is >50mL/min, no adjustment is required for rifampicin, isoniazid or pyrazinamide (although FBEs should be regularly monitored for bone marrow suppression induced by pyrazinamide). Ethambutol should be given at a dose of 15-25mg/kg.
- Pyrazinamide should be avoided with GFRs of <50mL/min and isoniazid dose halved if the GFR <10mL/min. Rifampicin can be given at standard doses for all levels of renal function.
- In general anti-TB drugs should be given after heamodialysis and should be given on a 3 times weekly schedule.

4.7.5. Liver disease

- Patients at risk of TB often have an increased incidence of underlying liver disease as TB is more common in people with alcohol abuse and hepatitis B and C than in the general population.
- Patients with severe hepatitis should have their treatment initiated and maintained by TB specialists as second line anti-TB drugs may need to be used.
- If LFTs (particularly the ALT) are abnormal at the start of treatment then they should be monitored frequently for the first 2 months of treatment (ie. weekly for the first 2 weeks and then at 2 weekly intervals) and then monthly for the remainder of the treatment period. Refer to Bibliograpgy; Saukonen J, et al, *An official ATS Statement: Hepatotoxicity of Antituberculous Therapy.*

4.7.6. HIV Infection

- HIV-related TB should only be managed by specialists familiar with both diseases.
- Short-course treatment of TB in patients with HIV has been associated with acceptable rates of treatment success and relapse. However, treatment should be prolonged if the clinical response is slower than expected or if sputum conversion takes longer than normal to occur.
- Interactions between drugs used for antiretroviral therapy and TB treatment are common and complex, often requiring drug avoidance or dosage adjustment. The toxicity profiles often overlap, which can make it difficult to discern the cause of drug-related adverse reactions.
- Rifabutin is usually used in place of rifampicin as it has fewer interactions with protease inhibitors and non-nucleoside reverse-transcriptase inhibitors. Not using Rifampicin/Rifabutin containing treatment regimens is associated with an unacceptable rate of treatment failure and/or relapse and should be avoided.
- Restoration of immune function with antiretroviral therapy in patients with HIV infection is associated with an increased incidence of paradoxical reactions (ie. an exuberant host response to TB antigens leading to transient worsening or emergence of TB-related clinical findings after anti-TB treatment has started). These usually begin within days to weeks and may be severe.

- Consideration should be given to delaying antiretroviral therapy by 1-2 months in patients not taking it at the time of TB diagnosis, as this enables full dose standard anti-TB treatment to be given during the critical intensive phase; minimises the possibility of drug interactions; makes it easier to identify the cause of adverse drug reactions and decreases the risk of paradoxical reactions.

4.8. Management of Relapse and Treatment Failure

- Relapse refers to the situation in which a patient becomes and remains culture negative while receiving therapy, but, at some point after completion of treatment becomes culture positive again or has clinical or radiological deterioration.
- Efforts should be made to determine, where possible by molecular testing, whether it is a true relapse (meaning the same *M tuberculosis* organism is able to be identified) or a re-infection from an exogenous source (pulmonary TB patient) causing new disease.
- Most relapses occur within the first 6-12 months after the completion of treatment.
- Empirical treatment should be based on the previous treatment scheme. If the initial TB was caused by drug susceptible organisms and the patient received DOT, a standard 4 drug regimen can be initiated while waiting for DST. If a patient did not receive DOT and dosing may have been irregular, drug resistance should be assumed and an expanded treatment protocol used in discussion with the TB specialist.
- Specimens are essential for DST.
- Treatment failure is defined as continued positive cultures during the course of treatment. Possible reasons include non-curative drug regimen because there is drug resistance, non-compliance or malabsorption.
- If failure is thought to be due to resistance and the patient is not unwell, an empiric 2nd line treatment regimen could be started until DST results are available.
- Importantly, never add a single new drug to a failing regimen.

4.9. Management of Smear-Negative/Culture-Negative Pulmonary TB

- At a minimum, patients suspected of having pulmonary TB should have 3 sputum samples collected.
- Patients who cannot produce sputum should either undergo an induced sputum or have a gastric aspirate obtained (see Chapter 2).
- Prior to making a diagnosis of culture negative TB other differential diagnoses should be excluded (see Chapter 2) and further diagnostic testing including bronchoscopy, CT/MRI and NAAT of any lung tissue should be considered.
- Following careful clinical and radiologic evaluation, patients who are thought to have pulmonary TB, should be initiated on treatment regardless of smear results.
  - If cultures return positive, treatment can then be continued.
  - If cultures remain negative a thorough clinical evaluation and CXR should be performed at 2 months. If improvement has occurred (clinical or radiographic) and no other aetiology identified, then treatment should continue. A decision as to whether 2, 3 or 4 drugs should be continued should be made with the TB specialist of the unit.

4.10. Management of Haemoptysis

Refer to Appendix 7.

4.11. ICU/HDU patients with significant risk of having tuberculosis

Refer to Appendix 8.

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5. BACILLE CALMETTE-GUÉRIN (BCG) VACCINE

5.1. The vaccine

BCG (Aventis Pasteur) is a suspension of live attenuated *M bovis* and remains the only vaccine available for TB. The aim of BCG vaccination is not to prevent transmission of MTB but rather to prevent progression of infection to disease. Its main role is in preventing meningeal and disseminated (miliary) TB in young children for whom its efficacy is >80%. The vaccines protective effect is thought to last approximately 10 years. Currently it is not recommended in Australia for routine vaccination of adults but is used in certain high risk groups. The effect of BCG vaccination on interpretation of subsequent Mantoux tests is discussed in Chapter 6.

5.2. Indications

- Aboriginal neonates.
- Neonates born to patients with leprosy or a family history of leprosy (refer to the Guidelines for the Control of Leprosy in the Northern Territory).
- Children under 5 years who will be living in Aboriginal communities or travelling to countries of high TB prevalence (>25 cases per 100,000 population per year – see map in Chapter 10 and Appendix 9) for periods longer than 3 months.

In addition to the above recommendations BCG may be considered in the following:

- Children over 5 who will be travelling or living in countries or areas with a high prevalence of TB for extended periods.
- HCWs who may be at high risk of exposure to drug resistant cases.

(see BCG fact sheet at Appendix 4)

5.3. Contraindications

BCG vaccination is contraindicated in individuals with:

- Mantoux test reactions ≥5 mm
- immunosuppression, including HIV infection; immunosuppressive drugs, including corticosteroids; radiation therapy; malignancies involving bone marrow or lymphoid systems.
- high risk of HIV infection when the HIV status is unknown (includes neonates of HIV-positive mothers)
- any serious illness including the malnourished
- generalised skin disease. eg. psoriasis or severe exzema
- pregnancy
- a past history of BCG vaccination
- a past history of TB.

BCG should be postponed

- BCG can be given at the same time as other live vaccines (in separate syringes in different sites) but should be **postponed** if another live vaccine has been given in the preceding 4 weeks.
- In the presence of significant febrile illness (in which case, BCG should be deferred for 1 month following recovery).

- Vaccination in premature or small for dates babies less than 2.5 kg should be delayed until discharge from hospital. No child should return to a remote community without vaccination.

5.4. Dosage and administration

- BCG should only be given by health staff who have been trained in the technique of BCG vaccination as specified in the National Immunisation Handbook.
- In the NT, the vaccine can only be obtained through neonatal nurseries for newborns or the CDC.
- A Mantoux test must be performed prior to BCG vaccination in all individuals except infants under 6 months of age with no history of MTB exposure. BCG can only be given to people with a Mantoux test result <5 mm.
- The dose is **0.05mL** for neonates and infants <12 months of age; and **0.1mL** for children.
- The vaccine does not contain a sterilising agent so extreme care must be taken to prevent bacterial contamination when reconstituting and handling the vaccine. The vaccine is unstable and should be used within 5-6 hrs of reconstitution.
- Protective eye-wear should be used when mixing and administering the vaccine to protect against the risk of eye splash.
- The use of a multi-dose vial is an accepted practice provided a strictly aseptic technique is adhered to but the vial **must be disposed of at the end of the vaccination session – it cannot be stored after a vaccination session.**
- The parents should be advised of what to expect and look out for following the injection (below). The importance of reporting suspected problems should be stressed.

5.5. Response to vaccination

- A small red papule normally forms and eventually ulcerates, usually within 2-3 weeks of vaccination. The ulcer heals with minimal scarring in several weeks.
- There may be swelling and tenderness in local lymph nodes.
- Subjects with LTBI who are inadvertently given BCG vaccination may experience an accelerated response characterised by induration within 24-48 hrs, pustule formation in 5-7 days and healing within 10-15 days.
- No more than 1 BCG is to be given, regardless of Mantoux test reaction.

5.6. Adverse reactions

- Serious complications from BCG vaccination including anaphylactoid reactions are rare.
- Regional lymphadenitis is the commonest adverse reaction. Lymphadenitis usually heals spontaneously but may take several weeks. Anti-TB drugs may be ineffective as BCG may have drug resistance. Where a node suppurates, starts to point or becomes adherent, surgical excision is the treatment of choice.
- Abscesses, lymphadenopathy and gross local reactions occur rarely. BCG abscesses should always have susceptibility testing performed.
- Keloid scar formation is minimised by giving BCG no higher than the level of the insertion of the deltoid muscle into the humerus.
- BCG may cause disseminated infection if inadvertently given to someone who is immunosuppressed or if inadvertently given with an incorrect technique.

- Gross local or disseminated infection can be treated with anti-TB drugs under the supervision of a TB specialist (usually rifampicin and isoniazid for 2-4 months; BCG is naturally resistant to pyrazinamide and may occasionally be resistant to isoniazid).
- Milder local reactions are usually self-limiting and can usually be managed expectantly by allowing pus to spontaneously discharge, keeping the site clean and dry (can be wiped with alcohol swabs) and covering the area with a gauze dressing rather than an occlusive dressing.
- Adverse reactions to BCG vaccine are a notifiable condition in the NT. An Adverse Event Following Immunisation form (Appendix 6, available from the Immunisation Project Officer 89228564) should be completed and forwarded to the Immunisation project officer. A BCG side effects questionnaire should also be completed (Appendix 10).

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6. LATENT TUBERCULOSIS INFECTION (LTBI) - DIAGNOSIS

6.1. Introduction

The risk of TB infection in close household contacts of an infectious case can be as high as 25-50%. Following infection, the subsequent lifetime risk of active TB is generally estimated at about 10% with half of these cases occurring within 2-5 years of infection. This risk is even greater in young children and people with impaired immunity. Diagnosis of LTBI followed by preventive treatment will reduce the risk of developing active TB by up to 90%. Current international guidelines emphasise targeted Mantoux testing of people at increased risk of TB infection and disease. In those guidelines, the decision to Mantoux test is usually regarded as an intention to give treatment for LTBI if the test is positive.

Although imperfect, the Mantoux method of testing with tuberculin purified protein derivative (PPD) derived from killed *M tuberculosis* is currently the most reliable and widely available diagnostic test for LTBI. IGRAs are blood tests which measure the release of interferon-gamma in whole blood from sensitized persons. It has a number of potential advantages: it only requires 1 patient visit; it may be less subject to errors in administration and interpretation; it can partly discriminate against false-positive results caused by non-tuberculous mycobacteria (NTM), BCG vaccination and false-negative results caused by poor immunity, and can be completed in <24 hr. The major limitations of this test are that it has not been as widely validated as the Mantoux test.

6.2. Mantoux testing

6.2.1 Indications

The main role of the Mantoux test, is to identify people who are ultimately at increased risk for active TB and who will benefit from treatment of TB infection. Generally, this includes people in population sub-groups at high risk of acquiring TB infection or with conditions associated with a high risk of progression of LTBI to active TB. Targeting testing at high risk groups has the potential benefit of maximising TB control efforts and minimising the number of people without LTBI who receive treatment. Routine screening of low risk persons is no longer encouraged, with the exception of establishing a baseline in those specific groups identified below or those who may face an increased risk of exposure to MTB through employment or travel. See Appendix 4 for a Mantoux test fact sheet for patients.

The indications for Mantoux test are therefore:

- recent contact with a case of infectious TB (Chapter 8)
- chest X-ray changes consistent with past inactive TB (eg. fibronodular apical or upper lobe infiltrates)
- screening of high-risk groups, including recent migrants/refugees and prisoners (Chapter 10)
- the presence (or in anticipation) of high risk medical conditions
  - these include HIV; diabetes; silicosis; prolonged immunosuppressive or corticosteroid therapy (eg. >15 mg prednisolone daily for >2 weeks); haematological malignancies; head, neck and lung cancers; chronic renal failure; gastrectomy or jejunal bypass; weight loss >10% body weight; malnutrition
- as a baseline and part of an ongoing program in employees whose work may involve an increased risk of TB exposure (eg. in hospitals, prisons, detention centres, hostels, drug and alcohol rehabilitation centres, night patrol, nursing homes – Chapter 10)
- prior to prolonged travel or employment in high prevalence countries/communities if the risk of exposure to TB is substantially increased

- prior to administering the BCG vaccine to individuals >6 months of age
- prior to donation in potential live organ donors
- as a diagnostic test in some cases of suspected active TB (generally in children, see Chapter 2).

6.2.2. Contraindications

The Mantoux test is contraindicated in the case of previous:

- confirmed TB infection (on Mantoux test and/or chest X-ray) or TB disease. The test will not provide any additional information in these cases and may cause more severe reactions
- Mantoux test causing severe skin reactions (vesiculation, ulceration, necrosis)
- Mantoux test causing a severe immediate hypersensitivity reaction.

The Mantoux test should be rescheduled in the case of:

- short-term immunosuppressive therapy that may cause false-negative response
- recent live virus vaccination (within 4 weeks) that may cause a false-negative response.

In some people who meet the criteria for a Mantoux test (eg. recent close contact of an index case with active TB) but in whom it is contraindicated, an alternative IGRA testing may be appropriate. An approach focussing on uncovering symptoms and signs of active TB with a baseline and follow up chest X-rays (eg. at 6 months, 1½ years and 2½ years) is also reasonable in close contacts.

6.2.3. Administration

- Tuberculin (PPD) should be protected from light and stored refrigerated at 2-8°C.
- PPD should only be used on the day it was opened and old vials thrown out.
- PPD should be administered as soon as possible after drawing up into the syringe because it can stick to the plastic and lose potency.
- Acetone or alcohol is used to clean an area of healthy skin free of veins on the anterior surface of the forearm (at the junction of the upper and middle thirds) and allowed to dry.

Administer **0.1mL** of 100 IU/mL strength PPD (ie. 10 International Units in total) intradermally using a 1mL insulin syringe with 29 gauge needle or 1mL syringe with 26 g needle.

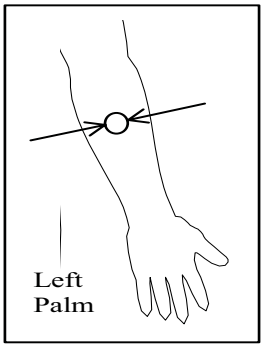
A palpable bleb between 5-8 mm diameter indicates that the test has been done correctly. If this does not occur or if PPD is observed to leak out, another test can be given immediately, either in the other forearm or in a site several cm away from the first.

The subject should be warned that the skin may become itchy but they should avoid scratching the area because irritation may lead to false-positive responses.

6.2.4. Reading

The reaction to PPD begins 5-6 hours after injection and produces maximum induration at 48-72 hours which is when the test is best read. Tests can be read up to 5 days after injection if necessary. Surrounding erythema is not included in the measurement.

- Mantoux test results are recorded in mm as a single* reading of the diameter of skin induration across the short axis of the forearm (the distance between arrowheads in diagram, right).



*The recording of Mantoux test results as a single transverse reading is based on standardisation with other guidelines, consistency with published literature and the possibility that longitudinal readings may be significantly greater than transverse ones.

- The tip of a medium ballpoint pen is pushed along the skin toward the site of injection, starting about 1 cm from the edge and stopping when resistance is felt. This is then repeated on the opposite side.
- The distance between the 2 pen marks is measured with callipers or a ruler.
- The **actual measurement** is recorded in mm along with the number of days following administration on which the test was read. Absence of induration should be recorded as 0 mm rather than as "negative" as this may be confusing.
- Vesiculation (blistering) if present should always be noted.
- A history of BCG vaccination (including age at vaccination, or ages in the case of multiple vaccination, and the presence or absence of BCG scars) should also be recorded. Scars should be looked for on both shoulders, at the top of the thigh (eg. in migrants) and wherever the person thinks they might have received BCG vaccination.

6.2.5. Adverse reactions

- Immediate hypersensitivity reactions such as wheals may occur, usually within 24 hours.
- Strong positive reactions including vesiculation, ulceration and necrosis may occur at the test site in highly sensitised individuals. Symptomatic relief can be provided with cold packs and the use of topical steroid preparations. Such reactions may cause scarring.
- Lymphangitis and regional adenitis can occur and is usually managed symptomatically.
- Residual erythematous lesions at the site of injection may rarely persist for extended periods (sometimes months to years) following a strongly positive reaction.
- Subcutaneous (rather than intradermal) injection will not cause a local reaction but may cause a general febrile reaction or inflammatory reactions around old tuberculous lesions in highly sensitised individual.
- Anaphylactoid and anaphylaxis reactions are extremely rare but it is advisable that Mantoux tests are done where access to adrenaline and resuscitation facilities is available.

6.2.6. Interpretation

Interpretation of the Mantoux test must be individualised after taking into account the size of reaction to PPD, the likelihood that false-negative or false-positive reactions may have influenced the result, and the risk of development of active tuberculosis. The main aim is to ensure that those at highest risk of infection or progression to active TB are offered preventive treatment and those at lowest risk do not receive treatment unnecessarily (see Chapter 7).

6.2.6.1. Causes of a false-negative Mantoux test (ie. negative in the presence of MTB infection)

- Use of PPD that is out of date or improperly handled.
- Subcutaneous injection or unrecognised leakage at the time of administration.
- Reading of the test within 48 hrs or longer than 5 days of injection.
- Test performed soon after TB infection (as it can take 2-12 weeks for a detectable immune response to MTB to develop, negative tests done early should be repeated at least 10 weeks following the exposure. This sometimes results in 2 Mantoux tests being done).
- Acute viral or bacterial infections, including active TB (up to 25% of TB patients). Impaired cellular immunity – eg. neonates, immunosuppression (including steroid therapy), HIV, malnutrition (eg. from living in refugee camps), renal failure, some malignancies.
- Waning cellular immunity to PPD (see 'Booster Effect' below). Recent live virus vaccination (within the preceding 4 weeks).

6.2.6.2. Causes of a false-positive Mantoux test (ie. positive in the absence of MTB infection)

- Ruptured small venule at time of injection.
- Trauma to the site (eg. scratching).
- Failure to distinguish erythema from induration.
- Past BCG vaccination or exposure to NTM (below).
- Sensitivity to preservatives in PPD.

6.2.6.3. Effect of BCG vaccination and non-tuberculous mycobacteria (NTM) on Mantoux testing

Most people vaccinated with BCG will develop a Mantoux test reaction ≥10mm within 8-12 weeks of vaccination but this reaction does not correlate with effectiveness of the vaccine. The likelihood and degree of persistence of this response is most strongly influenced by the age at vaccination. If BCG is given in infancy (ie. in the first year of life), it is very unlikely to cause Mantoux test reactions of ≥10mm after the age of 2 or 3 years. Those vaccinated later in childhood are more likely to have persistent responses but it can be expected that the majority of these will be <10 mm within 10 years of vaccination. Repeat BCG vaccination is also associated with persistent Mantoux test reactivity. Subsequent exposure to NTM and serial tuberculin testing may increase Mantoux test reactivity due to BCG but the extent of this effect can be difficult to judge. Exposure to environmental NTM in the absence of BCG may also cause induration in a Mantoux test (usually <10mm).

When reading Mantoux test reactions there is no reliable way to distinguish response caused by BCG from those caused by natural mycobacterial infections (whether MTB or NTM). The most important factor influencing the probability that a tuberculin reaction represents true infection with MTB rather than the effect of BCG is the prevalence of LTBI in the population sub-group being tested. Some authorities recommend that BCG vaccination status be ignored when performing the Mantoux test if the patient is in a high risk group for TB infection or if the vaccine was given in infancy. In these instances the likelihood of true infection with MTB relative to a false-positive reaction is increased. Treating these patients in a high risk group for progression of infection to active TB may mean some individuals are treated who are possibly not infected.

IGRA may have a role in more reliably determining Mantoux test response as their specificity is greater and there is no cross reaction with BCG and most NTMs (see 6.3).

6.2.6.4. Suggested cutoffs for interpreting Mantoux test reactions

The following guidelines are most useful when there is a low likelihood of false-negative or false-positive reactions. The cutoffs are chosen to enhance the sensitivity and specificity of the test for different population sub-groups. The aim is to maximise the chance that someone with infection will be offered treatment and minimise the chance that someone without infection will be offered treatment unnecessarily. This leads to lower cutoffs in people at highest risk and vice versa.

Induration*†	Suggested Positive Mantoux test Cutoffs
5-9mm	All children under 5 yrs without BCG. Children under 5 yrs with BCG who are contacts of an infectious case or are from a high risk group‡. HIV-positive persons. Patients with organ transplants and other immunosuppressed patients (receiving equivalent of >15mg/day prednisolone for >2 wks).
10-14mm	Children under 5 yrs with BCG who are not contacts of an infectious case and are not from a high risk group‡. Adults and children over 5 yrs with no BCG. Adults and children with prior BCG who are contacts of an infectious case or are from a high risk group for LTBI‡.
15mm+	Adults and children over 5 yrs with prior BCG who are not contacts of an infectious case and are not from a high risk group‡.

*Vesiculation, if present, is regarded as positive in all risk groups.

† For assessment of repeated testing of employees at increased risk of TB infection, see below.

‡ High risk groups include those: likely to have been infected with TB within past 2 years (includes contacts of all ages); chest X-ray consistent with past inactive TB; other high risk medical conditions including diabetes, silicosis, chronic renal failure, carcinoma of head and neck, leukaemias, lymphoma and malnutrition.

6.2.7. Follow up after a Mantoux test

The result of the Mantoux test in mm and the decision as to whether or not this was regarded as indicating LTBI should be carefully documented in the person's file. Generally people with negative tests can be reassured that they do not have TB infection provided they have no symptoms and normal immunity, and the test has been done at least 10 weeks following exposure. In very high risk contacts of an infectious case (ie. HIV-positive or immunosuppressed individuals and children < 5 years of age), it may be necessary to consider early treatment of primary progressive disease with anti-TB drugs prior to a Mx being carried out at 10-12 weeks after exposure. In this case, a chest X-ray should be taken and specialist advice sought.

The evaluation of all persons deemed to have a positive Mantoux test should include:

- clinical review directed at uncovering symptoms and signs of active pulmonary and/or extra-pulmonary TB (Chapter 2)
- a postero-anterior chest X-Ray (a lateral chest X-ray in children under 5 years may also be requested to look for mediastinal lymphadenopathy)
- sputum collection should be performed in the case of suspected active TB (Chapter 2), fibrotic non-calcified changes on chest X-ray or in HIV-positive persons with respiratory symptoms (regardless of chest X-ray findings)
- a discussion on LTBI and risk of progression to active tuberculosis (Chapter 7).

6.2.8. Boosted reactions and two-step testing

The 'booster effect' represents reactivation of waned cellular immunity by an initial negative Mantoux test such that a second test at any time from 1 week to 1 year later produces a greater, more accurate response. This effect will only be observed in individuals with prior cellular immunity to PPD (whether from MTB, BCG or NTM) and is more common in the elderly (age >55 years). Because the proteins in PPD are small in size, repeated skin testing with standard

doses of tuberculin will not induce a positive skin test reaction in individuals who have no cellular immunity to the antigens in PPD.

'Two-step' testing is used to avoid interpreting the effect of boosting as a new infection and is especially useful for people in whom Mantoux testing will subsequently be conducted at regular intervals or after exposure. If the first test is <10mm (and no Mantoux test has been done in the previous 12 months), it is repeated 1-3 weeks later and the second test is interpreted as measuring the degree of reactivity.

Baseline two-step testing should be routinely offered for:

- pre-employment testing of health care workers and staff of high risk workplaces (eg. prisons, detention centres,alcohol and drug rehabilitation centres and nursing homes)
- people with Chronic Renal Insufficiency
- people with lowered immunity including HIV
- the elderly who are entering care facilities
- people undergoing organ donation
- prior to treatment with some immunosuppressives eg. TNF-α.antagonists.

6.2.9. Ongoing screening of employees at increased risk of TB

A baseline two-step Mantoux test will make subsequent Mantoux testing much easier to interpret and minimise the chance that people will be inappropriately diagnosed and unnecessarily given treatment for LTBI. Because there is biological variation and unavoidable differences in even the most carefully performed tests, small increases in reaction size on post-employment testing may not be meaningful. Therefore, for persons with a Mantoux test regarded as not indicating LTBI initially, an increase in reaction size of less than 10mm within a period of 2 years should not generally be regarded as evidence of recent infection with TB. In selected circumstances, increases in reaction size of 6-10 mm within 2 years in people at particularly high risk may warrant consideration of treatment for LTBI. If in doubt, these people should be referred to the TB Control Unit for individualised assessment. Requirements for screening of health care workers and other at-risk staff are outlined further in Chapter 10. See Appendix 4 for fact sheet *Two step Mantoux test for high risk groups*.

6.2.10. HIV-positive persons

HIV-positive persons are at higher risk of both establishing LTBI infection following an exposure to TB and progression from LTBI to active disease. Decreased cellular immunity in HIV-positive persons leads to a higher rate of false-negative Mantoux test. Two-step testing (above) to look for a boosted reaction should be performed at the time of diagnosis and a positive cut-off of ≥5mm should be used. Negative (<5 mm) results should be reconfirmed if cellular immunity is subsequently partially restored with anti-retroviral therapy. HIV-positive individuals may have active pulmonary TB despite a normal chest X-ray so all patients with respiratory symptoms should be investigated with sputum cultures for TB and other mycobacteria. Because of the high risk of infection, active disease and false-negative reactions, the decision as to whether or not treatment is required to prevent active TB following a significant TB exposure should be made early and without regard to the Mantoux test result.

6.3. Interferon-γ Release Immunoassays (IGRAs)

IGRAs are in vitro diagnostic tests using peptide cocktails simulating ESAT-6 and CFP-10 proteins to stimulate cells in heparinized whole blood. These proteins are absent from all BCG strains and from most NTM with the exception of *M kansasii, M szulgai and M marinum* Individuals infected

with *M tuberculosis*-complex organisms usually have lymphocytes in their blood that recognize these and other mycobacterial antigens. This recognition process involves the generation and secretion of interferon-γ (IFN-γ). The detection and subsequent quantification of IFN-γ forms the basis of IGRA test.

IGRAs are not currently generally recommended for use in Australian TB programs. Their use has been recommended in limited situations in guidelines developed in the UK and USA.

The interim National Tuberculosis Advisory Committee (NTAC) position statement recognises that IGRAs are a novel test for a disease with a delayed onset where the 'gold standard' comparator test (ie, Mantoux test) is imperfect. The statement encourages further clinical and economic evaluation of IGRAs with a particular need for:

- comparative studies of the Mantoux test and interferon-γ assays undertaken by staff specially trained in the standardised application of the Mantoux test;
- companies producing IGRAs to conduct well-designed sequential testing studies (eg., at monthly intervals) on various patient groups to characterise and quantify conversion and reversion reactions;
- systematic research on the use of IGRAs in sub-groups such as children, immunosuppressed populations and in areas with a high incidence of infectious disease;
- an independent cost-benefit analysis (possibly through the Medical Services Advisory Committee) on the use of IGRAs using NTAC's preferred protocol of investigating LTBI in Australia to investigate the relative economic outcomes of changing from Mantoux test to immunoassays taking into account the structure of TB services and program delivery in Australia;
- a comparison of alternative IGRAs with the Mantoux test to determine differences between the assays and to help better assess the impact of indeterminate results.

The NTAC position statements on IGRA are updated regularly on http://www.health.gov.au/internet/wcms/publishing.nsf/Content/cdna-ntac-pubs.htm.

6.3.1. The Test and Indications

QuantiFERON®-TB Gold is currently the only IGRA licensed for use in Australia. Other tests including T-SPOT.*TB* may become available in the future.

IGRA can be used in most circumstances in which the Mantoux test is used. If a Mantoux test is contra indicated IGRA could be considered in its place. Availability of the test at a local laboratory would need to be considered before requesting the test.

6.3.2. Testing and Interpretation

It is essential to contact your local laboratory if you are considering using an IGRA. They will be able to provide up-to-date recommendations on sample collection and transport of specimens to the laboratory. As the test has to be completed within certain time constraints, usually 12-16 hours, liaising with the lab is essential.

A positive IGRA result should prompt the same public health response and interventions as a positive Mantoux test, including clinical review, CXR and sputum collection if indicated.

People diagnosed with LTBI by IGRAs should be offered treatment (Chapter 7).

6.3.3. Summary

In summary the following recommendations are made.

- currently Mantoux testing remains the preferred method of investigation for LTBI pending further evaluation of IGRAs
- Mantoux tests and IGRAs have almost no place in the diagnosis of active TB disease
- ongoing research will determine the use of IGRAs in the future.

6.4. Heaf testing

The Heaf test is similar to the Mantoux test but injects multiple samples of testing serum via a gun into the skin in a circular pattern of 6. It was carried out in the UK until 2005 but was not recommended in Australia.. The test is read between 3 and 10 days later.

The reading of the Heaf test is defined by a scale.

Heaf Reading	Defintion	Mantoux test eqivalent
negative	minute puncture scars, no induration	0mm
grade 1	at least 4 puncture points are indurated	0-4 mm induration
grade 2	coalescence of puncture points forming a ring of induration	5-14 mm induration
grade 3	extensive induration(5-10mm)	>15 mm induration
grade 4	severe induration (≥10mm)	>15 mm induration

Grades 1 and 2 may be the result of previous BCG or MAIC infection. People who have a grade 3 or 4 reaction require X-ray and follow-up.

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7. LATENT TUBERCULOSIS INFECTION (LTBI) AND TREATMENT

7.1. Introduction

The diagnosis of LTBI means that a person has been infected with *M tuberculosis* but the infection is inactive and there is no presence of disease. The diagnosis is made on the basis of a Mantoux test result (or IGRA test) as evidence of infection together with the patient's history, clinical, radiological and microbiological evidence ruling out active disease.

In people with LTBI, the rationale for treating those identified as latently infected is to kill any residual dormant bacilli in order to reduce or prevent later reactivation of TB disease.

Treatment of asymptomatic TB infection is an important strategy for decreasing the number of new cases of active TB in the future and therefore reducing TB transmission. In recent years there has been a move toward targeting Mantoux testing and treatment of LTBI for those individuals at highest risk of TB who stand to benefit the most from treatment. These include those with HIV infection, end-stage renal failure, insulin dependent diabetes mellitus, head and neck carcinoma, recently acquired LTBI (contacts), children, and those taking immunosuppressive medications. Conversely, it may be prudent to screen for TB with a chest x-ray rather than testing for LTBI with a Mantoux test, in circumstances where completion of a treatment course for LTBI is very unlikely (eg. persons in residential drug and alcohol rehabilitation programs lasting 12 weeks).

7.2. Diagnosis of LTBI

LTBI is a default diagnosis made in an individual with a positive Mantoux test or (IGRA) who has had active TB excluded by clinical, radiological, and possibly bacteriological assessments (Chapter 6).

It is essential that active TB disease is ruled out through a thorough history, clinical examination, CXR and possible microbiology specimens. Once a diagnosis of LTBI is made an assessment is made as to whether people are offered treatment for LTBI.

7.3. Indications for treatment of LTBI

Once a person has contracted LTBI, the risk for progression to TB disease varies. The greatest risk of progression occurs within the first 2 years after infection.

The decision on how to manage LTBI is based on the likelihood of active TB developing in the person's lifetime, risk of adverse reactions to the treatment, resources available to support treatment for LTBI, and individual decision making between the person and the TB Unit. The decision can be changed on the basis of any of these factors, for example, the development of renal disease long after the diagnosis of LTBI may lead to a decision to treat.

7.3.1. Treatment of LTBI should be recommended where:

- a child is under 5 years, due to the very high risk of progression to active TB
- infection with TB was likely to have occurred within the previous 2 years
  - through close contact with an infectious TB case
  - upon migration to Australia from a high TB prevalence country
- conversion of previously negative Mantoux test on regular screening

- risk factor(s) associated with increased progression of LTBI are present such as:
  - chest X-ray with fibrotic changes consistent with past untreated TB (after appropriate investigation to exclude active disease [Chapter 2])
  - HIV infection
  - immunosuppressive treatment eg. solid organ transplant recipients and use of TNF-α.antagonists (infliximab)
  - high-dose steroid treatment (equivalent to >15mg prednisolone daily for >2 weeks)
  - chronic renal failure
  - diabetes
  - weight loss >10% of ideal body weight
  - gastrectomy or jejunoileal bypass
  - carcinoma of lung or head and neck
  - leukaemia or lymphoma
  - silicosis.

The 'Lifetime Risk of Reactivation of Tuberculosis' table (see p 42) gives an estimation of the risk of developing tuberculosis on the basis of Mantoux test size, age, recent conversion of skin test and other risk factors.

The table can be used as a guide to decision making regarding treatment for LTBI.

People with a lifetime risk >10% should be strongly encouraged to have treatment. Especially if above risk factors present.

People with a risk between 5-10% who have any of the following risk factors should also be encouraged to have treatment.

- residents of most remote and some urban Aboriginal communities
- employees of high risk workplaces ie. hospitals, drug and alcohol rehab centres, prisons, detention centres, nursing homes
- migrants and refugees from high prevalence areas.

If no risk factors are present and lifetime risk is <5% education should be provided (Factsheet, Appendix 4).

7.3.2. Contraindications for treatment of LTBI

The following are relative contraindications to the use of treatment for LTBI. In some cases the benefit of treatment may outweigh the potential risks. This should be discussed with the TB Unit on an individual case basis

- prior completed anti-TB treatment/treatment for LTBI
- evidence of liver disease
- high alcohol intake
- pregnancy and lactation- treatment should be delayed until post partum if high risk case
- use of other hepatotoxic medications
- depression
- evidence of pre-existing neurological disorders.

Lifetime Risk of Reactivation Tuberculosis.*

Size of Induration on Skin Test and Age	Nonconversion Positive Skin Test	Recent Conversion of Skin Test	Immunosuppressive Therapy	Old, Healed Tuberculosis	Advanced HIV Infection
			percent (95 percent confidence interval)		
Induration of ≥15 mm					
0–5 Yr	13 (10–16)	17 (12–24)	25 (7–87)	66 (34–100)	100 (88–100)
6–15 Yr	7 (6–8)	8 (6–10)	14 (4–46)	37 (21–67)	70 (52–92)
16–25 Yr	8 (5–15)	13 (8–21)	17 (3–84)	44 (15–100)	83 (39–100)
26–35 Yr	7 (4–13)	12 (8–19)	15 (3–74)	39 (14–100)	73 (35–100)
36–45 Yr	4 (2–7)	7 (5–12)	8 (2–39)	21 (8–57)	40 (20–79)
46–55 Yr	3 (2–6)	6 (4–10)	6 (1–32)	17 (6–46)	32 (16–44)
56–65 Yr	3 (2–4)	3 (1–7)	5 (1–23)	13 (5–33)	25 (14–46)
≥66 Yr	2 (1–3)	2 (1–5)	4 (1–17)	9 (4–24)	18 (10–33)
Induration of 10–14 mm					
0–5 Yr	10 (6–15)	13 (8–21)	20 (4–82)	53 (22–100)	100 (56–100)
6–15 Yr	4 (3–5)	5 (3–7)	8 (2–30)	20 (10–44)	38 (24–61)
16–25 Yr	7 (3–13)	10 (6–17)	13 (2–73)	35 (12–100)	66 (30–100)
26–35 Yr	6 (3–12)	9 (5–15)	12 (2–64)	31 (10–93)	58 (26–100)
36–45 Yr	3 (2–6)	5 (3–9)	7 (1–34)	17 (6–50)	33 (15–68)
46–55 Yr	3 (1–5)	5 (3–8)	5 (1–8)	14 (5–40)	26 (12–55)
56–65 Yr	2 (1–4)	3 (1–6)	4 (1–20)	11 (4–29)	20 (11–39)
≥66 Yr	2 (1–3)	2 (1–5)	3 (1–14)	8 (3–20)	15 (8–28)
Induration of 5–9 mm					
0–5 Yr	3 (2–6)	6 (2–12)	6 (1–31)	16 (6–45)	31 (15–63)
6–15 Yr	2 (1–3)	3 (2–5)	4 (1–17)	11 (5–25)	21 (13–34)
16-25 Yr	6 (2–14)	8 (4–17)	11 (2–79)	29 (7–100)	55 (19–100)
26–35 Yr	5 (2–13)	7 (3–15)	10 (1–69)	25 (6–100)	48 (17–100)
36–45 Yr	3 (1–6)	4 (2–9)	5 (1–34)	12 (3–50)	24 (8–68)
46–55 Yr	2 (1–5)	4 (2–8)	4 (1–28)	10 (3–40)	19 (7–55)
56–65 Yr	2 (1–3)	2 (1–6)	3 (0–18)	8 (2–26)	15 (6–36)
≥66 Yr	1 (0–2)	2 (0–5)	2 (0–13)	6 (2–19)	11 (4–26)

* Data on the risk associated with recent conversion are from studies of household contacts of patients with active tuberculosis and are applicable to situations in which recent infection is likely, such as among persons with recent skin-test conversion, persons living in prison or a homeless shelter, intravenous-drug users, or persons who immigrated from a country with a high incidence of tuberculosis within the previous five years. Data on the risk associated with immunosuppressive therapy are from a study involving patients who were receiving infliximab and are applicable to patients undergoing long-term therapy with other medications that are known to impair cell-mediated immunity. HIV denotes human immunodeficiency virus.

Horsburgh CR (2004), Bibliography p 48

7.4. Prevention of primary progressive TB

Some individuals are at extremely high risk of progressing immediately from TB infection to active TB following exposure to an index case with infectious TB. In these situations, it is appropriate to start primary preventive treatment immediately following the TB exposure, with the aim of preventing establishment of primary TB infection. A baseline Mantoux test should be performed. Immunocompetent individuals may be able to cease treatment if a follow-up Mantoux test taken 10-12 weeks following TB exposure is negative (eg. children). In the case of immunosuppressed individuals, in whom the likelihood of false-negative Mantoux test reactions is increased, the treatment course should be completed regardless of the second Mantoux test result.

Chemoprophylaxis to prevent primary TB infection (using the same regimens recommended for treatment of LTBI) should be **strongly recommended** for close contacts of an infectious case who are:

- under 5 years of age
- immunosuppressed (eg. HIV infection, transplant patients)
- a neonate nursed by a mother with active pulmonary TB.

7.5. Pre-treatment clinical evaluation and advice

The goal of pre-treatment evaluation is to ensure that an individualised management plan can be established for patients taking treatment for LTBI. Because of the risks of toxicity, it is important that no more than 1 month of treatment is given at a time and regular follow-up of patients taking treatment is essential.

7.5.1. Patient history

Enquire about:

- risk factors for TB
- prior treatment for LTBI
- pre-existing medical conditions associated with increased risk of adverse events from treatment
- detailed drug history of current and previous medications, especially those that may interact with anti-TB drugs (eg. warfarin, anti-epileptics, oral or injectable contraceptives, contraceptive implants).

7.5.2. General advice for all patients

- The benefits of treatment for LTBI and importance of adherence should be stressed.
- Patients should be advised to avoid drinking alcohol while on treatment for LTBI as alcohol increases the risk of serious liver toxicity.
- Although anti-TB drugs are generally safe in pregnancy, women taking treatment for LTBI should be advised to use birth control and avoid pregnancy until their treatment course is completed because pregnancy increases the risk of drug-related liver toxicity.
- The oral contraceptive pill and other forms of progesterone based contraceptives (such as medroxy-progesterone acetate depot injections and etonogestrel implants) can be safely used with isoniazid but other methods of contraception should be used by women on rifampicin as it may reduce their efficacy.
- Patients should be asked to advise other health care providers they are taking anti-TB medication prior to taking any new drugs due to the possibility of drug interactions.

7.5.3. Baseline laboratory testing

Baseline liver function tests (**LFTs**) are indicated for all people over 15 years of age. Serology should be ordered if the likelihood of chronic hepatitis due to hepatitis B or C viruses is increased. A full blood examination (**FBE**) should also be ordered for patients taking rifampicin (or rifabutin).

If patients are HepBsAg positive with an elevated ALT, a HepBeAg should be requested. If positive rifampicin may be the preferred choice.

7.5.4. Advice on common side effects and toxicities of medications.

This is covered in detail in Chapter 4.

7.6. Treatment regimens and doses for LTBI

Factors to consider when choosing a regimen for treatment of LTBI include the length and complexity of the regimen, the possibility of adverse effects, and potential drug interactions.

Directly observed therapy (DOT) is mandatory for treatment regimens given intermittently because of a higher margin for error if doses are missed. Self-administration of medication intermittently may also be more difficult as the regimen is not linked to daily routines.

People eligible for treatment of LTBI who do not receive it for whatever reason should instead have a baseline chest X-ray and be provided with written information regarding the risk of disease progression and symptoms to be aware of.

7.6.1. Isoniazid

A 9 month course of isoniazid, given either daily or 3 times a week, is now the preferred regimen for treatment of LTBI in the NT due to its high efficacy, low toxicity and the considerable experience with use of the drug. The benefits of longer treatment are most apparent for those at greatest risk of active disease (eg. children and individuals with recent TB contact or other risk factors for TB progression), particularly if doses are missed. A 6 month isoniazid regimen still provides substantial protection in comparison to placebo (in the order of 65-75%) and may be justifiable in adults at lesser risk, although 6 month isoniazid regimens have not been properly evaluated in children.

Pyridoxine (Vitamin B6) supplements are given to patients receiving isoniazid treatment for LTBI to reduce the risk of peripheral neuropathy (nerve damage) that may sometimes occur because of interference with pyridoxine metabolism by isoniazid. The risk of neuropathy is highest in people with diabetes, alcohol abuse, chronic renal impairment, HIV infection, pregnancy, epilepsy or malnutrition.

Table: Drug Regimens for the Treatment of LTBI

Isoniazid 6 and 9 month regimens	Oral dose in mg/kg with maximum doses						
	Daily			3 times weekly			Tablet Formulation
	Adults	Children*	Adults and children*	Adults	children*	Adults and children*	
Drug	dose	dose	maximum dose	dose	dose	maximum dose	
Isoniazid	5mg/kg	10-15mg/kg	300mg	15mg/kg	15-20mg/kg	600mg	100mg

* children are defined here as <12 years

Pyridoxine - Vit B6 (to prevent side effects)	Dose
Adults	25mg (1 tab)
Children 5-11 yrs	12.5mg (½ tab)
Children <5 yrs	5mg† - 6.25mg (¼ tab)

† For a 5mg dose, crush a 25mg tablet, make up to 5 ml with water, give 1 ml (see p159 *Therapeutic Guidelines Antibiotic*)

7.6.2. Short-course rifampicin based regimens

Rifampicin alone given daily for 4 months is a rarely used alternative in cases at high risk of progression to active TB where isoniazid use is contraindicated or not appropriate due to known or strongly suspected isoniazid resistance, and adherence to treatment can be assured. **This regimen should only be prescribed and monitored by the senior staff of TB control units.**

Short course treatment with rifampicin and pyrazidamide for 2 months has previously been used to treat LTBI but reports of serious hepatotoxicity have emerged and this regimen is no longer recommended.

As rifampicin-containing regimens have only been evaluated in adults, their use is generally not recommended in children. Rifampin is contraindicated in HIV-infected persons being treated with certain combinations of antiretroviral drugs. In those cases, rifabutin may be substituted for rifampicin. The dose of rifabutin may require adjustment in patients taking other medications – specialist advice is essential.

7.7. Special considerations

- **Contacts of patients with TB (including drug-resistant TB)**

Close contacts of infectious cases (Chapter 8) in whom the Mantoux test indicates LTBI should receive treatment regardless of age. Because of the risk of severe disease, children <5 year and immunosuppressed contacts should receive treatment immediately to prevent primary progressive TB even if the initial Mantoux test is negative (see above).

It is essential that the drug susceptibilities on the source patient's TB isolate are reviewed as soon as they become available (usually 6-8 weeks after initiating culture). If the isolate is fully susceptible to first line drugs then any of the recommended regimens are appropriate. For contacts of patients with isoniazid-resistant, rifampicin-susceptible TB, rifampicin for 4 months is recommended. Specialist advice should always be sought for contacts of patients with known or suspected multidrug-resistant TB (ie. resistant to isoniazid and rifampicin). Treatment should be considered in those with a high probability of recent infection and an added risk factor (such as HIV co-infection). If there is a low probability of recent infection patients should be observed. When preventative treatment is indicated the consensus is that at least 2 drugs be used for 6-12 months based on DST(possibilities include pyrazidamide and a quinalone).

- **Pregnancy and lactation**

  Pregnancy itself is not thought to increase the risk of progression from LTBI to active TB and has minimal influence on Mantoux testing.

  If LTBI is diagnosed during pregnancy:
  - consider immediate treatment for LTBI if the woman is HIV-infected or a recent contact, and monitor
  - in the absence of risk factors, wait until after the woman has delivered to avoid administering unnecessary medication during pregnancy
  - supplementation with 50 mg of pyridoxine (vitamin B6) is recommended.

  No toxic effects have been reported in infants of breastfeeding mothers taking drugs for TB and the amount of anti-TB drugs delivered to infants in breast milk is minimal. Babies born to mothers with active pulmonary TB can be nursed by the mother provided that the baby immediately begins isoniazid to prevent primary TB infection.

- **HIV-positive persons**

  The choice of regimen will often be influenced by consideration of likely drug interactions, adverse effects and potential toxicity. Therefore, treatment should only be initiated after consultation with a specialist in HIV management. In general, recommendations for HIV-positive persons are similar to those for HIV-negative persons.

  The standard for preventive therapy in adult persons living with HIV/AIDS is isoniazid given daily for 9 months.

  Short course rifampicin regimines can also be used however rifabutin may need be substituted for rifampicin in cases where the latter drug is contraindicated because of potential toxicity or drug interactions. Dosage adjustment of rifabutin in these circumstances is beyond the scope of these guidelines and should be done in consultation with a specialist in HIV management.

  If the Mantoux test result is negative, treatment is recommended, in cases where the person has recent, prolonged exposure to infectious TB or if there is ongoing risk for exposure.

7.8. Monitoring of treatment and management of side effects

It is essential to ensure that all patients on treatment for LTBI are aware of the possible side effects of treatment and know what to do if they occur. The most serious potential adverse effect, hepatitis with liver failure, can usually be prevented by prompt recognition of early symptoms and appropriate action. All patients should be told to stop their anti-TB medication immediately and seek an urgent clinical review if any unexplained illness develops or if any of the following symptoms occur:

- **symptoms associated with hepatitis;** loss of appetite, nausea, vomiting, dark urine, jaundice, abdominal tenderness – especially over liver, easy bruising or bleeding, rash, persistent fatigue, weakness or fever lasting 3 days or more.
- **symptoms associated with other toxicities;** rash, easy bruising or bleeding, fever, persistent paraesthesias (tingling or numbness) of hands or feet, persistent fatigue or weakness, arthralgias, gout, gastrointestinal upset.

7.8.1. Clinical reviews and follow-up of laboratory tests

All patients taking isoniazid should be **reviewed monthly**. The indications for interrupting treatment and urgent review (above) should be reinforced at each one of these visits. Adherence to treatment, review of symptoms related to adverse drug effects and drug interactions, and the ongoing plan in relation to completion of treatment should all be discussed.

Repeat **LFTs** should be routinely ordered **at each visit** for anyone at increased risk of drug-induced hepatitis. This includes people >35 years of age; pregnant women, including those in the immediate post-partum period (ie. 3 months); HIV positive persons; alcohol drinkers and when there is a history of liver disease, including hepatitis B and C (see baseline testing above).

7.8.2. Management of common side effects

Because many of the adverse symptoms associated with drug treatment may be similar to, or coexist with those of drug-induced hepatitis, liver function tests should always be checked prior to proceeding to manage common side effects.

- **Drug induced hepatitis.** Drugs should be ceased and treatment for LTBI abandoned if the alanine aminotransferase (ALT) increases while on treatment to more than 3 times normal. In this event, LFTs should be monitored regularly (every 2 or 3 days initially) until they have begun decreasing toward normal. Specialist advice should be sought in the case of very high elevations (ie. ALT more than 10 times normal), or if any signs of acute liver failure are present. Patients with asymptomatic elevations of ALT can be monitored with more frequent LFTs (eg. 2 to 4 weekly) provided that they stay below the level of 3 times normal.

  Screening for viral hepatitis should be considered and concomitant use of hepatotoxic drugs of any type should be excluded.
- **Hypersensitivity reactions.** These usually occur within 8 weeks of initiating treatment. Minor reactions such as a slight itch that does not distress the patient may be self-limiting or require treatment with an anti-histamine (eg. loratidine 10 mg daily). The most common clinical features of hypersensitivity are rash (usually erythematous and may be macular or papular) and fever. Generalised and sometimes severe reactions may also occur and may follow the re-introduction of drug after a previous hypersensitivity reaction. For all but trivial reactions, medication should be stopped and specialist advice should be sought.
- **Gastrointestinal symptoms.** Gastrointestinal upset may occur with all anti-TB drugs. Medication should be ceased until LFT results have been checked and symptoms have subsided. Persistence of symptoms off medication for longer than 4 or 5 days should prompt a search for other causes. Reintroduction of treatment is often possible by changing the pattern of administration of medication (eg. taking before bedtime). Antacids can be used but should be avoided in patients taking isoniazid as they may interfere with the absorption of this drug. The rifampicin can then be restarted initially at half dose (increased to full dose after 2-3 days) and given after a small meal. If gastritis is persistent or severe then alternative treatment should be considered or treatment of LTBI ceased in favour of alternative follow-up (see below).

7.9. Completion of treatment and follow-up

7.9.1. Treatment success

Treatment success is defined as administration of the intended number of doses for each regimen, even if the duration is extended slightly by missed doses or minor treatment interruptions. In general, adherence to ≥ 80% of doses within the extended timeframes shown below is a reasonable indication of treatment success, provided that continuous treatment interruptions are brief. In the event of continuous treatment interruptions of 1 month or longer, active TB should be excluded by clinical examination and chest X-ray prior to fully restarting the same or different treatment regimen.

Aims for treatment success

- 9 month daily isoniazid – 270 doses within 12 months
- 6 month daily isoniazid – 180 doses within 8 months
- 9 month 3 times-weekly isoniazid – 117 doses within 12 months
- 6 month 3 times-weekly isoniazid – 78 doses within 8 months
- 4 month daily rifampicin – 120 doses within 6 months.

7.9.2. Follow-up

For those who have completed treatment for LTBI and were recent contacts of infectious TB case or likely to have been infected within 2 years

- repeat chest X-ray at end of treatment, educate patient and send letter to local doctor regarding small but possible risk of future active TB, discharge from follow-up.

For all others

- educate patient and send letter to local doctor regarding small but possible risk of future active TB, discharge from follow-up.

For those eligible for treatment of LTBI but incomplete or no treatment taken and

- were recent contacts of infectious TB case or likely to have been infected within 2 years
  - repeat chest X-ray and clinical review at 6 months, 1½ years and 2½ years, education and letter to local doctor regarding appreciable risk of future active TB.
- are lower risk patients
  - educate and send letter to local doctor regarding small but possible risk of future active TB, discharge from follow-up.

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8. CONTACT TRACING

8.1. Introduction

Every new case of TB was acquired through contact with an infectious case at some point. As the risk of disease is highest in the first 2 years following infection and disease can develop within 2-3 months of initial contact, the early identification of contacts and new cases infected by a new (index) case is the key priority for TB control programs and eventual eradication.

Once a suspected/confirmed case of infectious TB is identified the initiation of contact investigation should be prompt. Contact tracing in the NT uses a coordinated approach involving CDC staff working in partnership with hospitals and community health care providers and requires good coordination and a lot of time and effort to be effective. The process begins by evaluating those contacts at highest risk of infection and/or disease and then extending the investigation to lower risk contacts until a rate of infection no higher than the background rate for that community is found. This may range from limited examination of household contacts only in some cases through to screening of whole communities. The goal of this approach is to prioritise appropriately and to ensure that all those who will benefit from treatment of active TB or LTBI are identified as soon as possible.

8.2. The aims of contact tracing are to:

- identify new cases of active TB and initiate treatment
- identify TB-infected contacts by Mantoux testing in order to offer treatment for LTBI
- identify a source case for those index cases whose TB disease is likely to have been recently acquired (eg. where the index case is a child with any form of TB or an adult with primary progressive TB - including endobronchial, florid pneumonic and disseminated disease) (see section 8.4.5.)
- identify a source case in the case of extra-pulmonary disease (see section 8.4.5.)
- identify situations where community screening is required (Chapter 9)
- provide information and education about TB (see section 8.4.5.).

8.3. Defining the risk to contacts

The risk of a contact progressing to active TB depends on the likelihood that they have been infected by the index case as well as their own risk of progressing to active TB once infected. The **risk of disease progression** is higher in young children <5 years and individuals with underlying medical conditions: including HIV; renal failure; poor nutrition; diabetes; immunosuppression, including long-term corticosteroid therapy, and some forms of cancer (see section 7.3.1.). The **likelihood of TB infection** is affected by the infectivity of the index case, the susceptibility of the contact (eg. increased in HIV infection) and the degree of exposure, which in turn is dependent on the amount of time in contact with the index case and the environment in which that contact occurred.

8.4. Steps in Contact Tracing

1. Categorise the case according to the likely degree of infectiousness.
2. Obtain a list of contacts and categorise the contacts according to their estimated risks, ie. as high, medium and low risk.
3. Examine all high-risk contacts of pulmonary TB cases first.

4. Consider examination of medium risk (followed by low risk) contacts of pulmonary TB cases, depending on the results of the high-risk screen.
5. Whenever a case is diagnosed in an Aboriginal community setting the regional CDC unit staff should travel to the community to educate the family and close contacts, to educate and update the health service staff and to assist with contact tracing when appropriate. Likewise, this opportunity should be taken if a local Community Health Centre is involved in a patient's care.

8.4.1. Defining the infectivity of the index case

Information should be collected from the index case regarding:

- the presence, duration and nature of cough (productive/non-productive)
- the TB disease site(s) – pulmonary, laryngeal; and chest X-ray results (extent of disease, whether cavities are present)
- the sources, dates and results of microbiology tests (including sputum smears and cultures).

The index case infectivity can then be categorised as:

- **High** – Spontaneously collected sputum is smear-positive for AFB
- **Medium** – Smear negative, culture positive sputum samples or bronchial washings smear-positive **or** smear negative, nucleic acid detection positive
- **Low** – Clinical pulmonary TB **but** sputum smear and culture negative
- N**egligible** – Extra-pulmonary TB only.

It may not be possible to categorise sputum smear-negative index cases, unless NAAT is available, as medium or low infectivity until the results of culture are known (usually 4-6 weeks). The pace and extent of contact tracing for these cases will initially need to be guided by other factors including the degree of exposure (below) and the susceptibility of the contact to disease progression if infected (see below). Some sputum smear-positive cases will turn out to have non-infectious non-tuberculous mycobacteria (NTM) on culture. Unfortunately, this cannot be predicted on the initial sputum smear so initial contact tracing will need to proceed in most cases on the basis that the infecting organism is assumed to be *M tuberculosis*.

8.4.2. Defining the degree of risk in contacts

A list of close contacts, including names, age, addresses, telephone numbers and possible HRNs, should be compiled first.

Locations to be considered include homes, work, school and places of leisure (eg. church groups and bars). Basic environmental factors should be considered including size of enclosed spaces, crowding, adequacy of ventilation and exposure to UV light (includes sunlight - which kills MTB).

Contacts are to be categorised into the:

- **high risk group -** frequent, prolonged and close contact within the 3 months preceding diagnosis, or as far back as a clear history of active TB disease. This generally means ≥ 8 hr of cumulative physically close contact to the index case. This group includes:
  - all people living in the same household or dwelling
  - relatives and friends who have frequent, prolonged and close contact
  - any others who have had prolonged contact in a closed environment especially if small, poorly ventilated and not exposed to sunlight. (eg. workmates who daily share the same indoor small work area).

This high risk group should also include contacts with immunosuppresion and children aged <5 years.

- **medium risk group -** frequent but less intense contact. This group includes:
  - other close relatives, friends, schoolmates, work colleagues and neighbors.
- **low risk group.** This group includes:
  - other contacts at school or in the workplace or social environments.

  Obtaining details of low risk contacts is not necessary initially and need only be pursued if there is evidence of transmission in the high and medium risk groups.

8.4.3. Screening of High Risk Contacts

In setting priorities for contact screening, the infectiousness of the index case is the most important determinant. Rapid contact tracing is clearly indicated when the TB case has a productive cough, there is x-ray evidence of cavitary disease, and the sputum smear for AFB is positive. The investigation begins with those most likely to have been infected, those in the high risk group. As a guide, if 10 or more high exposure risk contacts have completed screening and no evidence of TB infection is detected, then it will usually be unnecessary to screen more remote contacts. In all cases, the aim should be to complete contact tracing within 3 months, unless community screening in needed.

Ideally:

- High risk contacts of highly infectious cases should be screened within 7 days of diagnosis (If AFBs are more likely to be an NTM rather than TB an extension of the time can be considered until PCR available).
- High risk contacts of cases of medium/low infectivity should be screened within 2 weeks of diagnosis.
- High risk contacts of cases with negligible infectivity should be screened once only.
- Contacts of children with active TB (who are usually smear-negative) and of adults with primary progressive TB or immunosuppressed adults should be screened with an emphasis on detecting the active source case, as infection in these cases is likely to have been recent.
- Screening of contacts of index cases with smear-positive NTM infection can usually be discontinued once culture results are known (MTB is excluded) or NAAT results are available, however, some individuals identified to be reactive on Mantoux testing may require follow up to be continued.
- Community screening should be considered in the event that an outbreak is suspected (ie. more secondary cases or TB-infected contacts than predicted based on the infectivity of the case and known exposure to contacts). This will be coordinated by the TB control unit involved in screening (Chapter 9).

8.4.4. Screening of Medium and Low Risk Contacts

- If evidence of transmission is discovered in high exposure risk groups then screening of medium exposure risk contacts will proceed.
- If <10 close contacts have been screened and the index case is high or medium level infectivity then medium contacts will be screened.

Screening should progress to the low risk group only if there is evidence of transmission in the medium risk group.

8.5. Screening Procedures

The mainstay of screening is a careful clinical evaluation and Mantoux test for potential contacts. A chest X-ray may be required for selected individuals. In populations with a high rate of BCG vaccination and exposure to NTM (eg. NT Aboriginal people, migrants from high prevalence countries), it may be impossible to determine the cause of Mantoux test reactivity. However, the vast majority of Territory school children aged 10-14 years screened in these groups have either a 0 mm or <10 mm Mantoux test result. As the risk of transmission of MTB to contacts increases, so does the likelihood that a Mantoux test result ≥10 mm diameter (≥5 mm in children <5 years and people with immune suppression) represents true infection with TB regardless of prior BCG status. Because the risk of disease is highest in recently infected contacts, the BCG status of an individual should not influence decision making in contacts of a highly or moderately infectious index case or contacts in a high or moderate exposure risk group. The decision in lower risk individuals must be individualised (Chapter 6).

It is important to remember that it can take 2-10 weeks for a person infected with MTB to develop an immune response that can be detected by Mantoux test. Therefore, the Mantoux test should be repeated at least 10-12 weeks following the last contact with an infectious index case in individuals who undergo earlier screening with Mantoux testing. It may be difficult to differentiate a boosted response (as seen with 2 step Mantoux test – Chapter 6) at this second visit from newly acquired infection with MTB. However, given the increased risk of disease in recently infected contacts and variable nature of boosting, it is wisest to assume TB infection if this second Mantoux test fulfils the criteria for a positive response.

8.5.1. Protocol for first ± second screening visit(s)

Interview contact to clarify past history related to TB, exposure risk, current risk factors for developing TB disease and potential symptoms of TB (Chapter 2).

Examine for signs of active TB (Chapter 2) and BCG scars.

If active TB suspected, then discuss with TB control unit urgently and institute infection control measures (Chapter 3).

If previous Mantoux test results were not regarded as indicating infection with MTB or are unknown, then perform and interpret Mantoux test according to guidelines in Chapter 6.

- If the Mantoux test is interpreted as negative for TB infection **and** the test has been done ≥10 weeks following last exposure to infectious index case, then discharge with no further routine follow up.
- If the Mantoux test is interpreted as negative **but** <10 weeks has elapsed since last exposure, then organise for a repeat Mantoux test between 10-12 weeks from the last exposure according to this same protocol. This will not be required if the index case was of negligible infectious risk (in which the main reason for screening is to detect the source case).
- If the Mantoux test is interpreted as positive on either occasion, then organise a chest X-ray and review by medical officer at TB control unit. In most cases, these individuals will be offered treatment for LTBI (Chapter 7) or further investigations to diagnose active TB.
- If previous Mantoux test result(s) were regarded as positive indicating infection with MTB, then repeating the Mantoux test will not provide any useful information. Such individuals are possibly less likely to develop disease following a new exposure but this risk will be higher in early childhood or in the setting of poor health. A chest X-ray should be ordered and the person referred to the TB control unit for evaluation. Further management will depend on the infectiousness of the index case and the degree of risk in the contact.

8.6. Special circumstances

Children <5 years and others at highest risk of early disease progression (eg. HIV infection, significant immune suppression) will usually require preventive treatment even if their first Mantoux test result is negative until the result of the second Mantoux test is known. They should be referred to the TB control unit for medical evaluation in all cases. Children will usually be able to discontinue preventive treatment if the second Mantoux test is negative, however immunosuppressed adults will often need to complete the treatment because of the higher risk of false negative Mantoux test reactions.

Pregnant women contacts should be screened by Mantoux testing but if a chest X-ray is required then it should be deferred until after pregnancy along with treatment for LTBI.

If however, the woman is symptomatic or develops symptoms during pregnancy, then she should be referred for medical evaluation and chest X-ray immediately to rule out active TB disease.

MDR-TB - The National Tuberculosis Advisory Committee (NTAC) has produced an information paper on multi-drug resistant TB in 2007 (see Bibliography).

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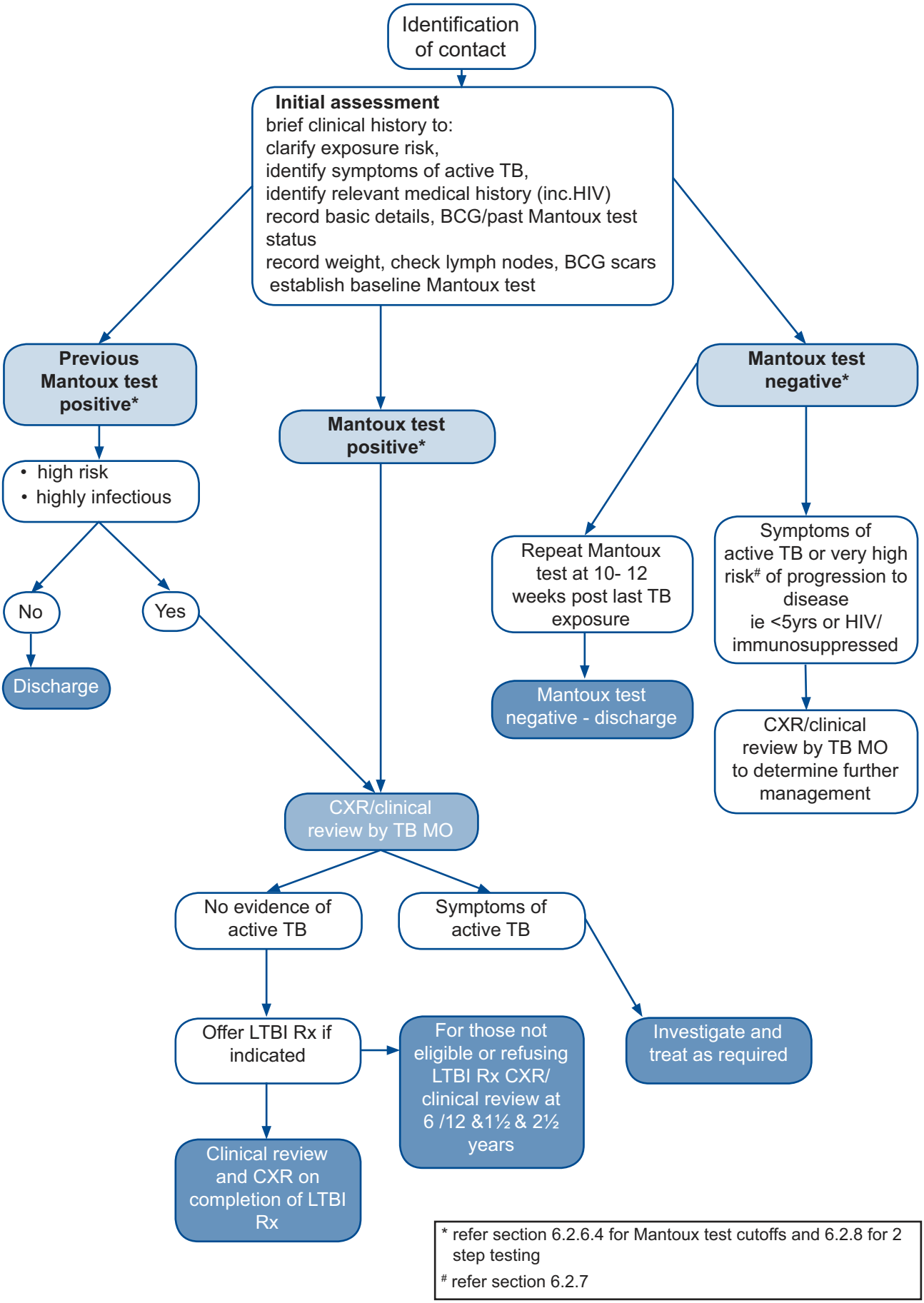
Contact tracing



* refer section 6.2.6.4 for Mantoux test cutoffs and 6.2.8 for 2 step testing

refer section 6.2.7

9. COMMUNITY SCREENING

Community screening is not meant to replace focussed contact tracing and in most cases will not be required. The indications for community screening are:

- when secondary cases are detected in a routine contact tracing investigation
- when 2 or more cases of active TB are diagnosed within 1 year in a community
- when the number of infected contacts exceeds that predicted based on the assessment of index case infectivity and exposure history
- when a case is detected in a "secondary community" named by an index case.

Depending on the size of the community involved, screening may involve the whole community or in large communities, be restricted to particular (eg. family, age or language) groups.

9.1. Preparation for community screening

The transmission of TB in the community is a problem that requires community ownership and community action. Health care providers, including the TB control units, need to share information about TB, its impact on families and community members and how it can be prevented and cured.

The assistance and participation of community elders, councils and local health care providers is essential and should be negotiated prior to carrying out screening. Community involvement is essential for the success of the program.

The TB control unit is primarily responsible for coordination and provision of resources for screening and education.

A population list for the community being screened and where possible a list of patients with chronic diseases is essential to identify all those at risk.

Data collected by the TB control unit should be analysed and reported back to the groups identified above at the completion of screening.

9.2. Procedures for community screening

The mobility and size of the population may make it difficult or impossible to screen everybody with Mantoux testing, therefore screening should be prioritised. As with contact tracing, the highest priority is to identify undiagnosed TB disease, followed by identification of individuals at the highest risk of developing disease if they have TB infection. In practice, this latter group includes children (especially those <5 yr) and those with underlying poor health. The aim of this approach is to prescribe treatment for those most likely to benefit from it and to concentrate on helping these people adhere to the treatment, which will hopefully benefit the whole community by decreasing transmission.

9.2.1. Methods

There are 2 methods of community screening based on the capabilities of the community involved.

9.2.1.1. Method A

In a stable community where LTBI can be identified and treated Method A should be followed.

Initial screening

- This provides an opportunity to identify close contacts who may have been missed or misclassified during contact tracing.
  - Urgent chest X-ray and clinical review for those with symptoms or signs of TB (with appropriate infection control measures [Chapter 3]).
  - Mantoux testing for everybody else. Note that the cutoffs used as indicating infection might be larger than for contact tracing, especially for BCG vaccinated subjects, as this population is on the whole at lower risk than identified contacts of an infectious index case.
  - Chest X-ray and clinical review for those with Mantoux test evidence of TB infection (Chapter 6).
  - Treatment for LTBI if indicated (Chapter 7).

Follow up

- Chest X-ray should be repeated at the end of treatment for LTBI with no further follow up if normal.
- If treatment for LTBI is declined or not completed, then a repeat chest X-ray should be done after 6 months then yearly for 2 years.

9.2.1.2. Method B

In a community with a mobile population which has less resources, or where immune suppressive factors are common and follow up of treatment for LTBI is difficult, the following is recommended.

Initial screening

- This provides an opportunity to identify close contacts who may have been missed or misclassified during contact tracing
- Urgent chest X-ray and clinical review for those with symptoms or signs of TB (with appropriate infection control measures [Chapter 3]).
- Mantoux test all children ≤10 yr of age (≤15 yr if resources permit).
- Chest X-ray and clinical review for those children with Mantoux test evidence of TB infection (Chapter 6). Treatment for LTBI if indicated (Chapter 7).
- Chest X-ray and clinical review for those >10 yr of age, to detect active disease.

  Note - Children <5 yr of age are the highest priority for Mantoux testing and treatment of LTBI. If resources do not allow for Mantoux testing in the 6-10 yr age group, then chest X-ray and clinical review (as above) should be done instead in this age group.

Follow up

- For those who have a positive Mantoux test, Chest X-ray should be repeated at the end of treatment for LTBI with no further follow up if normal.
- If treatment for LTBI was recommended after initial screening on the basis of Mantoux test or chest X-ray, but was declined or not completed, than a repeat chest X-ray should be done after 6 months, then yearly for 2 years.
- For those Mantoux test negative or with a chest X-ray only, repeat chest X-ray and clinical review in those >10 yr of age after 6 months and discharge if normal.

Further follow up

- If further cases are being found, and resources permit, then further follow up of those children who declined or did not complete treatment for LTBI and all of those 10 yr and over whose Mantoux test status is unknown with a chest X-ray and clinical review yearly for the next 2 years is advised.

9.3. Documentation

Those carrying out the community screening should establish an appropriate database, document the screening, the results and the follow up and a copy of this report should be kept in an electronic form in the responsible CDC unit. Information from the community screen should also be entered onto CCIS to provide an important resource for the follow-up of potential TB cases.

10. SCREENING IN SPECIAL GROUPS

10.1. School screening

10.1.1. Introduction

Tuberculosis screening in schools using the Mantoux test has previously been scheduled for remote communities who have had cases of active TB in the previous 10 years and was also carried out in all urban settings. The aim was to identify Mantoux test positive children who were at risk of LTBI and to provide clinical review, chest-xray and possible treatment for LTBI. Between 2003-2005, 2.6% of Indigenous students and 9% of overseas born students screened were identified as Mantoux test positive. These relatively low rates in Indigenous students have led to a revision of the school-screening program.

10.1.2. Aims and outcomes

The main aim of Mantoux test school screening is to reduce the rate of TB in the community by diagnosing and treating LTBI. Its success is proportional to the **number of students diagnosed with LTBI who complete treatment**, and this should be considered as the primary outcome measure. A secondary aim is to monitor the level of TB infection in the community so as to guide planning and implementation of TB control services. Although not intended for case finding, active TB cases are occasionally detected during school screening, which necessitates further contact tracing and follow-up.

10.1.3. Target group

Mantoux test screening is indicated in the following groups of students:

- overseas-born students attending urban schools
- Indigenous students in urban schools
- students in communities where there has been a case of pulmonary TB in the previous 3 years and where resources allow in communities where there has been a recognised higher historical rate of TB in the previous 10 years.

These recommendations are based on data that shows primary outcome measures are best achieved in these groups.

In urban areas screening is carried out in Year 8 while in remote areas is incorporated into the Healthy School Aged Kids (HSAK) school screening for 10 year olds.

10.1.4. Interpretation of Mantoux test and treatment for LTBI

Mantoux tests should be administered and interpreted according to Chapter 6. All students with Mantoux test reactions of ≥10 mm require a chest X-ray and review. Treatment for LTBI should be recommended and provided according to Chapter 7.

10.1.5. Planning and organisation

Organisation is the key determinant of the success of Mantoux test school screening programs. The ultimate goal of screening is to supervise the completion of treatment for LTBI. The resources required to perform a school screening depend on the location and should be discussed with CDC or TB Unit staff prior to screening.

10.1.5.1. Human resources

The HSAK program co-ordinates school screening in all communities. Communication between the TB and the HSAK program will identify those communities that require screening. For urban centres direct communication can be made between the TB unit and the school nurse.

A CDC staff member should be involved in the school screening process.

Local health staff or school health staff are normally responsible for the following tasks:

- liaising with the school to organise the screening and obtain consent from parents
- assisting with organising follow-up
- ongoing TB education of students and families
- assisting with supervision of treatment, where needed
- identifying family contacts of those students identified as Mantoux test positive.

CDC TB staff are normally responsible for the following:

- administration and reading of the Mantoux test
- providing advice concerning planning, resources and infrastructure required for screening programs
- organising and performing all follow-up (including chest X-rays)
- recommending and prescribing treatment for LTBI
- recording the data
- educating other staff about TB
- organising Mantoux testing of contacts of Mantoux test positive students.

Supervision of treatment is usually done by local health staff following liaison with CDC but this may vary as required.

10.1.5.2. Health service infrastructure

It is important to consider the local health service infrastructure prior to commencing school screening. Although the requirements are minimal, some remote communities or outstations may have their screening performed by mobile clinics which will need to bring the infrastructure with them. It is important to consider the local cold chain, the availability of PPD and insulin syringes, local and immediate disposal of sharps and the hardware required for screening (a room, tables, chairs etc).

10.1.5.3. School attendance

Performing screening programs through schools (as distinct from local GPs or health centres) makes it logistically easier to contact most children in the target age group. However, if school attendance is very poor the effectiveness of this approach is lost and screening, in these high risk communities, should occur through the community health service with assistance from the TB Unit.

10.1.6. Contact Tracing of Mantoux test positive students

Prevention of disease and increased compliance with LTBI treatment can be increased if several members of a family unit are being treated at the same time.

If a child is identified as having LTBI all family contacts should be screened to either identify a case of active disease or to identify other people with LTBI.

Treatment for LTBI with isoniazid should be offered to all members of the family where appropriate (see Chapter7).

10.1.7. Barriers to successful outcomes

Review of past Mantoux test results from school screening has revealed that there are many barriers to achieving successful outcomes of the program and it is worthwhile having them in mind during the planning phase. Recognised barriers are listed below.

Consent

- Gaining informed consent from parents is important, however, it can be time-consuming and difficult so it pays to have the process streamlined. In some high schools, consent is obtained at the time of enrolment into school.

Administering and reading Mantoux tests

- Because Mantoux testing requires a second visit to have the result read, some students test will be missed if they are absent on the day it is read. They may need to be contacted out of school to get their Mantoux test read. The efficiency of the program is reduced if there is a large proportion of students regularly absent from school.

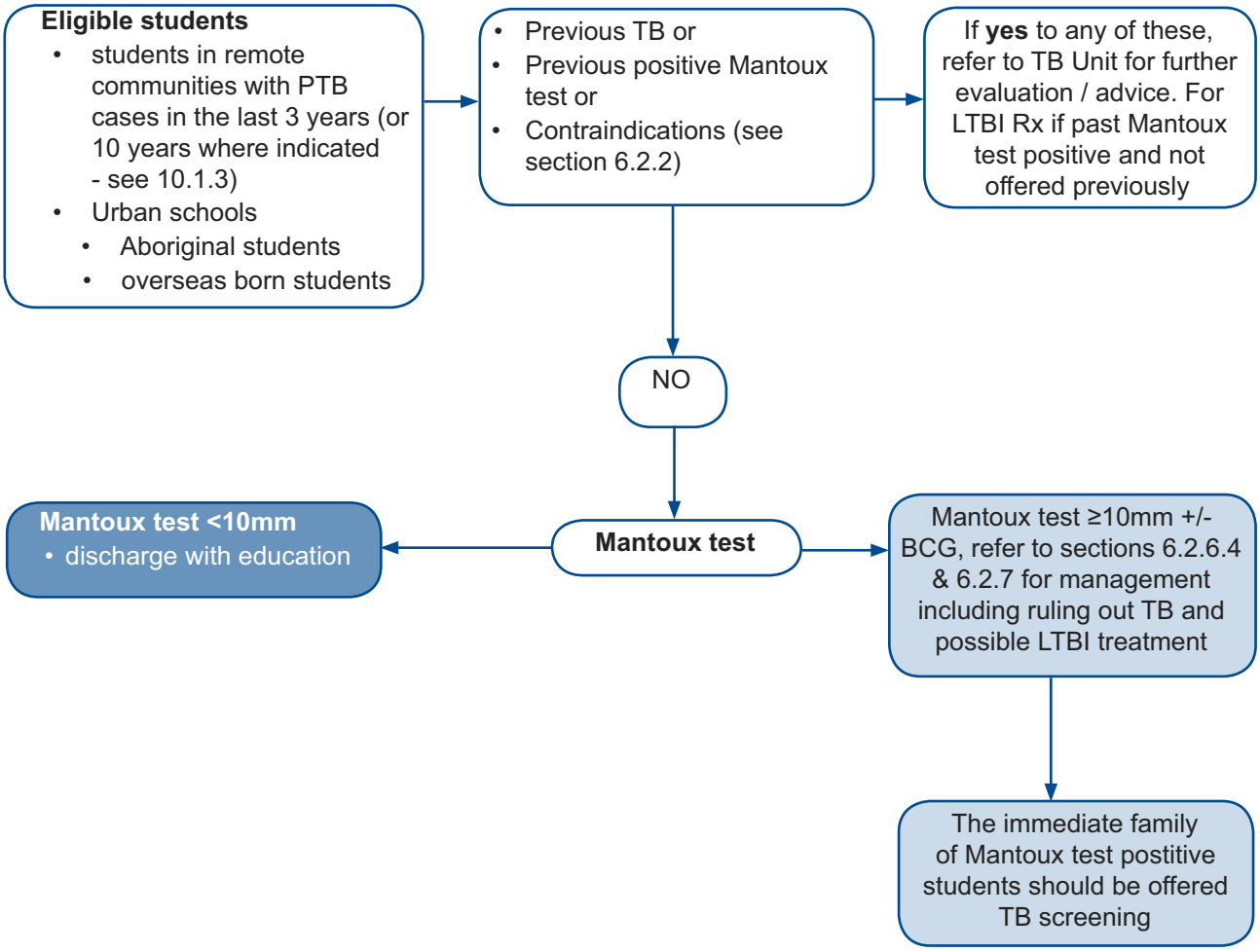
Follow-up and chest X-ray

- In larger remote communities, it is usually more efficient to arrange X-rays and follow-up in the community. This requires resources and planning and often takes several days to complete. Moreover, it relies on the availability of a radiographer and possibly mobile X-ray equipment from the local hospital, which can result in unforeseen delays.

Education, counselling and provision of treatment for LTBI

- In the absence of contra-indications **all students with LTBI should be offered treatment.** The decision (by students and parents alike) to start treatment needs to be taken with a full understanding of the natural history of LTBI, the risk of progression to active TB, the risk of side effects with treatment and the requirements for supervised follow-up. In most situations this will need to be done across language and/or cultural barriers which can be both difficult and time-consuming. The use of Aboriginal Health Workers, interpreters, visual aids, diagrams and other resources available from CDC may assist.

School screening flowchart for TB Control Unit



10.2. Health care workers and other staff at occupational risk of TB

Screening for TB is recommended for anyone who engages in direct contact with people at risk of having active TB. Such screening for NT Department of Health and Community Services (DHCS) staff is a **compulsory** component of employment conditions. Other workers at risk who are not employed by DHCS are **strongly recommended** to undergo the same screening procedures as outlined below. These guidelines cover staff, volunteers and students. Employers/managers are encouraged to provide education to their personnel in relation to the following recommendations. Screening and any necessary treatment is provided free to employees of both the public and private sectors.

10.2.1. Components of TB education program

It is recommended that all staff, students and volunteers who may potentially be exposed to people with active TB receive education about TB, and the rationale for screening, appropriate to their particular employment circumstances. This should be an integrated part of the induction process for new employees whether full time or casual.

Education should include the following:

- how TB is transmitted (refer section 1.1.)
- the natural history of TB infection (refer section 1.3.)
- clinical features of active TB (refer section 2.2.)
- the importance of prompt diagnosis (refer section 1.4.) and isolation (refer section 3.1.) for patients with infectious active TB
- measures that can be taken to prevent acquisition of TB, both at the personal and institutional level (refer section 3.1.)
- the role of Mantoux testing and regular screening programs (refer section 6.2. and below)
- procedures for contact tracing, referral, treatment of LTBI and counselling for people infected with TB during the course of their employment
- the policies and procedures of the institution regarding TB prevention and control.

10.2.2. Reasons for screening

- To screen employees for LTBI so that appropriate counselling, follow-up and possibly treatment (Chapter 7) can be offered.
- To establish a Mantoux test baseline for the employee that will enable future Mantoux tests done for screening purposes or for contact tracing to be interpreted more accurately.
- To identify possible active TB cases. This is for both the employees health and to reduce the possibility of the employee infecting patients or other staff.

10.2.3. Recommendations for DHCS and other staff at occupational risk

All health staff or other staff at occupational risk who engage in **direct patient contact** or **handling of potentially TB infected materials** are advised to have a baseline Mantoux test unless contraindicated. This is a **compulsory** pre-requisite to employment for DHCS staff. The requirement for a baseline Mantoux test might be waived if a documented two-step Mantoux test was done within the previous 3 months.

10.2.3.1. Contraindications to baseline Mantoux tests are:

- previously confirmed TB infection (ie. a Mantoux test and/or chest X-ray consistent with LTBI) or active TB disease. This includes previous treatment for LTBI or active TB
- previous Mantoux test causing severe skin reactions (vesiculation, ulceration, necrosis)
- previous Mantoux test causing a severe immediate hypersensitivity reaction
- relative contraindications (that require rescheduling of baseline Mantoux testing) such as:
  - short-term immunosuppressive therapy that may cause false-negative response
  - recent live virus vaccination (within 4 weeks).

10.2.3.2. Health personnel with the NT public service who must undergo TB screening and those outside the public service recommended for TB screening include:

- health care workers
- Aboriginal Health Workers

- doctors
- nurses
- physiotherapists
- radiographers
- cleaners
- admissions clerks etc
- laboratory staff who handle suspected or known TB materials (eg. specimen reception, microbiology, histopathology)
- mortuary staff.

10.2.3.3. Other staff at occupational risk who should undergo screening include:

- prison officers
- nursing home staff with direct patient contact
- staff of drug and alcohol rehabilitation centres
- staff who care for the homeless (eg. night patrol, homeless shelters)
- ambulance officers
- staff caring for asylum seekers, illegal fishpersons and refugees in institutional settings
- customs and quarantine staff
- interpreters.

10.2.3.4. Baseline Testing

All staff commencing work with DHCS and involved in patient care or pathology work are required to have a Mantoux test at the beginning of their employment.

People working in high-risk areas are encouraged to have a two-step test. These high-risk areas include:

- emergency departments
- wards that care for TB patients
- bronchoscopy theatre
- pathology
- mortuary
- ICU
- TB clinics.

The **two-step test** (ie. an initial Mantoux test followed by a second test 1-3 weeks later if the first is <10 mm (refer section 6.2.8.) is given in these cases unless the individual has had a Mantoux test in the previous 12 months. Two-step tests provide a more accurate baseline in the case of previous BCG vaccination or distant infection with mycobacteria (TB or NTM), which may cause a boosted response (refer section 6.2.8.) on the second of the two-step tests. An initial two-step test will decrease the chance that the next Mantoux test (done for annual/2 yearly screening or contact tracing) is misinterpreted as representing conversion due to TB infection.

For example: If a single (one-step) Mantoux test is done at baseline (and is negative) and a repeat test done for contact tracing or screening afterwards shows conversion to positive, then it is difficult to know whether the positive test represents recent TB infection or a boosted response of the baseline one-step Mantoux test. This may lead to unnecessary treatment with anti-TB

medication as recently infected individuals are at highest risk. A baseline two-step test eliminates the possibility that the repeat test is a boosted response and therefore potentially limits the number of people who are advised to take treatment for LTBI. **At-risk personnel should be strongly advised that it is in their own interest to have a baseline two-step Mantoux test.**

- A careful **clinical history** should be taken at the time of the baseline Mantoux test directed at uncovering symptoms and signs of possible active TB (eg. prolonged cough > 3 weeks, fever, night sweats, weight loss, lymphadenopathy; (refer section 2.2)).
- A **baseline chest X-ray** should be done instead of a Mantoux test for those in whom a Mantoux test is contraindicated (above) unless a chest X-ray has been done within the previous 12 months, in which case, the X-ray films or report may be accepted as a suitable alternative.
- Staff with a past or present baseline or follow-up **Mantoux test ≥10 mm** (ie. second reading of a two-step test) must be **referred to the nearest TB clinic** or CDC Unit for a clinical review to assess the likelihood of TB infection (Chapter 6). In most cases this will also involve a chest X-ray. If they have had a chest X-ray within the previous 12 months, then the film or its report may be an acceptable alternative to a repeat chest X-ray. These staff will receive advice on whether or not treatment for LTBI is recommended and the need for ongoing follow-up as appropriate.

10.2.3.5. Ongoing Screening

Staff with a **baseline Mantoux test <10mm** (ie. second reading of a two-step test) should be advised to undergo **regular annual or biennial (ie. every 2 years) screening** with a one-step Mantoux test depending on the likely degree of contact with TB patients.

Second yearly screening is generally appropriate for all lower risk patient care settings and community care facilities, as well as other workplaces with occupational risk as identified above.

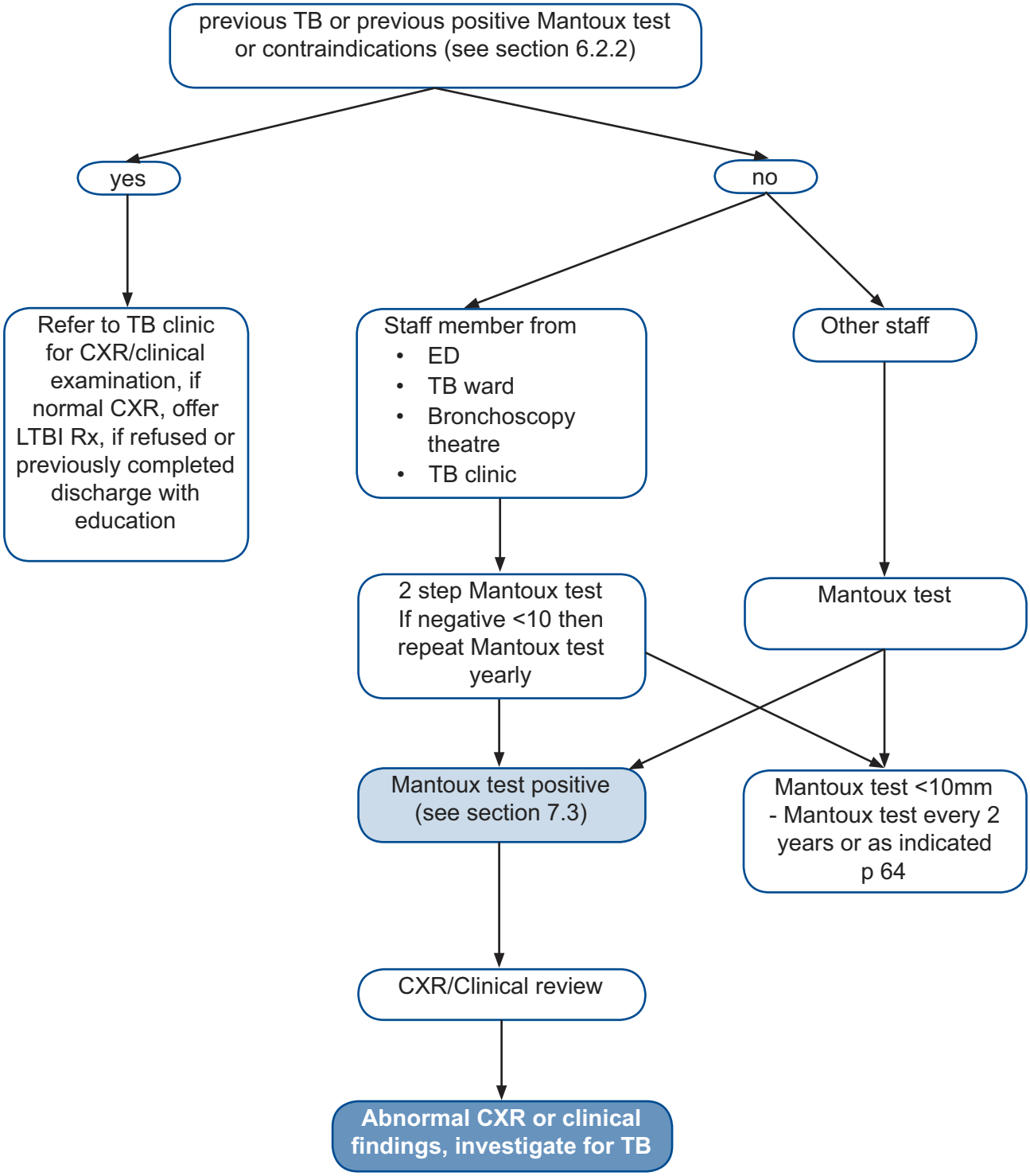
Those at high risk who require annual screening include those working in:

- bronchoscopy theatres
- wards that care for TB patients
- TB clinics
- radiology departments
- physiotherapy (eg. if involved in collection of induced sputums)
- intensive care
- emergency departments
- laboratories handling infected TB materials (eg. specimen reception, microbiology, histopathology)
- a mortuary
- prisons
- staff caring for asylum seekers, foreign fisherpersons and refugees.

Annual or biennial screening should be rescheduled based on the above guidelines if interrupted by an earlier Mantoux test done as part of a contact tracing investigation.

It is strongly recommended that staff have an exit Mantoux test (if not contraindicated; above) at the **termination of employment**. Staff should be provided with copies of all their Mantoux test results, chest X-ray reports and information regarding treatment or follow-up for LTBI.

Screening for Health Care workers and others at occupational risk of TB



10.3. Chronic renal failure and dialysis patients

In 2005, there were approximately 180 people undergoing dialysis and 50 people living with a renal transplant in the Top End of the NT, and approximately 166 and 25 people respectively in Central Australia. Around 20 people commence dialysis annually in the Top End with around 35 people commencing dialysis in Central Australia.

Significant immunosuppression is present once a person's glomerular filtration rate (GFR) has declined to **20ml/min**. This threshold of GFR also indicates the need for referral to a renal unit, with case management including construction of a fistula and commencement of erythropoietin (EPO) in anticipation of eventual dialysis. Dialysis is usually started once the GFR declines to <**10ml/min**.

Compared with the general population, the relative risk of active TB is 37 times higher for those with a renal transplant, and 10 to 25 times higher for those undergoing haemodialysis.

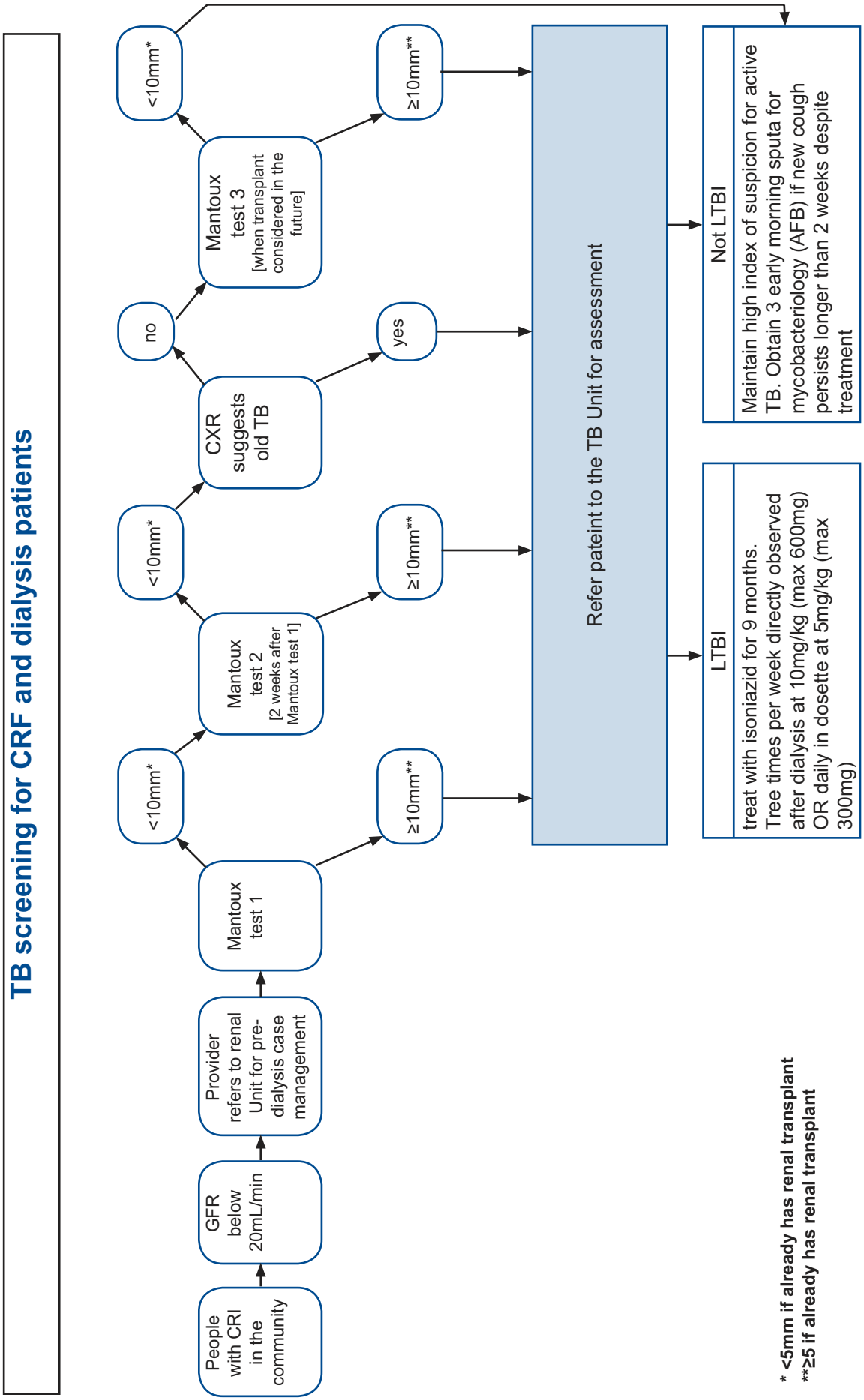
Patients with chronic renal insufficiency (CRI) and a GFR <20 ml/min should have a **two-step** Mantoux test (refer section 6.2.8.) as part of their routine case management as cutaneous anergy (ie. false negative Mantoux test) in this setting is common. Results ≥5 mm are considered positive following renal transplant, therefore the second step of the two-step test need only be done if the first step is <5 mm in transplant patients.

Renal patients should be referred for further assessment in the TB Unit (clinical review and chest X-ray) if either the first or second step of the Mantoux test is ≥10 mm in patients with CRI who have not been transplanted, or ≥5 mm in transplant patients.

Patients with negative Mantoux test but with evidence of past or present TB infection on chest X-ray (eg. upper lobe fibrosis or consolidation, calcification or volume loss) should also be referred to the TB Unit. Patients with negative Mantoux test and normal chest X-rays should be re-tested if a decision is made later for a renal transplant. This is to ensure that subsequent infection with TB has not occurred, as the risk of reactivation is markedly increased in the setting of the profound immunosuppression that accompanies the transplantation process.

If LTBI is diagnosed and there are no significant contraindications, treatment with 9 months of isoniazid should be commenced without delay. Directly observed treatment 3 times per week on dialysis days can be utilised at a dose of isoniazid 10 mg/kg (maximum 600 mg per dose). If daily dosing is used the dose of isoniazid is 5 mg/kg (maximum 300 mg per dose). Pyridoxine 25 mg is given with each dose of isoniazid to prevent peripheral neuropathy.

The assessing TB Unit doctor should correspond with the appropriate renal unit physician about the diagnosis of LTBI and the recommendation for treatment. The renal physician will then organise the prescription using the unit's computerised system.


TB screening for CRF and dialysis patients
People with CRI in the community
GFR below 20mL/min
Provider refers to renal Unit for pre-dialysis case management
Mantoux test 1
<10mm*
≥10mm**
Mantoux test 2 [2 weeks after Mantoux test 1]
<10mm*
≥10mm**
CXR suggests old TB
no
yes
Mantoux test 3 [when transplant considered in the future]
<10mm*
≥10mm**
Refer pateint to the TB Unit for assessment
LTBI
treat with isoniazid for 9 months. Tree times per week directly observed after dialysis at 10mg/kg (max 600mg) OR daily in dosette at 5mg/kg (max 300mg)
Not LTBI
Maintain high index of suspicion for active TB. Obtain 3 early morning sputa for mycobacteriology (AFB) if new cough persists longer than 2 weeks despite treatment
* <5mm if already has renal transplant
**≥5 if already has renal transplant

10.4. People born overseas (migrants)

Persons born overseas constituted 86% of Australia's TB notifications in 2005, the proportion steadily increasing from 60% in 1986. Among the overseas born, the highest rates are in those originating from countries with a high incidence of TB, and occur in the first few years after migration.

Migrants account for approximately 16% of the NT population, many coming from countries known to have an extremely high rates of TB, such as Indonesia, East Timor, Vietnam, the Philippines, Papua New Guinea and Sub Saharan Africa. Over 50% of TB cases in the NT in 2005 occurred among persons born overseas, therefore **screening should be offered to all new migrants to Australia.**

10.4.1. Screening to be offered to all new migrants to Australia and can be achieved by:

- education and contact with the migrant population
- following up family members and household contacts of people who have arrived in Australia under a Commonwealth TB Undertaking (see below)
- screening overseas-born children in school (refer section 10.1.3.)
- facilitating screening of all refugees on arrival in the NT
- screening health care workers on commencement of employment with DHCS.

10.4.2. Special considerations

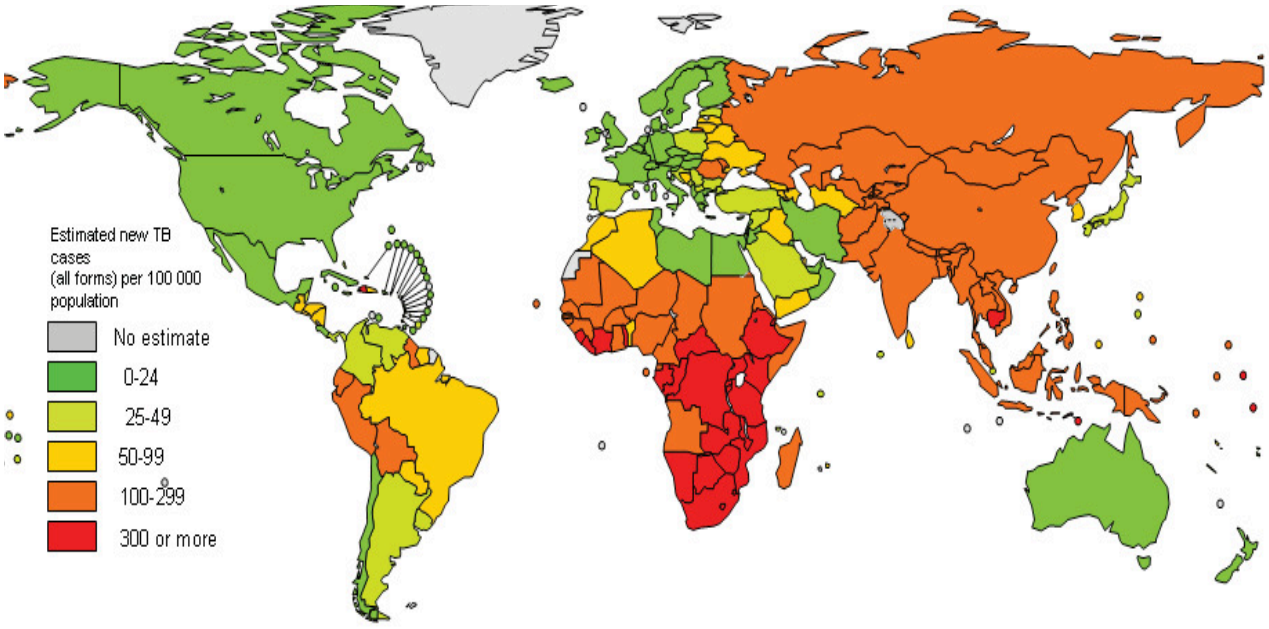
- Language and cultural considerations. An interpreter may be needed.
- Cultural barriers to prevent presenting for screening or if symptoms of active TB.
- Concern regarding the cost of health care. Diagnosis and treatment for TB is free in Australia without restriction.
- Unfounded fears regarding the possibility of deportation if diagnosed with TB.

10.4.3. TB Undertakings (TBUs)

Some migrants on arrival in Australia are required to comply with a health undertaking for TB, as coordinated by the National Health Clearances Unit. TBUs usually result from an abnormal chest X-ray report, an inadequate standard of chest X-ray from the country of origin, or following past treatment of TB. People on TBUs are required to report to a TB Unit within 25 days of arrival in Australia.

- All migrants on a TBU require a chest X-ray and clinical review.
- If the chest X-ray is normal, or has changes unrelated to TB then no further follow-up is required. However, the first visit to a TB Unit is an opportune time to offer Mantoux testing to recently arrived migrants from high risk countries, as well as to other family members or friends in a similar situation.
- In the setting of a positive chest X-ray and/or positive Mantoux test, treatment for LTBI should normally be offered (Chapter 7). If isoniazid is not given or is incomplete, then patients should be followed up with repeat chest X-ray and clinical review at 6 months, 1½ years and 2½ years, followed by education and a letter to the local doctor regarding appreciable risk of future active TB.
- If past treatment for TB was given and there is no evidence of active TB on examination or X-ray, then follow-up should continue with clinical reviews and X-rays for 5 years, at the end of which time education should be given about the future risk and presentation of recurrent disease.

World: Estimated new TB cases 2005*



* Source: World Health Organisation. Public Health Mapping and GIS Library. http://gamapserver.who.int/mapLibrary/Files/Maps/TB_newcases_2005.png. accessed November 2007.

- The TB Unit doctor should promptly forward a letter to the Health Undertakings Service (HUS) confirming the patient's attendance, and detailing the findings and the plans for treatment or follow-up. This will avoid the patient being further approached unnecessarily by the HUS.

10.4.4. Follow Up of New Arrivals

Newly arrived migrants who do not fall into the category of TBUs will also benefit from screening. Currently 2 further groups are formally referred for screening:

1. recently arrived refugees as part of their arrival medical review; and
2. health care workers when they commence work with DHCS.

All migrants from high prevalence TB countries are recommended to be screened and treated for LTBI. This beneficial screening relies on awareness of such screening services by newly arrived migrants or referral to screening services by NT health care professionals.

- If a positive Mantoux test is detected, a chest X-ray and clinical review is required.
- Free diagnosis and treatment for LTBI should be offered to recently arrived migrants.

- If isoniazid treatment is not given or is not completed, then patients should be followed up with repeat chest X-ray and clinical review at 6 months, 1½ years and 2½ years.

10.5. Prisoners in Correctional Facilities

10.5.1. Introduction

In the NT there are currently 2 primary detention populations:

- prisoners in the NT's Correctional Facilities
- Illegal Foreign Fisherpersons (IFF) detained at either the Northern Immigration Detention Facility (NIDF) or Berrimah Correctional Facility in Darwin.

This section will address all prisoners in correctional facilities, including IFFs. For IFF detained at NIDF, and for other detention populations, see section 10.6.

Residents of correctional facilities are at an increased risk of TB compared with the general population. The primary reason for this is that prisoners disproportionately represent groups with a high burden of TB disease. These groups include the homeless, malnourished, overseas-born, Indigenous Australians, mentally ill and substance abusers. Indigenous Australians in particular are over-represented in NT prisons. In the quarter to March 2006, 82% of the daily average adult prison population, and 94% of the juvenile prison population, were Indigenous. By comparison, 29% of the 2006 NT population was Indigenous.

The past decade has also seen an influx of foreign nationals, particularly Indonesians, into NT prisons. Initially this population group comprised those charged with people smuggling offences. From 2000-2002, just over 20% of the NT prison population were classified as 'people smugglers'. Since then, this population has been declining and has been replaced by IFF apprehended off the Northern Coast of Australia. Of 1784 prisoners between 2000 and 2006 who had Mantoux test recorded in the TB Unit's Mantoux test database, 525 (29.4%) were Indonesian nationals.

The TB Unit's Mantoux test database confirms the high incidence of LTBI in these population groups. From 2000-2006, the proportion of NT prisoners who had a Mantoux test reading ≥10mm recorded in the database were:

- Indigenous Australian prisoners – 66%
- non-Indigenous Australian prisoners – 51%
- Indonesian-born prisoners – 64%
- non-Indonesian overseas-born prisoners – 88%.

The incidence of active pulmonary TB is also high in these population groups. In 2004, the TB incidence rate for Indigenous Australians in the NT was 31.9 per 100 000. This compares with an overall rate for non-Indigenous Australians of 1.2 per 100 000. In the same year, the World Health Organisation reported incidence rate in Indonesia was 245 per 100 000, while the fisherperson rate recorded in 2006 by the TB Unit's Fisherperson Screening database was 1091 per 100,000.

Other reasons for the increased TB risk in prison populations include:

- The high turnover of prisoners serving short sentences increases the potential exposure of long-term inmates. On a prison census undertaken on 30 June 2005, 42% of prisoners in NT prisons were serving sentences of less than 12 months and 21% were serving sentences of less than 6 months.
- The physical structure of correctional facilities often involves close living arrangements coupled with restricted ventilation, thus leading to an increased risk of transmission if a prisoner did have infectious TB.

This combination of structural risk factors and high prevalence of disease means that different screening protocols may be appropriate for different population groups.

Indigenous Australians are over-represented in NT prisons. In 1998/99, 79% of all sentenced prisoners incarcerated in the NT were indigenous (NT Correctional Services Annual Report 1998/99, page 95), compared to the Indigenous proportion in the general NT population of 28% in 1999. From September 1999 there was an influx of overseas-born prisoners into NT prisons charged with people smuggling under new legislation which provided longer sentences than previously. By mid-2000, over one-third of the inmates in Darwin Correctional Centre were Indonesian nationals.

Prisoners have higher rates of LTBI than the general population because they disproportionately represent groups with a high burden of TB disease. These groups include the homeless, malnourished, mentally ill, overseas-born, indigenous Australians, and substance abusers. Of 3206 prisoners between 1989 and 2000 who had Mantoux test recorded in the Darwin TB Unit's Mantoux test database, the following group had high proportions with results ≥ 10 mm:

- Indonesian-born – 80%.

Of 310 Indonesian prisoners (people smugglers and fishermen) in Darwin assessed by the TB Unit in the 3 years 1999 and 2001, 14 cases of pulmonary TB were diagnosed. This high prevalence of disease justifies separate screening protocols for overseas nationals from high prevalence countries who are incarcerated in NT prisons.

10.5.2. General Prisoners

Prisoners falling into this category include those who are Indigenous, non-Indigenous Australian born, and foreign nationals from countries with a low TB prevalence. TB should be considered as a potential diagnosis for all general prisoners undergoing a reception health assessment.

Initial assessment at reception should include:

- symptom review – all prisoners should be asked about new cough of >2 weeks, worsening chronic cough, haemoptysis, weight loss, fever, and night sweats
- medical history review – previous personal history of TB, family or other contact history of TB, HIV status if known, conditions or medications causing immunosuppression
- examination – particularly for focal chest signs and lymphadenopathy.

Any prisoner who has symptoms suggestive of pulmonary TB should be given a mask to wear, have an immediate chest x-ray and, if it is abnormal, be admitted to Royal Darwin Hospital for sputum tests. The TB Unit should be notified immediately.

All prisoners who are HIV positive, or take medications causing immunosuppression, should have a chest x-ray irrespective of their Mantoux test result. If the chest x-ray is abnormal, a plan should be made for further investigations in consultation with the TB Unit.

All prisoners should have a reception Mantoux test unless:

- a previous Mantoux test ≥10mm has been recorded
- the prisoner has had a previous serious reaction to a Mantoux test
- TB has previously been diagnosed.

All prisoners with a previous positive Mantoux test, a reception Mantoux test ≥10mm, or previously treated TB should have a chest x-ray and clinical review with the TB Unit to exclude active TB.

If latent TB infection is diagnosed, there are no significant contraindications, and the sentence is sufficiently long to complete the course of treatment, LTBI treatment should be offered to the prisoner. Although generally a nine month course of isoniazid is preferred, a four month course of rifampicin can be offered to those with shorter sentences.

10.5.3. Prisoners serving long sentences

- If, at any time, a prisoner presents to the prison medical staff with symptoms or signs suggestive of TB, urgent consultation with the TB Unit, investigations (CXR and sputum samples), and isolation in hospital should be considered. This should occur irrespective of the results of previous screening.
- Prisoners who have a reception Mantoux test <10mm should have their Mantoux test repeated annually. Any prisoner who converts his/her Mantoux test while incarcerated should undergo a CXR and clinical review with the TB Unit. Contact screening will be required.
- Mantoux test negative prisoners who are transferred from other correctional facilities should have a Mantoux test undertaken upon reception into the new facility. If conversion has occurred, the site of transmission can be located to the previous prison and contact screening can be undertaken.
- Long stay prisoners who have been fully evaluated and either decline or are unable to take LTBI treatment should have an annual clinical assessment for TB by the TB Unit medical officer.
- All prisoners who have been previously treated for active TB should have an annual clinical assessment for TB by the TB Unit medical officer.
- Prisoners who have completed a course of LTBI treatment do not require annual clinical assessments.

10.5.4. Prisoners from countries with a high prevalence of TB

10.5.4.1. Illegal Foreign Fisherpersons

Although the number of prisoners convicted of people smuggling offences has decreased since the 2001/2 peak, the number of IFF incarcerated in the Northern Territory is continuing to rise. During 2004/5, 186 adult foreign nationals were received into NT prisons, a 54% increase from the previous year attributable primarily to the incarceration of illegal foreign fisherpersons.

All illegal foreign fisherpersons undergo a comprehensive medical and public health screening assessment upon entering Australia (see section 10.6). This screening assessment includes a CXR and clinical review to exclude active TB. It can be reasonably assumed that all illegal fisherpersons entering correctional facilities in the NT have had infectious active pulmonary TB excluded.

On reception to prison, all illegal fisherpersons should be screened for latent TB infection by means of a Mantoux test unless:

- A previous Mantoux test ≥10mm has been recorded (for example if previously incarcerated in Australia).
- The prisoner has had a previous serious reaction to a Mantoux test.
- TB has previously been diagnosed.
- All illegal fisherpersons with a previous or reception Mantoux test ≥10mm should be offered treatment for LTBI provided there is no known contraindication and the sentence is sufficiently long for the prisoner to complete the course of treatment. Although generally a 9 month course of isoniazid is preferred, a 4 month course of rifampicin can be offered to those with shorter sentences.

- If, at any time, an illegal fisherperson presents to the prison medical staff with symptoms or signs suggestive of TB, urgent consultation with the TB Unit, investigations (CXR and sputum samples), and isolation in hospital should be considered. This should occur irrespective of the results of previous screening.

10.5.4.2. Other prisoners from countries with a high prevalence of TB

Foreign nationals entering correctional facilities without first being in the custody of the Australian Customs Service (ACS) or the Department of Immigration and Citizenship (DIAC) will not have undergone medical and public health screening prior to reception. Countries considered to have high prevalence of TB ie. ≥25/100,000 are shown on p 69 and listed in Appendix 9.

- These prisoners should be considered to be at high risk of TB and should undergo a CXR and clinical review, as well as a Mantoux test, on reception.
- Any prisoner with symptoms or signs suggestive of TB, or with an abnormal CXR, should be provided with a mask and discussed urgently with the TB Unit so that sputum samples can be organised and isolation in hospital considered.
- Asymptomatic prisoners with normal CXRs, or those cleared after investigations, should be managed according to their Mantoux test results. All who have a previous or reception Mantoux test ≥10mm should be offered treatment for LTBI provided there is no known contraindication and the sentence is sufficiently long for the prisoner to complete the course of treatment. A 9 month course of isoniazid is preferred, but a 4 month course of rifampicin can be offered to those with shorter sentences.
- Prisoners with a negative Mantoux test should have their Mantoux test repeated annually.

This process can be summarised by the algorithm page 74.

10.5.5. Prison and prison clinic staff

Prison officers and staff of prison clinics should be screened in accordance with Section 10.2 *Health care workers and other staff at occupational risk of TB.*

10.6. Residents of Detention Facilities, Including Illegal Foreign Fisherpersons

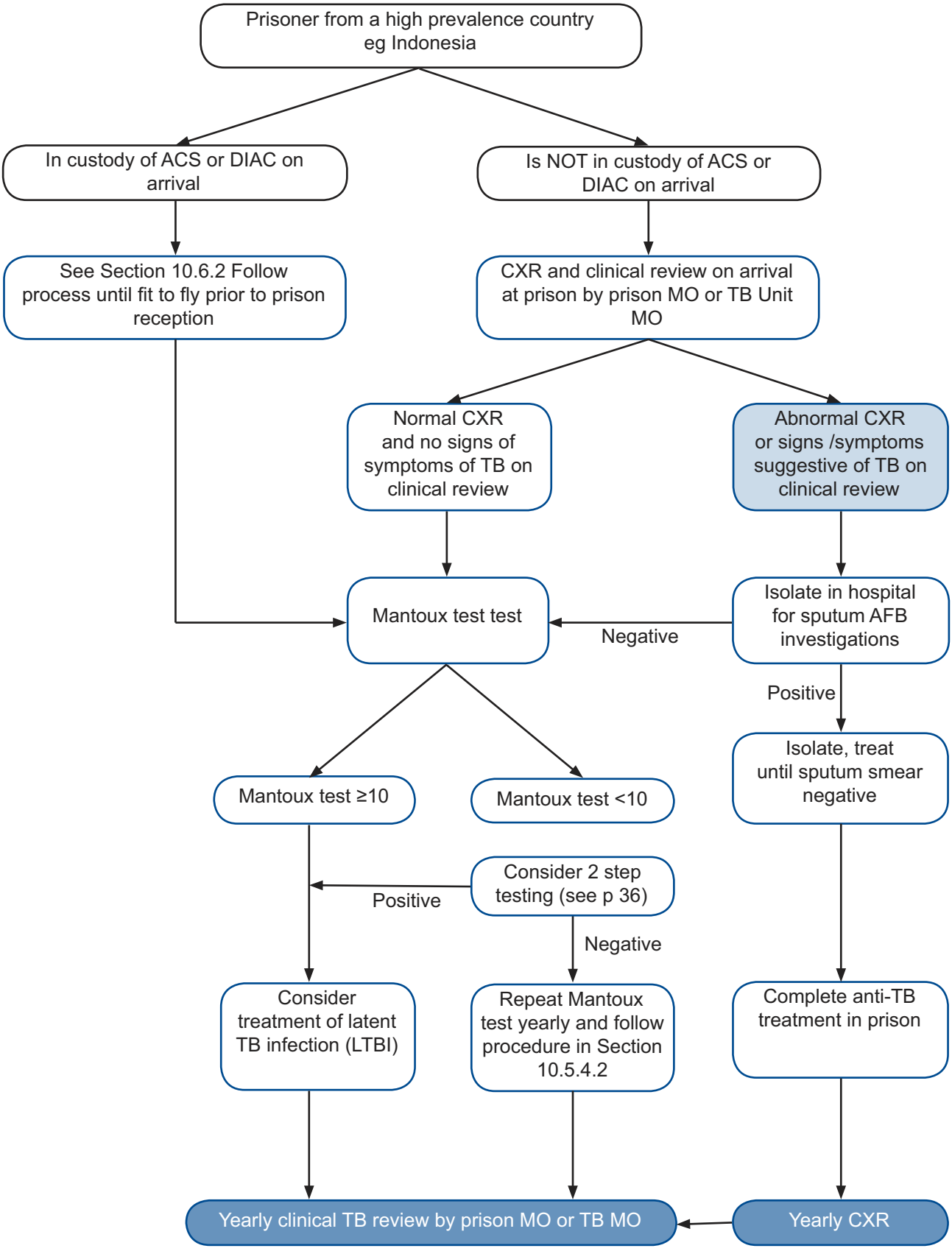
10.6.1. Background

The Northern Immigration Detention Facility (NIDF) was opened in 2006 after a significant upgrade. When fully operational it will have a capacity of 600 detainees. The primary purpose of NIDF is to detain illegal foreign fisherpersons until they are either repatriated back to their country of origin, or enter Australian Correctional Facilities. Although there is a possibility that unauthorised boat arrivals (UBAs) could be detained at NIDF in the future, this has not yet occurred.

The residents of NIDF are at a higher risk of TB than the rest of the Australian population as:

- Detainees come from countries with high TB prevalence and themselves often experience risk factors for TB including poor nutrition, overcrowded living conditions, limited access to health care in their home countries, and substance abuse. According to the TB Unit's Fisherperson Database, the rate of TB amongst illegal foreign fisherpersons in 2006 was 1091 per 100 000.
- The risk of exposure is high due to the high turnover of detainees. At the time of writing, the average stay in NIDF was three weeks. This high turnover also means that there is insufficient time to identify and treat detainees with latent TB infection.
- It has been demonstrated from fisherpersons entering Correctional Facilities that the rates of LTBI infection in this population are also high. According to the TB Unit's Mantoux test database, 64% of Indonesian fisherpersons had a positive Mantoux test from 2000-2006.

Approach to the detection of TB disease and infection in prisoners from countries with a high prevalence of TB.



- Detention environments usually involve close living arrangements and restricted ventilation, thus further increasing the risk of transmission of airborne communicable diseases.

This combination of high prevalence of both disease and LTBI systemic factors increasing the risk of transmission, and high rates of recidivism amongst illegal fisherpersons justified the development of separate screening protocols for this detention population.

10.6.2. Health Screening Process for Illegal Foreign Fisherpersons

A summary of the 'Procedure for Health Assessments of illegal foreign fisherpersons apprehended off the Northern Coast of Australia" is set out in the Figure pp77-78. In this Figure, 'temporary accommodation' refers to either the holding and processing facility in Nhulunbuy, or the medical separation area of NIDF. These areas have been developed to ensure that fisherpersons who have not yet undergone health screening are physically isolated from those who have. Following screening, fisherpersons are accommodated in either the Northern or Southern Compounds of NIDF.

- As soon as possible after apprehension, all fisherpersons should undergo the standard "TB and General Health Questionnaire" with the assistance of an interpreter. This form is designed to identify fisherpersons at high risk of having pulmonary TB, and requires that they wear a mask until cleared.
- If Health Assessments cannot be conducted at CDC that day (for example, for night arrivals) any fisherperson who is obviously unwell or has haemoptysis, a fever, or recent history of TB should be transferred immediately to the Emergency Department of the nearest hospital.
- All other fisherpersons should attend CDC for their Health Assessments at the pre-arranged times. This Health Assessment consists of:
- A CXR for ALL fisherpersons, and
- A clinical review with a CDC medical officer who fills out the standard "Health Assessment" form and certifies whether active TB can be excluded, and whether the fisherperson is 'fit to travel'.
    - If active TB can be excluded, and the fisherperson is 'fit to travel', the original Health Assessment forms should be returned to the medical clinic at NIDF. These should detail any investigations undertaken (eg. malaria screens) and any treatments given (eg. for STIs).
- If active TB cannot be excluded the fisherperson should be admitted to hospital for 3 sputum samples for AFB smear and culture. No more than 2 samples should be taken in a 24 hour period. If two samples are taken within a 24 hour period the laboratory should be notified that the patient is an illegal fisherperson.
- Sputum induction and bronchoscopy should be undertaken only if the diagnosis is in doubt and it is thought that the empiric commencement of treatment would be inappropriate. The TB Unit should be consulted in all of these cases.

10.6.2.1. TB Suspect Smear negative fisherpersons

- A fisherperson with 3 consecutive smear negative sputum samples can be discharged from hospital and return to either the Northern or Southern Compounds of NIDF.
- In cases with highly suggestive chest x-rays or signs and symptoms of TB, it will be decided to commence smear negative fisherpersons on treatment. Fisherpersons whose sputum samples are smear negative and were not commenced on treatment should be followed closely by IHMS while still in Australia (see Appendix 11). If symptoms suggestive of TB develop, repeat sputum samples should be taken.
- Fisherpersons whose sputum samples are smear negative but culture positive for TB should, if still in Australia, have their fitness to travel revoked so as to commence treatment, ensure that the medications are well tolerated, and arrange follow-up in their country of origin.

It is hoped this will be an infrequent occurrence.

10.6.2.2. TB Suspect Smear positive fisherpersons

- If smear positive pulmonary TB is diagnosed, the fisherperson should remain isolated in hospital and commence treatment in accordance with Chapter 4 of these Guidelines. Discharge should not occur until the fisherperson has 3 consecutive smear negative sputum samples, irrespective of how long this takes.
- DOT will be provided by the health service provider at NIDF (currently International Health and Medical Services - IHMS) for any fisherperson requiring ongoing TB treatment following discharge from hospital.
- All fisherpersons who have commenced treatment for active TB in Australia require a medical referral (translated into their local language) and a supply of medications to take home to their country of origin. Attempts to contact local TB control units should also be made.
- Fisherpersons who commence treatment for MDR-TB in Australia should not be repatriated until they have at least 3 negative sputum cultures. Difficulties in patients accessing second line medications in their home countries should be considered when deciding appropriate times for repatriation. This decision should be made in consultation with the TB Unit.

10.6.2.3. Fisherpersons with probable old TB

- Fisherpersons with a chest x-ray suggestive of old, healed inactive TB may not warrant isolation and hospitalisation. For these patients, a spot sputum for AFB smear and culture may suffice. Always consult with the TB Unit before making this decision. If suspicion of active TB cannot be ruled out always collect 3 sputum samples and put in isolation.
- Fisherpersons awaiting spot sputum results should remain in medical separation at NIDF until they are confirmed to be smear negative.

10.6.3. Health Screening Process for Unauthorised Boat Arrivals

To date, no unauthorised boat arrivals have been held at NIDF. The arrangement with the Department of Immigration and Citizenship (DIAC) is that, if this were to occur, all unauthorised boat arrivals should be screened in accordance with the process set out above for illegal foreign fisherpersons.

10.6.4. Personnel with frequent contact with Illegal Foreign Fisherpersons

All personnel in frequent contact with illegal foreign fisherpersons should be screened in accordance with Section 10.2 *Health care workers and other staff at occupational risk of TB.*

Figure. Procedure for Health Assessment of Illegal Foreign Fisherpersons apprehended off the Northern Coast of Australia.

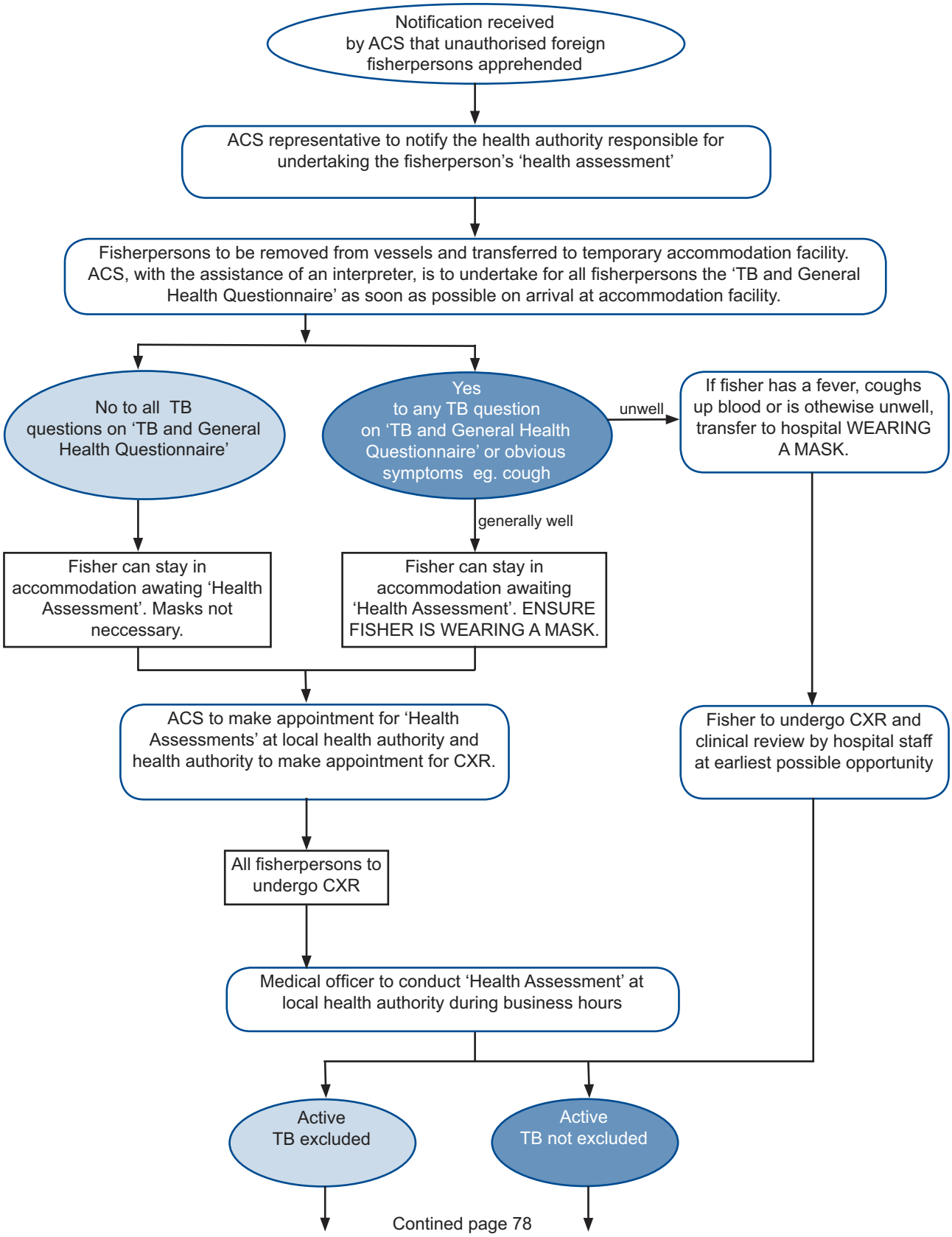
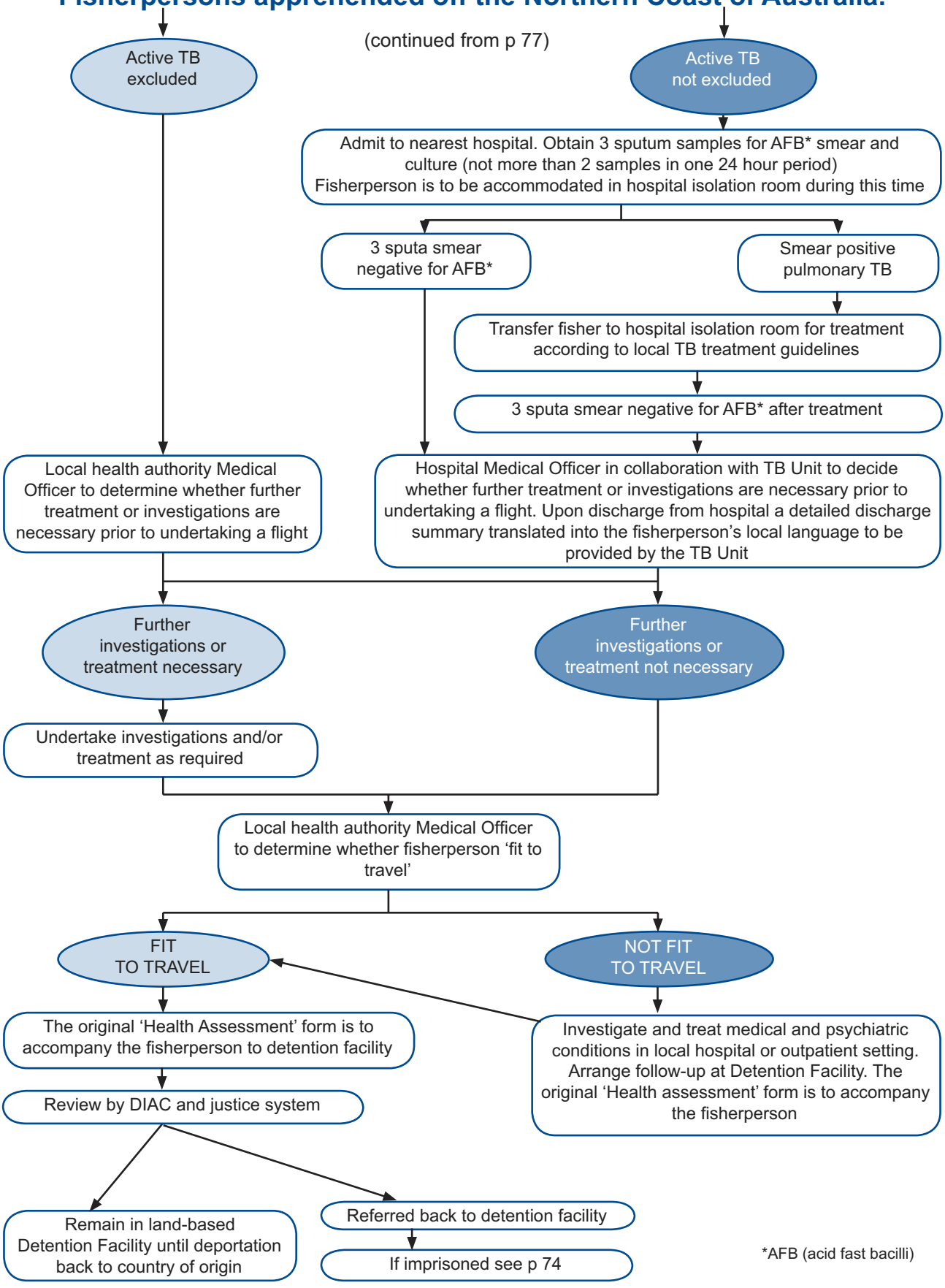


Figure. Procedure for Health Assessment of Illegal Foreign Fisherpersons apprehended off the Northern Coast of Australia.



10.7. Residents of long stay care facilities

Recommendations for elderly residents of nursing homes and hostels.

Elderly persons residing in a nursing home are almost twice as likely to acquire TB as those living in the community.

All new residents therefore should have a baseline clinical evaluation and two-step Mantoux test unless contraindicated (refer section 6.2.3). Because the likelihood of false-negative Mantoux test is increased in the elderly, they should also routinely have a baseline chest X-ray unless an X-ray or report from the last 12 months is available. These results should be recorded in an easy to access section of the person's chart (eg. inside the front cover).

New residents with symptoms or signs suggestive of active TB may require admission to hospital with appropriate infection control procedures for evaluation (Chapter 3).

Residents with a **past or present Mantoux test result ≥10mm** (ie. second reading in two-step test) or chest X-ray suggesting LTBI (inactive but past TB activity) should be reviewed by TB clinic staff either at the TB clinic or by home visit for consideration of treatment for LTBI. Consideration of treatment will take into account the time of likely acquisition of TB infection, as well as coexisting medical conditions and risk of drug toxicity. In many cases, treatment will not be prescribed in favour of follow-up (below).

On the basis of their medical history, Mantoux test result and chest X-ray, those with a positive Mantoux test or chest X-ray indicating LTBI (whether or not they have been prescribed treatment) or with a past-history of untreated or treated active TB are at higher risk.

The following should be done for people at higher risk

- It should be noted in an easily accessible section of the person's chart that they are at increased risk for active TB. This should be taken into consideration during acute illnesses.
- A letter should be sent to the person's GP informing them of the risk of active TB.
- Annual review for clinical evidence of TB (which may include a chest X-ray) by TB clinic staff. This can most conveniently be done at the time of the yearly inservice (below).
- Staff of the long stay care facility should be particularly vigilant for symptoms and signs that may indicate active TB (eg. cough, fever, night sweats, weight loss).

A **yearly inservice** by the TB clinic will be provided to staff of the long stay care facility to increase awareness through education regarding TB. Staff of the facility should have a low threshold for seeking advice for suspected cases of active TB. Facilities for ordering sputum AFBs and chest X-ray should exist.

There is no requirement for residents of long stay care facilities to have regular Mantoux test or chest X-rays other than in the event of contact tracing.

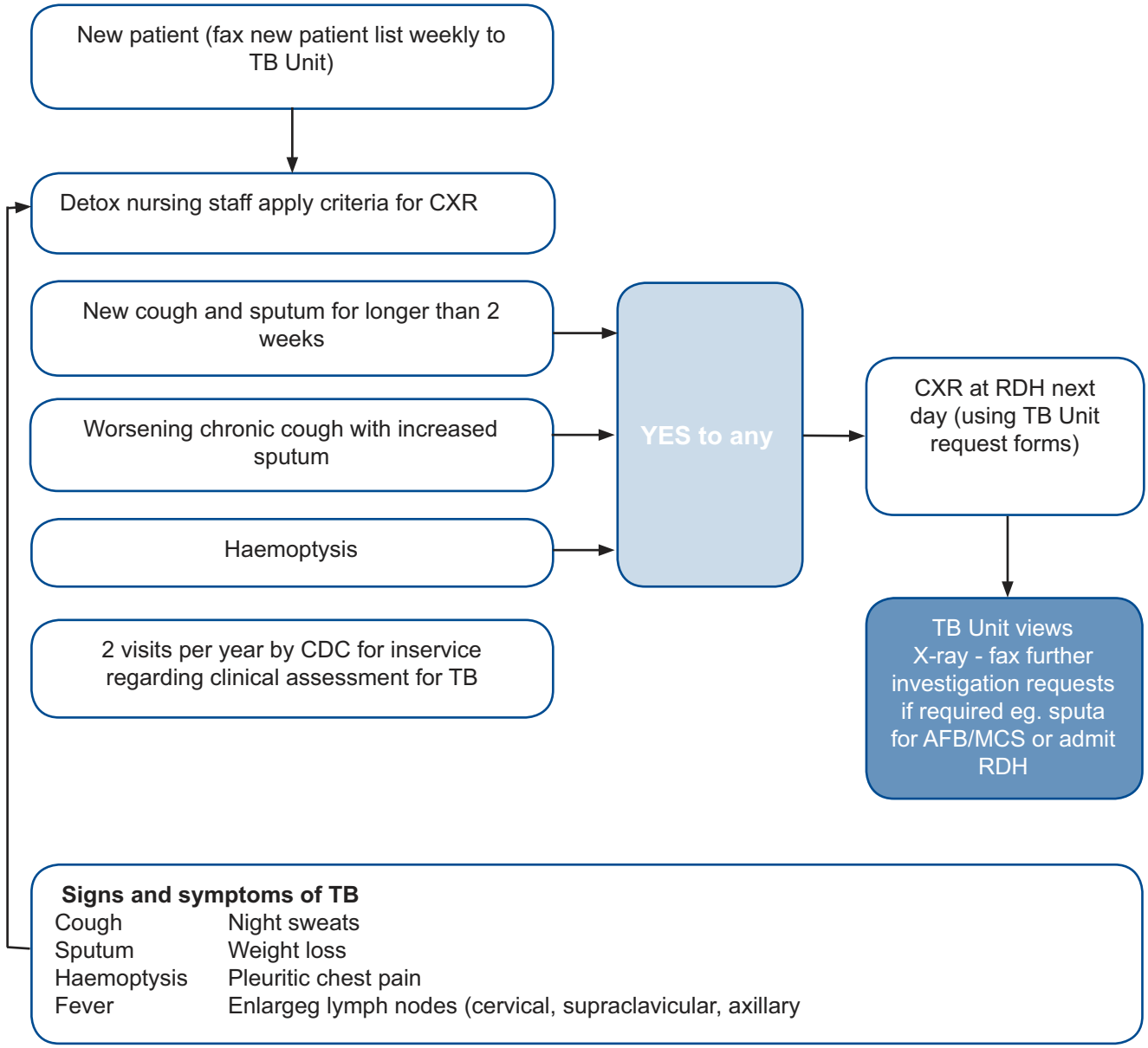
10.8. Residents of drug and alcohol rehabilitation centres

10.8.1. Detoxification program

Since the duration of this program is usually a few days, the likelihood of completion of Mantoux testing and treatment of LTBI is low. The main aim of screening is to opportunistically detect active disease.

A laminated clinical algorithm (overpage) is available for Detoxification program staff.

Detoxification - TB screening protocol



The algorithm should briefly be applied for all new patients. If patients have a new cough, which has been present for longer than 2 weeks, or a chronic cough which has been worse for the last 2 weeks (increased volume, stickiness, or colour of sputum), the TB Unit should be immediately contacted.

A chest X-ray will be organised for the same or following day at the RDH, and will be immediately read by staff at the TB Unit.

The TB Unit staff will organise with Detoxification staff further investigations (eg. sputum tests) or admission to the RDH based on the chest X-ray and clinical presentation.

10.8.2. Alcohol and Drug Rehabilitation Centres

The major centres involved with alcohol and drug rehabilitation in the NT have residential programs with durations ranging from 6 weeks to 12 months.

Opportunistic clinical screening of all residents should occur, followed by a chest X-ray if active TB is suspected.

Centres should contact the designated staff member at the TB Unit each month. A list of their new patients is faxed to the TB Unit, and a monthly visit to the Centre is arranged. Staff and patients will receive training about TB screening and treatment. New patients will receive a clinical review for symptoms and signs of active TB, and those who have not previously been diagnosed with LTBI or active TB will receive a Mantoux test.

Those people identified as having a positive Mantoux test should go on to have a CXR.

New clients who have previously had a positive Mantoux test, or previous active TB should have a symptom review and a CXR if one has not been carried out in the previous 12 months.

Staff employed at the centres should have initial screening on employment and ongoing yearly Mantoux tests as directed in section 10.2.3.

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APPENDIX 1. Fine needle aspiration of lymph nodes

- This is a sterile technique done by an operator wearing a particulate filter mask.
- Prior to starting, prepare a slide by writing on the frosted end **in lead pencil only** the date, patient's name, HRN and FNA site.
- EMLA cream may be applied under an occlusive dressing (eg. Opsite™) for 30 minutes prior to beginning.
- Prepare the area using aqueous chlorhexidine with alcohol and then inject a local anaesthetic if EMLA was not used. Allow the area to dry.
- Using a 19 gauge needle attached to a 10 mL or 5 mL syringe, make three passes through the node, aspirating each time on withdrawal.
- Place one drop of the FNA onto the centre of the slide without touching the slide with the needle. Using a wooden applicator stick, spread the FNA drop over an area of approximately 15 x 30 mm. Allow to air dry.
- Transfer the remainder of the contents of the needle and syringe to a sterile container with 5 mL of sterile saline. Aspirate some saline into the syringe and then ensure that all of the contents are evacuated into the container. Take care not to aerosolise the contents. Dispose of the needle/syringe into a sharps container.
- Securely tighten the lid on the specimen container and wrap the lid/container interface with Parafilm™.
- It is **very important** to label the specimen and write on the pathology request form, "FNA of (eg.) left supraclavicular lymph node in 5 mL sterile saline for AFB smear, culture and cytology" in addition to name, HRN etc.
- Specimen container goes into BioHazard bag and then into Esky with freezer brick for long-distance transport. It should get to the laboratory within 24 hours (48 hours at most).

APPENDIX 2. Non-Tuberculous Mycobacteria

Clinical disease	Common etiologic species	Diseases ever notified in the NT	Unusual etiologic species	Diseases ever notified in the NT
Pulmonary disease	*M abscessus*	√	*M asiaticum*	-
	M avium complex (MAC)*	√	*M branderi*	-
	M kansasii	√	*M celatum*	-
	M malmoense	-	*M fortuitum*	-
	M xenopi	-	*M haemophilum*	-
			M scrofulaceum	-
			M shimoidei	√
			M simiae	-
			M smegmalis	-
			M szulgai	-
Lymphadenitis	MAC*	√	*M abscessus*	-
	M malmoense	-	*M chelonae*	-
	M scrofulaceum	-	*M fortuitum*	-
			M haemophilum	-
			M interjectum	-
			M kansasii	-
			M szulgai	-
Skin and soft tissue disease[#]	*M abscessus*	√	MAC*	-
	M chelonae	√	*M branderi*	-
	M fortuitum	√	*M haemophilum*	-
	M marinum	√	*M kansasii*	-
	M ulcerans	√	*M mageritense*	√
			M mucogenicum	-
			M scrofulaceum	-
			M simiae	-
			M smegmatis	-
			M szulgai	-
			M terrae complex[φ]	-
Disseminated disease	MAC*	√	*M abscessus*	-
	M chelonae	-	*M conspicuum*	-
	M haemophilum	-	*M fortuitum*	-
	M kansasii	-	*M genavense*	-
			M gordonae	-
			M malmoense	-
			M marinum	-
			M scrofulaceum	-
			M simiae	-
			M szulgai	-
			M xenopi	-

*[*]*M avium* complex (MAC) consists of 2 distinct species *M avium* and *M intracellulare*.
[#]*M marinum, M fortuitum*, MAC, *M scrofulaceum, M haemophilum* and *M szulgai* are also causative organisms for osteomyelitis.
[φ]*M terrae* complex includes *M terrae, M nonchromogenicum*, and *M triviale.*

NTM whose pathogenicity is unclear

M gastri	*M aichiense*
M flavescens	*M aurum*
M mageritense	*M celatum*
M neoaurum	*M chubuense*
M phlei	*M gadium*
M thermoresistible	*M lentiflavum*
M vaccae	*M triplex*

NTM growth rate classification

Slow growing NTM (>7 days)	Rapidly growing NTM (<7 days)
MAC	*M abscessus*
M asiaticum	*M aichiense*
M branderi	*M aurum*
M celatum	*M chelonae*
M conspicuum	*M chubuense*
M flavescens	*M fortuitum*
M gastri	*M gadium*
M genavense	*M mageritense*
M gordonae	*M mucogenicum*
M haemophilum	*M neoaurum*
M interjectum	*M phei*
M kansasii	*M smegmatis*
M lentiflavum	*M thermoresistible*
M malmoense	*M vaccae*
M marinum	
M scrofulaceum	
M shimoidei	
M simiae	
M szulgai	
M terrae	
M triplex	
M ulcerans	
M xenopi	

APPENDIX 3. Aerial Medical Service tuberculosis transport policy

1. We depend on the DMO's to inform flight staff if there is **any** suspicion of TB.
2. People with suspected active pulmonary or laryngeal TB should only travel by air on commercial aircraft if definitely known to be smear negative on 3 adequately collected sputum smears.
3. Patients who are smear-positive or whose sputum smears have not been examined should only travel by air with NTAMS.
4. Ideally there should be no other patients on board and certainly none that may be immunocompromised.
5. The patient and all personnel on board should wear the particulate filter duckbill masks stocked on all NTAMS aircraft.
6. If the patient needs to cough/sneeze, then this should be done into a handful of tissues that effectively seal the nose and mouth. Tissues should then be disposed of in line with other contaminated waste.
7. It is not possible to guarantee contamination of the aircraft has not occurred; therefore, consider the following:
   - For the aircraft to be completely decontaminated 6 air exchanges are required. This will occur naturally by diffusion over 6 hours but the process is considerably hastened by ventilation.
   - The cabin air within a King Air B200/B200c with pneumatic flow packs installed, is changed every 3.6 to 5.8 minutes during normal pressurised flight with all systems operating normally. With both engines running and the air-conditioning system operating on the ground, this cabin air replacement will occur in a time less than with the aircraft in flight and being pressurised.

In view of this, it is recommended that:

a. the aircraft be left for 6 hours with the cargo door open, **OR**

b. all persons on board wear a mask for the first 35 minutes from start up time on the next flight.

Further information on TB and air travel can be obtained from:

The World Health Organisation. *Tuberculosis and Air Travel: Guidelines for Prevention and Control.* http://whqlibdoc.who.int/hq/2006/WHO_HTM_TB_2006.363_eng.pdf.

APPENDIX 4. Fact sheets

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WHAT YOU NEED TO KNOW ABOUT TUBERCULOSIS

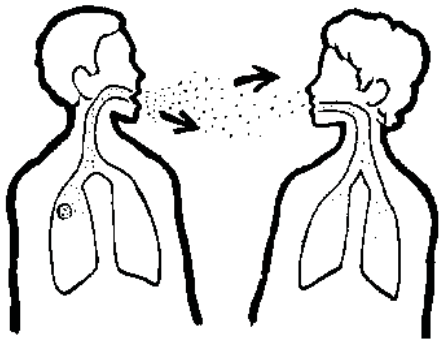
People of all ages, all nationalities and all incomes can get tuberculosis (TB). Each year about 1,000 people in Australia get TB disease. Between 20 and 30 cases occur in the Northern Territory each year. In almost all instances, ***TB can be cured***.

What is Tuberculosis?

TB is an infectious disease caused by the germ *Mycobacterium tuberculosis.* TB usually affects the lungs but can affect any part of the body.

How is TB Spread?

TB is spread when people who have active untreated TB bacilli (germs) in their lungs or throat, cough, sneeze or speak and send their germs into the air. Other people who breathe these germs into their lungs can become infected. People who breathe in TB germs usually have had close contact with someone who has the disease. TB is not spread by handling objects that the patient has come in contact with eg. dishes, drinking glasses, sheets or clothing.



TB germs spread through the air

Is TB hereditary?

No. This belief arose because those in closest contact to the patient are those most likely to get infected and are often family because they share the same air.

What does having 'TB infection' mean?

After TB germs enter the body, in most cases, body defences control the germs by building a "wall" around them, the way a scab forms over a cut. The germs can stay alive inside these walls for years in an 'inactive' state. While TB germs are inactive, they cannot harm the person and ***they cannot spread to other people***. The person is infected but not sick and is unlikely to be aware that he or she is infected. The only way to tell the germs are there is by having a tuberculin skin test (Mantoux test). Inactive TB germs cannot hurt you but, if the body defences are weakened for any reason, inactive TB germs may weaken the "wall" and become active and multiply to become disease.

What is TB Disease?

TB disease is a serious illness caused by ***active*** TB germs. If body defences are weak, it is possible to get TB disease shortly after the germs enter the body. It is also possible, even after many years, for inactive TB germs to become active when body defences are weakened. This may be due to aging, a serious illness, developing diabetes, drug or alcohol abuse, or HIV infection.

What are the signs of TB?

TB can affect any part of the body but the lungs are the most common target. People with TB disease may have some or all or the following symptoms: persistent cough for more than 3 weeks, fevers, weight loss, night sweats, feeling tired and weak, loss of appetite, enlarged glands.

A person with TB disease may cough up blood stained sputum. People with active TB disease may only have mild symptoms. They may be spreading their germs to others without even knowing that they have TB.

What are the tests for TB?

There are a variety of tests, depending on the part of the body infected, but nearly all cases of TB have 3 tests. These are:

1. The **tuberculin skin test** shows if a person has been infected with TB germs. It does not mean that he/she has TB disease.
2. A **chest X-ray** shows if any damage has been done to the lungs and the extent of the damage. A large amount of the lungs may be involved before major signs and symptoms occur.
3. A **sputum test** shows if TB germs are present in the sputum. Their presence is proof of active pulmonary TB. The germs may be seen under the microscope called "a smear" or they may take up to eight weeks to grow in a medium called a "culture".

Who should get checked for TB?

- People who have symptoms of TB.
- Recent contacts of someone who has active TB disease. This could be a family member, friend, or co-worker.
- Those who have a chest X-ray suggesting that they have had untreated TB disease in the past.
- People who have lowered immunity such as HIV infection or certain medical conditions.
- People who are required to be tested for employment reasons or as part of a school screening program.
- People who are about to undergo organ donation or transplantation.
- People travelling to a high-risk country should have a tuberculin skin test to establish a baseline of previous exposure.

What is the treatment for TB?

Most people who have TB will begin treatment by taking at least 4 different types of tablets. After several months this may be reduced.

These tablets can cure TB if taken for at least 6 months. The tablets are given to the patient by direct supervision usually by a health care worker 3 times a week.

Sometimes TB germs are resistant. This means that the TB tablets that are most often used do not kill the TB germs. When this happens, combinations of other medications are given. Resistant TB is harder to cure and it takes more time to control, but most people with resistant TB can be treated. Your doctor will make sure specific tests are done to check for drug resistance.

Is TB curable?

Yes. TB is almost 100% curable with modern treatment. To be effective, treatment requires the full co-operation of the patient. Early diagnosis, followed by prompt treatment, helps in preventing spread to others and reducing disability after cure.

Can TB patients infect other people?

Only lung or throat TB is infectious. Usually, after 3 or more weeks of taking effective medication, most patients with lung or throat TB will stop spreading germs. Most TB patients can then be discharged from hospital and can resume normal activities ***but are not yet cured***. It is important to continue to take the tablets as ordered and the person is checked regularly by the clinic staff. Should any side effects develop speak at once with health care providers.

For further information contact the TB Clinic in your region:

Alice Springs	8951 7548
Darwin	8922 8806
Katherine	8973 9049
Nhulunbuy	8987 0282
Tennant Creek	8962 4259

April 2008

TUBERCULOSIS (TB) TREATMENT

Can TB be cured?

Yes. Today in almost all cases, ***TB can be cured.*** It is important to take the TB drugs regularly, on schedule and for the full duration of treatment.

Most people who have TB will begin treatment by taking at least 4 different types of tablets. After several months this may be reduced.

These tablets can cure TB if taken for at least 6 months. The tablets are given to the patient by direct supervision usually by a health care worker 3 times a week. If this is not possible tablets are given daily in a weekly administered dosette box.

Sometimes, TB germs are resistant. This means that the TB tablets that are most often used do not kill the TB germs. When this happens, combinations of other medications are given. Resistant TB is harder to cure and it takes more time to control, but most people with resistant TB can be treated. Your doctor will make sure specific tests are done to check for drug resistance.

Are TB medicines safe?

As with any medicines, TB tablets can sometimes cause side effects, although most people do not experience any problems. Tell your doctor or health care worker immediately if any unexplained illness develops or if any of the following symptoms occur:

- Nausea and/or vomiting
- Jaundice (Yellowish skin or eyes, dark urine)
- Unexplained fever or tiredness
- Tingling or numbness of hands or feet or joint pains
- Skin rash/itch, bruising
- Blurred vision or colour blindness to red/green colour.

It is important to tell your health care worker if you are taking any other medication especially oral contraceptives, diabetic tablets, anti-epileptic drugs, or anti-coagulation tablets so that drug interaction can be considered. Rifampicin (one of the TB drugs) causes discolouration of urine, sweat and tears to pink-orange. This is a normal reaction and causes no problem unless you wear contact lenses.

Why do I have to take the tablets for so long?

You have to make sure that the medicine gets to ***all*** the TB germs. Some of the germs may be killed when you start to take your medicine but it takes a long time for all of them to die.

I feel better! Why should I keep taking tablets?

Even after you feel well, do ***NOT*** stop taking your tablets. There are still many active TB germs in your body. If you stop taking your tablets, the germs that have not been killed will multiply and you can get sick again.

Drug resistant TB can develop when a person does not take the TB medication as prescribed. A person with untreated drug resistant TB of the lungs or throat can spread these drug resistant germs.

How should I take my tablets?

It is easier to remember to take your tablets if you take them at the same time each day. It is also best to take them on an empty stomach half an hour before meals or at bedtime.

You should also:

- Take the tablets with milk, water or a glass of juice.
- Tell your doctor or health care worker about other medications you are taking (including birth control pills).
- ***Avoid drinking alcohol while being treated for TB.*** Alcohol increases the risk of serious liver problems if taken while on TB medication.
- Eat healthy food and get enough rest.

What happens if I forget to take my tablets?

If you miss your tablets one day, do not worry. Just continue taking your next dose as usual. If you forget too many times however the medicine will not work.

Monthly check-ups

While you are on TB medication, a monthly visit to the TB Clinic is required. The purpose of this visit is to:

1. Make sure the medicine is working and that you are taking the tablets correctly.
2. Check your weight and general health, ensure your sputum has cleared of germs and your chest X-ray is improving.
3. Make sure you are not having any side effects from the tablets.

How can I keep TB from spreading?

- The medicine will usually stop you from spreading the TB germs within a few weeks, if you take the tablets as directed. But remember, ***you are not yet cured.*** The most important thing is to continue taking your tablets as prescribed until the doctor says you can stop.
- Always cover your mouth when you cough and sneeze.
- Tell all the people who you spend a lot of time with to contact the TB Clinic so that they can have a tuberculin skin test (Mantoux test). These could be family members, friends or co-workers.

Can I live as I always did?

If you have pulmonary (lung TB) or extensive disease, you may need to be admitted to hospital for the first few weeks of treatment for TB. Your contacts and activities will initially be restricted until your doctor tells you that you are no longer infectious. In most cases this is only for a few weeks.

When no longer infectious most patients with TB live at home and continue their normal activities. When you are no longer spreading TB germs, you can be near anyone, including children. You can continue your regular activities and return to work ***as long as you continue taking your medicine.***

For further information contact the TB Clinic in your region:

Alice Springs	8951 7548
Darwin	8922 8806
Katherine	8973 9049
Nhulunbuy	8987 0282
Tennant Creek	8962 4259

April 2008

TUBERCULOSIS VACCINATION (BCG)

What is BCG?

BCG (Bacille Calmette–Guérin) vaccine is a live vaccine made from an attenuated or weakened strain of the tuberculosis bacteria. BCG vaccination does not prevent TB infection however its use is in providing protection against invasive disease eg. TB meningitis in children under 5 years of age.

BCG is only useful if it is given before the child is infected with the tuberculosis bacteria.

BCG is also highly protective against leprosy.

It is recommended for children at high risk of contact with active tuberculosis or leprosy.

These include:

- Aboriginal newborn babies
- Children under 5 years old with no previous BCG who will be living overseas in countries of high TB prevalence, or in the NT in high risk Aboriginal communities for more than 3 months at a time
- Newborn babies whose parents have leprosy, or an immediate family history of leprosy.

What are the contraindications?

- Immune compromised children
- Newborn babies of mothers with known HIV infection, known risk factors for HIV or AIDS
- Children with a past history of tuberculosis
- Children with a tuberculin skin test (Mantoux test) result greater than 5 mm
- Febrile (Current Temperature >38.5ºC) at time of consultation
- Septic skin disease
- Another injectable live vaccine was given in the preceding 4 weeks (ie. need to postpone BCG administration).

Is a tuberculin skin test necessary before vaccination?

Children over 6 months of age should have a tuberculin skin test prior to BCG vaccination to establish if BCG administration is appropriate.

How is BCG administered?

The vaccine is given intradermally in the left arm.

Children under 12 months should receive 0.05ml.

Children over 12 months and over should receive 0.1ml.

Response and care of the BCG injection site

A small red papule forms and eventually ulcerates (it may discharge pus). This usually occurs within 2 - 3 weeks, forming a crust or ulcer. There is no pain or tenderness around the site of injection, and there are no signs of general ill health. However this ulcer may persist for 2 to 3 months. Keloid (raised and overgrown scar) formation can occur but is minimised if the injection is given at the correct site.

The ulcer may be covered with dry sterile gauze if discharging pus, and should be kept as dry as possible. Antiseptics and sticking plasters are to be avoided. The ulcer will eventually heal.

Adverse reactions are rare but need to be reported to the TB unit and the local immunisation coordinator.

Please seek medical advice If your child develops:

- Fever >38.5º
- Soreness, redness and swelling around the ulcer (larger than a 50c piece)
- Swollen glands under the arms, around the neck or in the groin.

Please note:

BCG immunisation provides some immunity to tuberculosis but should not be presumed to be 100% effective against contracting tuberculosis. The Australian Immunisation Handbook 9th Edition (2008) states that the overall protective efficacy of BCG for preventing serious forms of TB in children is over 80%. Therefore the vaccine is recommended for high risk infants.

For further information contact Centre for Disease Control

Darwin	89228804
Nhulunbuy	89870282
Katherine	89739049
Tennant Creek	89324259
Alice Springs	89517548

Further fact sheets and treatment protocols are available at http://www.nt.gov.au/health/publications.

April 2008

THE TUBERCULIN SKIN TEST (MANTOUX TEST)

Why do a skin test?

Sometimes people can become infected with tuberculosis (TB) germs without getting the actual disease. The tuberculin skin test (Mantoux test) can show if the person has ever been infected by TB germs. TB infection does not mean the person has the disease, but if someone has been infected there is a chance they might get sick with TB in the future.

Who needs a skin test?

- Recent contacts of someone who has active TB disease. This could be a family member, friend, or co-worker.
- Those who have a chest X-ray suggesting that they have had untreated TB disease in the past.
- People who have lowered immunity such as HIV infection or certain medical conditions.
- People who are required to be tested for employment reasons or as part of a school screening program (providing they have not had a previous positive tuberculin skin test).
- Before administering a BCG to infants greater than 6 months of age.
- People about to undergo organ donation.
- People travelling to a high risk country.

The tuberculin skin test

A tuberculin skin test is a simple and safe test. A small amount of tuberculin is injected just under the top layer of skin on a person's arm using a small sterile needle and syringe. The skin reaction (lump) is measured 2 to 3 days later and the result recorded.

Possible side effects

Side effects are uncommon. However, a person who has been exposed to TB germs may occasionally have a sizeable reaction, which may cause some discomfort. This swelling should disappear in about 2 weeks.

The reaction can get itchy. It is best not to scratch the arm – a cold compress can help relieve any itching.

What does a negative result mean?

If the lump is below a certain size the result of the test is negative. Usually this means that the person has not been infected with TB germs. However, under some circumstances it can be negative even when someone has been infected. This can happen if the exposure to TB has been in the last few weeks and the body has not had time to develop a reaction or if the body's defences are weakened and unable to react to the skin test. In these situations the test may need to be repeated or interpreted differently.

What does a positive test mean?

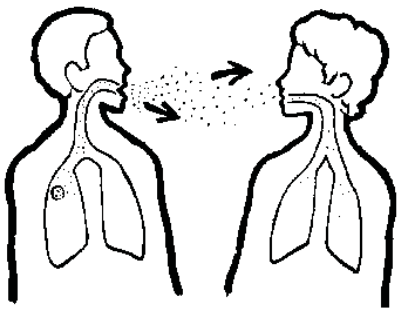
It means that the person is infected by TB germs, but does not mean that he or she has TB disease. This person cannot pass TB onto anyone else unless they progress at some later date to active TB disease.

How can a person be infected and not have TB disease?

After TB germs enter the body, in most cases, body defences control the germs by building a wall around them, the way a scab forms over a cut. The germs can stay alive inside these walls for years in an 'inactive' state. While TB germs are inactive, they cannot harm the person and ***they cannot spread to other people***. The person is infected but not sick and is unlikely to be aware that he or she is infected.

What is TB disease?

Tuberculosis is an infectious disease which usually affects the lungs but can affect other parts of the body. It is spread from person to person through the air by droplet infection. It is possible to get TB disease shortly after the germs enter the body, if body defences are weak. It is also possible, even after many years, for inactive TB germs to become active when body defences are weakened. This may be due to aging, a serious illness, developing diabetes, drug or alcohol abuse, or HIV infection.



TB germs spread through the air

What happens after the tuberculin skin test is read?

If the test is negative, no further testing is needed at this time, but you may need another test a few months later, depending on the reason for the test.

If the test is positive, a chest X-ray and physical examination will be needed to ensure there is no sign of active disease. If there are no signs of active TB the doctor will discuss the possibility of taking medication to prevent the development of TB disease. The benefits of taking the medication depend on the person's age, health and underlying risk of TB disease.

For further information contact the TB Clinic in your region:

Alice Springs	**8951 7548**
Darwin	**8922 8806**
Katherine	**8973 9049**
Nhulunbuy	**8987 0282**
Tennant Creek	**8962 4259**

Further fact sheets and treatment protocols are available at http://www.nt.gov.au/health/publications

April 2008

TWO STEP TUBERCULIN SKIN TESTING (MANTOUX TESTING) FOR HIGH RISK GROUPS

The Mantoux test

A Mantoux test is a simple and safe test. A small amount of Tuberculin is injected just under the top layer of skin on a person's arm using a small sterile needle and syringe. The skin reaction (lump) is measured 2-3 days later and the result recorded.

Boosted reactions and two-step skin testing

Two step testing is given to detect individuals previously infected with TB or vaccinated with BCG who may test negative to tuberculin testing initially, but who show a strong reaction to tuberculin if the same procedure is repeated 1 - 2 weeks later. The 2 step test is important to establish the true baseline reaction when further tuberculin testing is required as part of contact tracing or monitoring of high risk groups.[1]

The 'booster effect' represents bolstering of waned cellular immunity by an initial negative Mantoux test such that a second test at any time from 1 week to 1 year later produces a greater, more accurate response. This effect will only be observed in individuals with prior cellular immunity to PPD (whether from *Mycobacterium tuberculosis*, BCG or Nontuberculous Mycobacteria) and is more common in the elderly (age >55 years). Because the proteins in PPD are small in size, repeated skin testing with standard doses of tuberculin will not induce a positive skin test reaction in individuals who have no cellular immunity to the antigens in PPD.

'Two-step' testing is used to avoid interpreting the effect of boosting as a new infection. If the first test is <10mm (and no Mantoux test has been done in the previous 12 months), it is repeated 1-3 weeks later and the second test is interpreted as measuring the true degree of reactivity.

Possible side effects

Side effects are uncommon. However, a person who has been exposed to TB germs may occasionally have a sizeable reaction, which may cause some discomfort. This swelling should disappear in about 2 weeks.

Who needs a 2 step skin test?

- People who have chronic renal insufficiency.
- People who have lowered immunity such as HIV infection or certain medical conditions.
- The elderly who are entering care facilities.
- Baseline two-step testing should be routinely offered for pre-employment testing of health care workers and staff of high risk workplaces (eg. prisons, alcohol and drug rehabilitation centres and nursing homes).
- People about to undergo organ donation.

What happens after the tuberculin skin test is read?

If the test is negative, it is recommended that you undergo yearly or second yearly Mantoux testing.

If the test is positive, a chest X-ray and physical examination will be needed to ensure there is no sign of active disease. If there are no signs of active TB the doctor will discuss the possibility of taking medication to prevent the development of TB disease. The benefits of taking the medication depend on the person's age, health and underlying risk of TB disease.

Ongoing screening of employees at increased risk of TB

A baseline two-step Mantoux test will make subsequent skin testing much easier to interpret and minimise the chance that people will be inappropriately diagnosed

and unnecessarily given treatment for latent tuberculosis infection (LTBI). Because there is biological variation and unavoidable differences in even the most carefully performed tests, small increases in reaction size on post-employment testing may not be meaningful. Therefore, for persons with Mantoux tests regarded as not indicating LTBI initially, an increase in reaction size of less than 10 mm within a period of 2 years should not generally be regarded as evidence of recent infection with TB. In selected circumstances, increases in reaction size of 6-10 mm within 2 years in people at particularly high risk may warrant consideration of treatment for LTBI. If in doubt, these people should be referred to the TB Control Unit for individualised assessment. Requirements for screening of health care workers and other at-risk staff are outlined further in the *Guidelines for the Control of Tuberculosis in the Northern Territory*.

What does a positive test mean?

It means that the person is infected by TB germs, but does not mean that he or she has TB disease. This person cannot pass TB onto anyone else unless they progress, at some later date, to active TB disease.

How can a person be infected and not have TB disease?

After TB germs enter the body, in most cases, body defences control the germs by building a wall around them, the way a scab forms over a cut. The germs can stay alive inside these walls for years in an 'inactive' state. While TB germs are inactive, they cannot harm the person and they cannot spread to other people. The person is infected but not sick and is unlikely to be aware that he or she is infected.

1. ATAGI. The Australian Immunisation Handbook. October 2008. 9th Edition

Tuberculin skin testing for Health staff and those in designated risk groups

• Initial Mantoux test ≥10mm refer to p36 TB Guidelines
• Initial Mantoux test <10mm (no previous Mantoux test within the past 12 months)
• Repeat Mantoux test in 2-3 weeks
• Second Mantoux test <10mm repeat 1-2 yearly
• Second Mantoux test ≥10mm refer p36 TB Guidelines

For further information contact the TB Clinic in your region

Alice Springs	**8951 7548**
Darwin	**8922 8806**
Katherine	**8973 9049**
Nhulunbuy	**8987 0282**
Tennant Creek	**8962 4259**

Further fact sheets and treatment protocols are available at http://www.nt.gov.au/health/publications

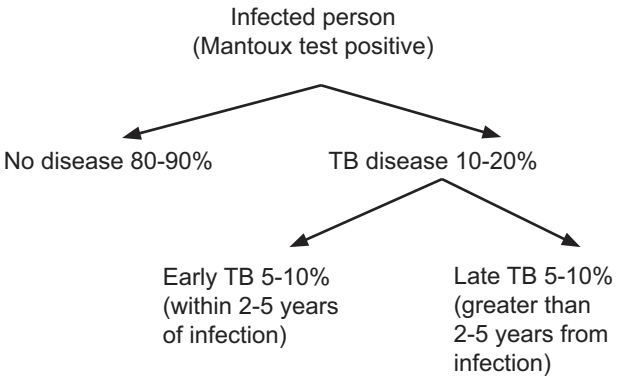
April 2008

TREATMENT OF LATENT TUBERCULOSIS INFECTION (Preventive Treatment)

Why do I need treatment to prevent TB?

Your positive Mantoux test indicates that you have been infected with the tuberculosis (TB) germ (*Mycobacterium tuberculosis*). Your chest X-ray and examination indicate that you **DO NOT** have the **disease** tuberculosis and **cannot pass the germ on to anyone else**. Being infected or having latent TB infection (LTBI) means that you may be at risk of developing disease sometime in your life especially if your body defences are weakened for any reason. By taking isoniazid (INH) tablets for 9 months, you can **reduce** your chance of infection developing into TB **disease** by 92%.

The risk of developing TB disease us outlined below



So if 100 people were infected (Mantoux test positive), 10 to 20 would be likely to go on to get TB over their lifetime with 5 to 10 of these TB cases occurring within 2-5 years of infection. If all 100 Mantoux test positive people took INH then less than 1 to 2 people would develop TB as the INH works to eliminate the dormant infection.

What medicine do I take to prevent TB?

A 9 month course of INH is taken to prevent TB disease from developing. INH is given according to your weight and for adults the daily dose is 300mg (3 X 100mg tablets). INH is sometimes given 3 times per week, at a higher dose, as a directly observed treatment by a health care worker. A vitamin B6 supplement (pyridoxine) is also given to reduce the risk of possible side effects.

Blood test before starting INH medication

INH can occasionally cause drug-induced hepatitis, (liver inflammation). Before taking INH, your liver function will be tested to check that your liver is working properly. INH is not recommended for people with liver disease or for those who consume alcohol regularly and heavily. ***It is very important that you avoid/ minimise drinking alcohol while taking INH as alcohol increases the risk of serious liver toxicity.***

Is INH safe?

INH has been taken by millions of people around the world and is generally well tolerated. However, as with any medicine, it can sometimes cause side effects. Tell your doctor, Aboriginal health worker or TB nurse immediately if any unexplained illness develops or if any of the following symptoms occur:

- upset stomach
- loss of appetite
- nausea
- vomiting
- skin rash/itch
- yellowish skin
- dark urine (tea colour)
- tingling or numbness of hands or feet
- fever lasting 3 days or more
- initital drowsiness (usually goes within the first month).

Monthly check-ups

While you are taking INH, a monthly visit to the TB Clinic is required. The purpose of this visit is to:

- check your weight and general health
- check for any side effects from the tablets
- check you are taking the tablets correctly
- collect another month supply of tablets.

What happens if I forget to take my tablets?

If you forget to take your tablets one day, do not worry. Just continue taking your daily dose the next day as usual. If you forget too many times, however, the medicine will not be effective.

It is easier to remember to take your tablets if you take them at the same time every day. It is also best to take them on an empty stomach.

General advice while taking INH

- take your INH tablets at least half an hour before meals or at bedtime.
- take the tablets with milk, water or a glass of juice.
- eat healthy food and get enough rest.
- **avoid drinking alcohol**.
- tell your doctor, Aboriginal health worker or TB nurse about any other medications you are taking and before beginning any new ones.
- **women** taking INH should avoid pregnancy until the treatment course is completed. This is because pregnancy can increase the risk of side effects related to the liver. If pregnancy does occur inform the TB clinic as soon as possible.
- the **oral contraceptive pill** can be safely used while taking INH.

What if I am exposed to someone with active TB again after completing a course of INH

Completing a course of treatment for LTBI (preventive treatment) kills the dormant TB germs in your body. Later, if you are exposed again, the risks of progressing to disease are much lower (about one quarter as much)*. Treating your initial Mantoux test conversion is most important. However, should you be re-exposed (ie. be identified as a TB contact) a clinical review and chest X-ray follow up would be recommended.

*Sutherland et al. The Development of Clinical Tuberculosis Following Infection with Tubercle Bacilli. *Tubercle* 63(1982) 255-268.

TB fact sheets are available at website: http://www.nt.gov.au/health/publications

For further information contact the TB Clinic in your region

Alice Springs	89517548
Darwin	89228806
Katherine	89739040
Nhulunbuy	89870282
Tennant Ck	89624259

April 2008

APPENDIX 5. Drug side effects and common drug interactions

<table>
<tr><th colspan="2">DRUG SIDE EFFECTS</th><th colspan="2">COMMON DRUG INTERACTIONS</th></tr>
<tr><td colspan="4">ISONIAZID</td></tr>
<tr><td>Nausea
Vomiting
Hepatitis
Rash
Peripheral neuropathy
• CNS effects
• drowsiness
• fatigue
• headache
• psychiatric
• giddiness
convulsion</td><td>Acne
Haemolytic anaemia
Aplastic anaemia
Agranulocytosis
Lupoid reaction
Arthralgia
Gynaecomastia</td><td colspan="2">Phenytoin (both INH and phenytoin levels increase)
Carbamazepine (Carbamazepine levels increase, INH can degrade to hepatotoxic metabolites)
Paracetamol (more of paracetamol's toxic metabolites form)</td></tr>
<tr><td colspan="4">RIFAMPICIN</td></tr>
<tr><td>Pink/orange
• urine
• sweat
• tears (stains contact lenses)
Nausea
Vomiting
Hepatitis
Rash
Drug induced fever</td><td>With prolonged unscheduled breaks:
• shock
• acute renal failure
• thrombocytopenia
• purpura
• haemolytic anaemia
• shortness of breath
• flu like syndrome (myalgia, arthralgia, fever, malaise, mild haemolysis)</td><td>Antacids may reduce the absorption of rifampicin.
Rifampicin causes decreased activity of:
• oral anticoagulants
• anticonvulsants
• antiarrhythmics
• antifungals
• barbiturates
• beta blockers
• calcium channel blockers
• chloramphenicol
• corticosteroids
• oral hypoglycaemics (sulphonylureas only)
• levothyroxine
• narcotic analgesics
• macrolide antibiotics (including clarithromycin, erythromycin and azithromycin</td><td>• methadone
• ondansertron
• quinine
• tacrolimus
• cyclosporin
• cardiac glycosides (digoxin),
• clofibrate
• hormonal tamoxifen,
• theophylline,
• tricyclic antidepressants,
• zidovudine
• contraceptives,
• dapsone,
• benzodiazepines,
• doxycycline,
• fluoroquinolone,
Rifampicin interacts with: enalapril, atovaquone, PAS, halothane</td></tr>
<tr><td colspan="4">PYRAZINAMIDE</td></tr>
<tr><td>Arthralgia
Gout
Nausea
Vomiting</td><td>Hepatitis
Flushing
Rash (photosensitive)
Disturbed diabetic control</td><td colspan="2"></td></tr>
<tr><td colspan="4">ETHAMBUTOL</td></tr>
<tr><td>Optic neuropathy
• Loss of visual acuity
• Loss of red green discrimination</td><td>Nausea Vomiting
Hepatitis
Rash
Arthralgia
Peripheral neuropathy</td><td colspan="2"></td></tr>
</table>

APPENDIX 6. FORMS

Tuberculosis treatment card 102
Tuuberculosis notification form 106
Adverse event following immunisation form 109
Contact tracing form 112
Isoniazid LTBI treatment form 113

Northern Territory Government
Department of Health and Community Services

HRN

TUBERCULOSIS TREATMENT CARD

CCIS Case ID

NT Department of Health and Community Services

Name:_____ DOB: / / Age: _____ Sex: _____
Ethnic group:_____ COB:_____ Notification date: / /
Address:_____ Phone: _____
Place of work:_____ Phone: _____
Next of kin:_____ Phone: _____
Treatment centre (CHC etc):_____ Supervisory centre:_____
CDC Case Manager:_____

DIAGNOSIS (Please circle)

PULMONARY Sputum: Pos/Neg
Culture: Pos/Neg
CXR: Consistent

PLEURAL Aspirate: Pos/Neg
Culture: Pos/Neg

LYMPH NODES Bx: Pos/Neg
Asp: Pos/Neg

CNS CSF: Pos/Neg
Cullture: Pos/Neg

PERICARDIUM CXR: Consistent
Asp: Pos/Neg

BONE X-ray: Consistent
Bx: Pos/Neg

PERITONEUM Asp: Pos/Neg
Bx: Pos/Neg

OTHERS _____

Treatment started: / /
Treatment due to stop: / /
Treatment actually stopped: / /

TYPE OF TREATMENT
(Please tick)

Initial	
Defaulter	
Relapse	
Resistance	

REASON TREATMENT STOPPED
(Please tick one)

Completed	
Transferred out	
Lost	
Died	

Compliance /

WEEKLY WEIGHTS

Week	Date	Weight (Kg)
0		
1		
2		
3		
4		
5		
6		
7		
8		
9		
10		

Initial AFB Smear result*_____ / / Culture result*_____ / / * Use report dates
Smear result*_____ / / Culture result*_____ / /
Smear result*_____ / / Culture result*_____ / /

Sensitivity results Date reported / /
Sensitive to: _____ _____
_____ _____
Resistant to: _____ _____
_____ _____

Baseline visual examination / / Result R eye _____
Result L eye _____
Ishihara _____

Baseline LFTs Date / / Results _____
_____
_____
_____

Name:

MONTH				MONTH				MONTH				MONTH				MONTH				MONTH			
	Rx	Defaulter Action			Rx	Defaulter Action			Rx	Defaulter Action			Rx	Defaulter Action			Rx	Defaulter Action			Rx	Defaulter Action	
	X				***X***				***X***				***X***				***X***				***X***		
		Visit type*	Sig			Visit type*	Sig			Visit type*	Sig			Visit type*	Sig			Visit type*	Sig			Visit type*	Sig
1				1				1				1				1				1			
2				2				2				2				2				2			
3				3				3				3				3				3			
4				4				4				4				4				4			
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29				29				29				29				29				29			
30				30				30				30				30				30			
31				31				31				31				31				31			

End of month Wt __________ Kg	End of month Wt __________ Kg	End of month Wt __________ Kg	End of month Wt __________ Kg	End of month Wt __________ Kg	End of month Wt __________ Kg
Compliance Daily /30	Compliance Daily /30	Compliance Daily /30	Compliance Daily /30	Compliance Daily /30	Compliance Daily /30
MWF /	MWF /	MWF /	MWF /	MWF /	MWF /
	Cumulative Total /	Cumulative Total /	Cumulative Total /	Cumulative Total /	Cumulative Total /
Review Date / /	Review Date / /	Review Date / /	Review Date / /	Review Date / /	Review Date / /

Name:

MONTH				MONTH				MONTH			
	Rx X	Defaulter Action			Rx X	Defaulter Action			Rx X	Defaulter Action	
		Visit type*	Report			Visit type*	Report			Visit type*	Report
1				1				1			
2				2				2			
3				3				3			
4				4				4			
5				5				5			
6				6				6			
7				7				7			
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30				30				30			
31				31				31			
End of month Wt				End of month Wt				End of month Wt			
_____ Kg				_____ Kg				_____ Kg			
Compliance				Compliance				Compliance			
Daily				Daily				Daily			
/30				/30				/30			
MWF				MWF				MWF			
/				/				/ **78**			
Cumulative Total				Cumulative Total				Cumulative Total			
/				/				/ **182**			
Review Date				Review Date				Review Date			
/ /				/ /				/ /			

End of treatment review / /

Clearance sputum result

Smear / /

Culture / /

TBMO comment

_____
_____
_____
_____
_____
_____
_____
_____
_____
_____
_____

Drug toxicities Yes / No

If 'yes' list drug/s and side effects

_____
_____
_____
_____

HIV result:_____ / /

Defaulter action

If pt. misses treatment - home visit

If pt. misses more than 1 treatment - report case to supervisory centre

Defaulter

If pt. on daily treatment misses more than 28 days in a row (MWF 12 doses) or takes longer than 8 months to complete a 6 month course. The course must then be restarted.

Missed doses for 6 month treatment regimens

Provided that >or = 80% of doses are taken within 8 months and no more than 1 month of treatment in a row has been missed, then every attempt should be made to continue treatment beyond 8 months so that all of the intended doses are given.

*Visit type = H (home visit) C (clinic visit by patient)

Name

TB Treatment

Drug	Dose (mg)	Frequency	Commenced	Completed	MO Signature

Initial home visit on discharge from hospital / /

Visit to supervisory health centre / /

Initial Contact tracing completed / /

3 month contact tracing completed / /

TUBERCULOSIS NOTIFICATION FORM

CORE DATA

Surname_____

First Name_____**Other Names** _____

Date of Birth / / **Age** _____**HRN** _____**Sex:** M / F

Indigenous Status (Please circle appropriately)

Aboriginal but not TSI / TSI but not A / A+TSI / Not A or TSI / Not Stated

Address when diagnosed_____

Suburb / Community (resident location)_____

CDC Unit Notifying *A/SP DARWIN EAR KATH Barkley*

Notification received date / / (date when TB Unit first informed)

Notification date (diagnosis date) / / (date 1st positive AFB/culture/histology collected)

True onset date (Date TB symptoms began or signs noted) / /

Case found by (please circle) *Clinical presentation / Contact tracing / Screening / Unknown*

Clinical Presentation	Contact tracing	Screening	
☐ *Clinical Referral (list symptoms and CXR findings)*	☐ *Contact Tracing*	☐ *TBU*	☐ *Health Staff Screening*
		☐ *Unauthorised person screening*	☐ *Migrant Screening*
		☐ *Community Screen Rural*	☐ *School Screening*
		☐ *Darwin Urban Screening*	☐ *Prisoner Screening*
☐ *Post Mortem*		☐ *Worker Screen (not Health)*	

Case found by other reason (please explain)_____

Hospitalised *Yes / No / Unknown* **Date admitted** / / **Date discharged** / /

Doctor notifying_____

Died from TB *Yes / No / Unknown* **Date of death** / /

LABORATORY DATA

Laboratory (please circle): *RDH, ASH, Kath, Gove, Tennant creek, Western Diagnostic, Qld Medical, IMVS, Path Centre, MedVet, Sullivan Nicolaides, Gribbles, Other, Unknown, No specimen requested*

Micro specimen type#: *Sputum, Induced Sputum, Brain, Bronchial Washing, Cerebro Spinal Fluid, Gastric Aspirate, Node, Node Aspirate, Pleura, Pericardial Fluid, Pleural Fluid, Peritoneal Fluid, Spine, Tissue, Urine*

Specimen type# (micro) date taken	AFB smear (microscopy)	AFB culture	PCR/DNA (NAT†)	Result (TB, *M bovis*, MAIC)
/ /	Neg / Pos	Neg/ Pos/ Pend/ ND	Neg / Pos/ND	
/ /	Neg / Pos	Neg/ Pos/ Pend/ ND	Neg / Pos/ND	
/ /	Neg / Pos	Neg/ Pos/ Pend/ ND	Neg / Pos/ND	

If extra-pulmonary TB was sputum taken Yes / No Smear Pos/Neg Culture Pos /Neg

† Nucleic acid testing, ND = not done, Pend = Pending

Histology specimen type List choices: *Sputum, Brain, Bronch Washing, Gastric Aspirate, Node, Node Aspirate, Pleura, Pleural Fluid, Peritoneal fluid, Spine, Tissue, Urine*

Specimen type (date taken)	Histology	AFB Smear	Culture	PCR	Result (TB, M bovis, MAIC)
/ /	Neg / Pos	Neg / Pos / ND	Neg/ Pos/ Pend/ ND	Neg/Pos/ND	_____
/ /	Neg / Pos	Neg / Pos / ND	Neg/ Pos/ Pend/ ND	Neg/Pos/ND	_____

ND = not done, Pend = Pending

ENHANCED DATA

First health contact / /

Country of birth_____**Year of first arrival**_____

Australian status (please circle)

Refugee / humanitarian	Visitor	Student	Unknown
Permanent resident	Unauthorised person (not IFF)	IFF	TSI Treaty
Other	N/A		

Health undertaking (tuberculosis undertaking) *Y / N / unknown*

HISTORY

New or relapsed case

New Case (less than 1 month of Tb Rx ever) ☐

Relapse after full Rx overseas ☐

after full Rx in Australia ☐

Other Relapse after partial Rx overseas (> 1 month Rx but less than full Rx) ☐

Relapse after partial Rx in Australia (> 1 month Rx but less than full Rx) ☐

Case found by (for data entry staff—use selection from core data)

Has patient had Mx in last 3 months Yes / No Size _____mm___**Date given** / /

Size of largest previous Mx (may be 0mm)_____mm **Year of largest previous Mx** / /

IGRA test *QuantiFERON Gold / T-Spot TB / Not done* **Date** / /

IGRA result *Positive / Negative / Indeterminate*

History of LTBI (identified by medical officer) *Yes / No*

LTBI Treatment *Didn't start / Started and completed / Started and didn't complete / Unknown*

Estimated date LTBI treatment completed / /

No. of BCGs or scars 0, 1, 2, 3, 4 or "U" **Year of most recent BCG**_____

Transfer In From outside NT Yes / No **Transfer in From Where?**_____

Year of previous Treatment _____**Place of previous treatment**_____

Name of contact index case(s) with TB (if known)_____

HIV *Positive / Negative / Not tested / Refused*

HTLV-1 *Positive / Negative / Refused / Not tested* (Reason not tested _____)

Risk Factors (please tick appropriate choices)		
Unknown	*No risk*	*Health Care Worker / Laboratory Worker*
lived / resident overseas >3 months	*HIV positive*	*Institution Worker (prison, aged care, homeless shelter)*
Resident Aged Care Facility	*Resident correctional facility*	*Household member or close contact with TB*
Kava	*Hepatitis B positive*	*Previously defaulter*
Diabetes	*Current Corticosteroid use*	*Chronic Lung Disease*
History of cancer < 5 yrs	*Renal Failure*	*Petrol Sniffing*
Post-partum	*Old TB*	*Malnourished*
History of leprosy	*Excessive alcohol intake*	*Defence*
Meatworker/Cattleman	*Miner*	

Pulmonary site *Pulmonary only / Pulmonary plus other sites / Extrapulmonary only*

Extrapulmonary site

Pleural	*Lymph nodes*	*Bone/Joint*
Genito-urinary	*Miliary (including blood culture pos)*	*Meningeal*
Peritoneal	*Other*	*None*
Brain	*Breast*	*Bowel*
Laryngeal	*Liver*	*Pericardial*
Skin	*Mediastinal*	*Other*

ICD10 code _____

Sputum clearance

Collection date 1st sputum smear +ve ___/___/___ Collection date 1st sputum culture +ve ___/___/___
Collection date 1st sputum smear -ve ___/___/___ Collection date 1st sputum culture -ve ___/___/___
Collection date 2nd sputum smear -ve ___/___/___ Collection date 2nd sputum culture -ve ___/___/___
Collection date 3rd sputum smear -ve ___/___/___ Collection date 3rd sputum culture -ve ___/___/___
Time to clear (time in weeks between treatment start date and first sputum smear negative)_____weeks

Treatment *Yes / No* **Treatment comm date** ___/___/___ **Treatment completion date** ___/___/___

Therapy		**Drug reaction**	**Drug Resistance**
INH	*Yes / No*	*Yes / No*	*Yes / No / NA (neg or no culture)*
Rifampicin	*Yes / No*	*Yes / No*	*Yes / No / NA (neg or no culture)*
Pyrazinamide	*Yes / No*	*Yes / No*	*Yes / No / NA (neg or no culture)*
Ethambutol	*Yes / No*	*Yes / No*	*Yes / No / NA (neg or no culture)*
Streptomycin	*Yes / No*	*Yes / No*	*Yes / No / NA (neg or no culture)*
Other_____		*Yes / No*	*Yes / No / NA (neg or no culture)*
Other_____		*Yes / No*	*Yes / No / NA (neg or no culture)*
No treatment	*Yes / No*		

Outcome - What was the outcome of TB Case? (tick only one choice)

☐ Cured (bacteriologically confirmed — smear and culture negative)

☐ Completed Treatment (completed at least 80% of doses)

☐ Interrupted treatment (interrupted for 2 months or more but completed treatment)

☐ Died of TB (please ensure this is the same as core data)

☐ Died of other cause (state cause)

☐ Defaulter (failed to complete treatment)

☐ Failure (completed treatment but failed to be cured)

☐ Transfer out to an interstate unit Where _____ Date / /

☐ Transfer out to an overseas unit Where_____ Date / /

☐ Outcome pending

Conversion at 3 months *Yes / No / Unknown*

No of doses taken_____**No. of doses prescribed**_____

Notifier's Name (print)_____Phone No. _____

Put on TB database / / Signature _____

ADVERSE EVENT FOLLOWING IMMUNISATION (AEFI) NORTHERN TERRITORY

PART A: INITIAL REPORT

HRN		
Family name (first two letters, only)		
Given name (first two letters, only)		
Date of Birth	**/ /**	
Ethnicity	**Aboriginal**	**Other**
Date of onset of adverse event	**/ /**	
Sex	**F**	**M**

1. Vaccine(s) given preceding the adverse event

Vaccine	Dose No.	Date given	Manufacturer	Batch No.	Post code of clinic where administered
Hepatitis B **(EngerixB or HBVax11)**					
Diphtheria-tetanus-acellular pertussis-HepB-inactivated polio vaccine **(Infanrix Penta)**					
Haemophilus influenzae type b **(PedvaxHib)**					
Pneumococcal conjugate **(Prevenar)**					
Rotavirus Vaccine (**Rotarix)**					
Measles-mumps-rubella **(Priorix)**					
Meningococcal C conjugate **(NeisvacC or Menjugate)**					
Hepatitis A **(VAQTA)**					
Pneumococcal polysaccharide **(Pneumovax 23)**					
Varicella Zoster **(Varilrix /Varivax)**					
Diphtheria-tetanus-acellular pertussis-inactivated polio vaccine **(Infanrix-IPV)**					
Adult Diphtheria Tetanus Pertussis **(Boostrix)**					
Influenza **(Fluvax,Vaxigrip,Fluarix,)**					
Human Papillomavirus **(GARDASIL)**					

HRN		
Family name (First 2 letters)		
Given name (First 2 letters)		

2 Were other vaccines administered within the four weeks prior to the suspected vaccines?

YES ☐ NO ☐ DON'T KNOW ☐

If YES – specify what vaccines _____

_____

3 Was the person ill at the time of administration of the suspected vaccine(s)?

YES ☐ NO ☐ DON'T KNOW ☐

If YES, describe the clinical features _____

_____

4 Previous medical history

Gestation age at birth (If less than 6 months old at time of AEFI) _____

Birthweight (If less than 6 months old at the time of AEFI) _____

Congenital abnormalities _____

Neurological disorders _____

Allergies _____

Other significant medical conditions _____

5 Describe the adverse event(s). ie clinical symptoms, time between vaccine administration and onset, duration, and any treatment performed during this event. Attach any relevant documentation such as progress notes. _____

_____

_____

_____

6 Was the person hospitalised? **YES ☐ NO ☐**

7 Did the person recover? **YES ☐ NO ☐**

If NO, describe the current situation _____

_____

If YES, in what time period? _____

Details of person reporting this event	
Name	
Clinic name and address	
Date of report	

Received at CDC	Date	Signature

PART B: 60-DAY REPORT

ADRAC sequence		
HRN		
Family name (first two letters, only)		
Given name (first two letters, only)		
Date of Birth	/ /	
Ethnicity	Aboriginal	Other
Date of onset of adverse event	/ /	
Sex	F M	

1 Did the person recover? **YES** ☐ **NO** ☐

If NO, describe the current situation _____

_____

If YES in what time period? _____

_____

2 Other comments

_____

_____

_____

_____

3 Details of health professional reporting the event

Name _____

Address _____

Phone number _____

Date of report ___/___/___

Person receiving the report _____

Date ___/___/___

January 2007

Northern Territory Government
Department of Health and Community Services

CONTACT TRACING **CONFIDENTIAL**

(INDEX TB CASE) NAME:_____ **HRN:**_____ **CCIS Case id no:**_____

ICD10 Code:_____ **Index Case Notification Date (use as Referral in date for contacts):**_____

NAME	M or F	Eth	HRN / DOB	Country of Birth	BCG Date (or no. of scars)	Current weight	Date prev Mantoux test / Size prev Mx	Mantoux test 1 Date / Reading in mm	Mantoux test 2 Date / Reading in mm	Review due / Review due date	Comments Include if known: address, contact ph, relationship to index

ISONIAZID LTBI TREATMENT

DEPARTMENT OF HEALTH & COMMUNITY SERVICES

Principal name
Other name (s)
DOB/Sex
Specialist

Public/Private
HRN
Ward

Status: Refugee ☐ Migrant ☐ Prisoner ☐ School screen ☐ Contact ☐

Employment ☐ Other ☐ If other please specify .....

Liver function test (if abnormal repeat monthly or prn) Date ...../...../20..... Normal ☐ Abnormal ☐

Drug ..... Dose ..... Drug ..... Dose .....

Date Commenced ...../...../20.... Date completed ...../...../20.....

MONTHLY CHECK LIST

LFTs to be performed monthly
Yes ☐ No ☐

Date	Weight	Dose Correct	Drowsy	Liver S & S	Nausea	Rash	Periph Neuritis	LFTs Taken	
								Yes	No
1.									
2.									
3.									
4.									
5.									
6.									
7.									
8.									
9.									

SIDE EFFECTS OF INH

Drowsiness, insomnia, irritability, feeling happy, dizziness, tinnitus, anorexia, nausea, epigastric pain

LIVER PROBLEMS

Hepatitis, jaundice, dark urine

PERIPHERAL NEUROPATHY

Fever, Skin rash

Prescription Dates	Next Appointment
1.	
2.	
3.	
4.	
5.	
6.	
7.	
8.	
9.	

IF NEW CONVERSION OR CONTACT THEN FOR CLINICAL REVIEW + /OR CXR ON COMPLETION

Date: ...../...../20…… Results: ..... Adherence: ____/____ _____%

Signature: …… Designation: ..../...../20.....

NAME:																									HRN		
Month			Month			Month			Month			Month			Month			Month			Month			Month		
Date	Taken	Ini	Date	Taken	Ini	Date	Taken	Ini	Date	Taken	Ini	Date	Taken	Ini	Date	Taken	Ini	Date	Taken	Ini	Date	Taken	Ini	Date	Taken	Ini
1			1			1			1			1			1			1			1			1		
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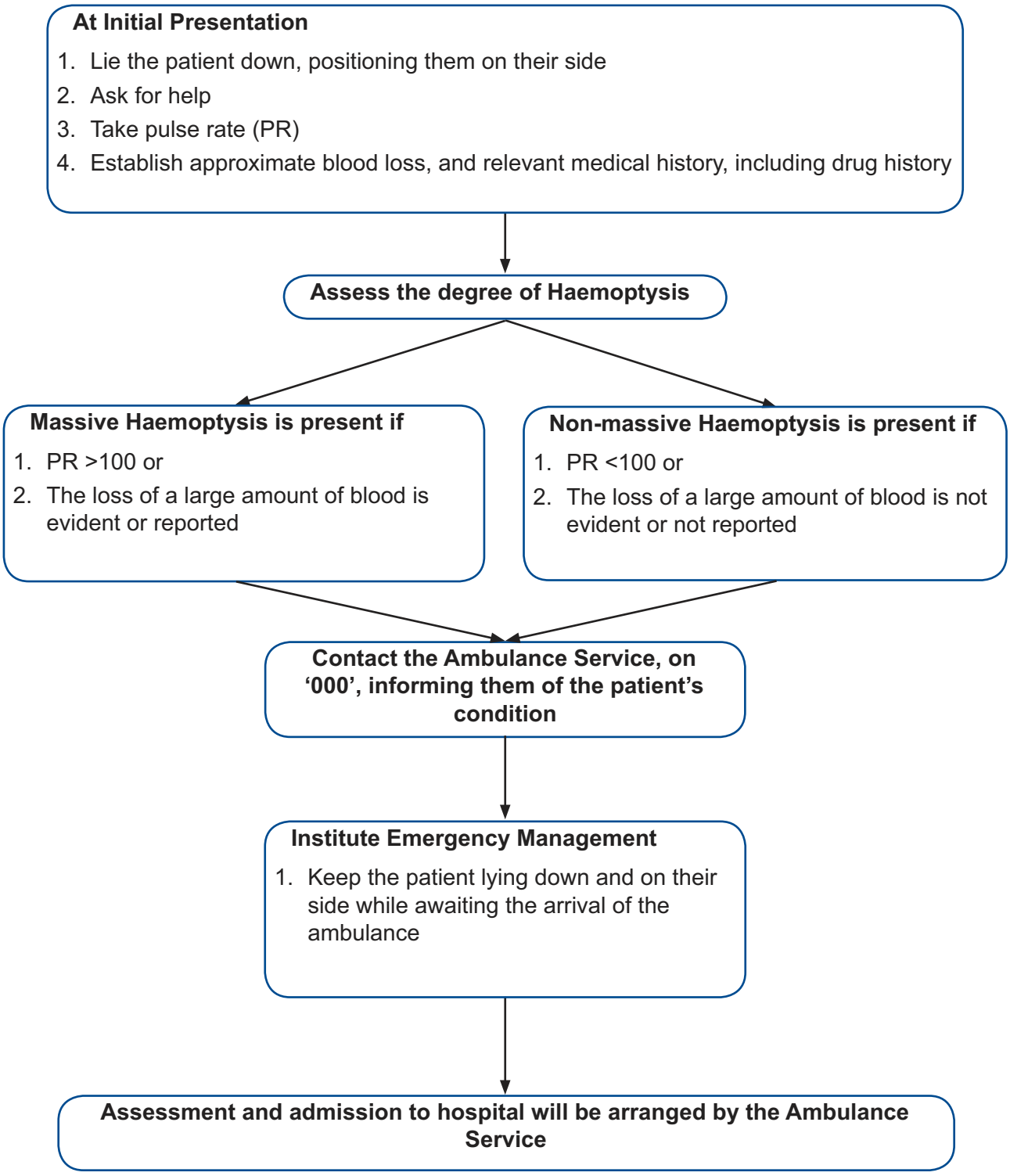
APPENDIX 7. Haemoptysis Protocol

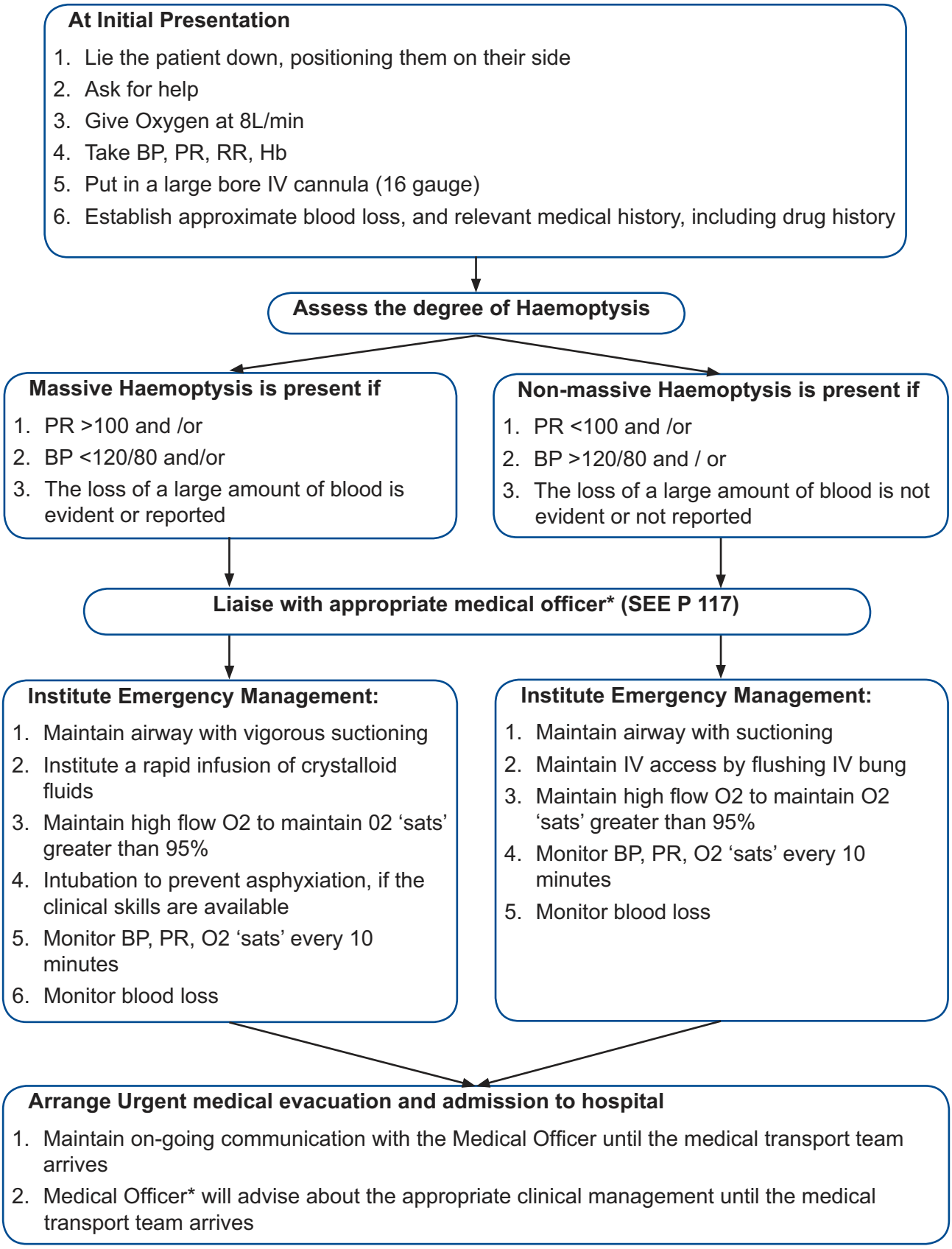
EMERGENCY MANAGEMENT OF HAEMOPTYSIS

IN THE HOME



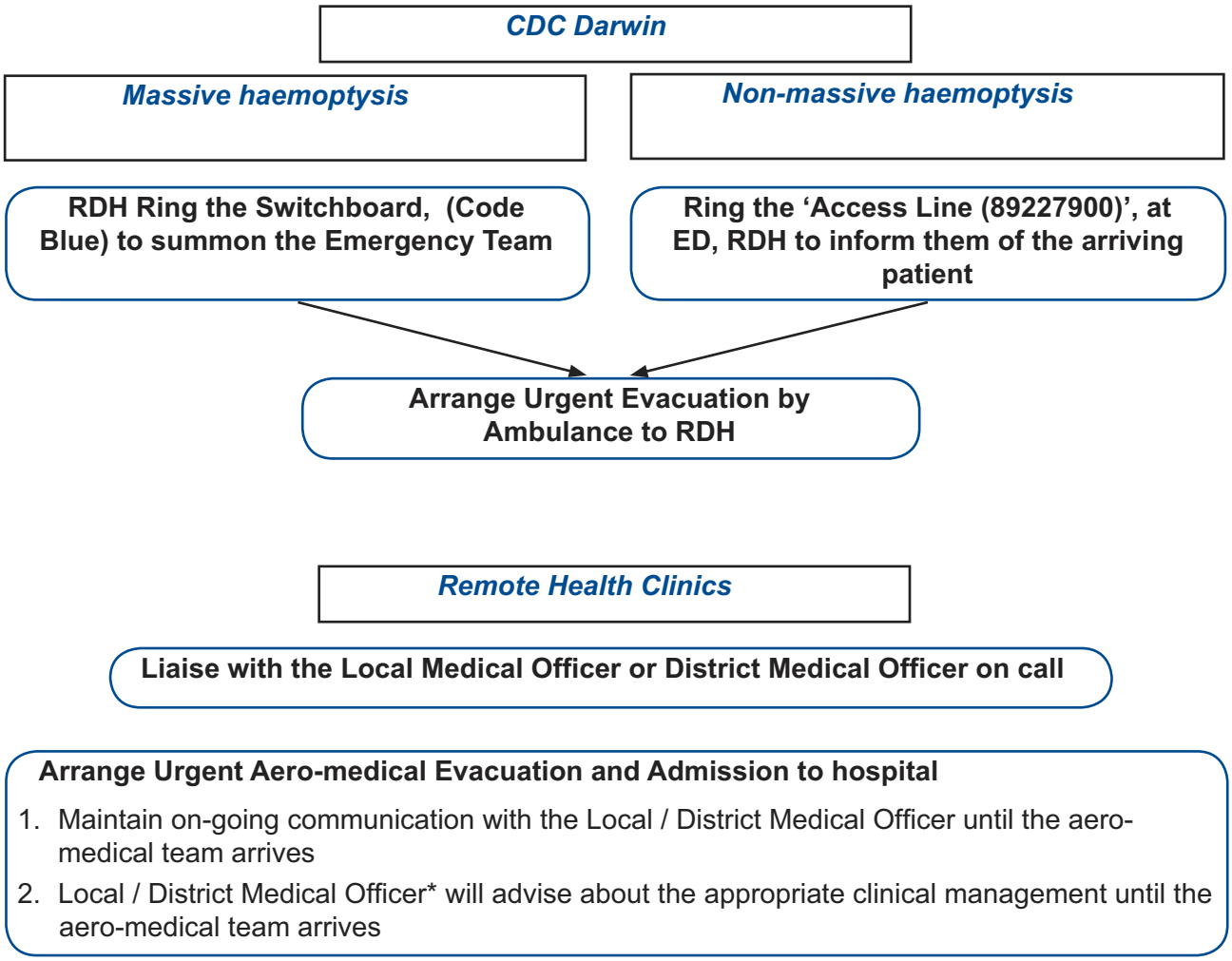
EMERGENCY MANAGEMENT OF HAEMOPTYSIS

IN A CLINIC SETTING



EMERGENCY MANAGEMENT OF HAEMOPTYSIS

Procedure for contacting an appropriate medical officer



APPENDIX 8

Royal Darwin Hospital Intensive Care Unit

ICU/HDU PATIENTS WITH SIGNIFICANT RISK OF HAVING TUBERCULOSIS (TB)

1. If a patient is assessed as having a significant risk of TB, the patient is to be admitted to 1 of the 2 negative pressure rooms (Iso 2 and Iso 3).
2. The isolation room is to have the corridor door closed at all tomes to maintain negative pressure.
3. All staff entering the room need to enter via the anteroom in the CCU back corridor.
4. Personal protective equipment including P2 mask (duckbill mask) will be put on in the anteroom by all staff entering the room.
5. Masks will be discarded when leaving the room and a new one applied when re-entering the room - do not reuse masks.
6. Notify the TB Unit in CDC that a patient with possible TB is in the unit so they can assess the situation and provide advice.
7. Precautions will remain in place until 3 sputums have been reported as negative for acid fast baccilli as per the RDH/CDC protocol and/or the patient has been declared by an ICU specialist as no longer having a significant risk of having TB.
8. Ventilator circuits with closed suction systems do not provide 100% protection for staff and therefore masks must be worn even if the patient is ventilated and has a closed suction system.

This policy is conservative and provides ICU/HDU staff with the greatest degree of work place safety and will over ride any other policy or opinion relating to infection control measures for patients with suspected TB.

Dr Dianne Stephens

APPENDIX 9 Countries of High TB Prevalence*

Country	Cases per 100,000/yr 2006	TB Prevalence ≥25/100,000
Afghanistan	161	X
Albania	19	
Algeria	56	X
American Samoa	9	
Andorra	19	
Angola	285	X
Anguilla	26	X
Antigua and Barbuda	6	
Argentina	39	X
Armenia	72	X
Australia	6	
Austria	13	
Azerbaijan	77	X
Bahamas	38	X
Bahrain	41	X
Bangladesh	225	X
Barbados	11	
Belarus	61	X
Belgium	13	
Belize	49	X
Benin	90	X
Bermuda	4	
Bhutan	96	X
Bolivia	198	X
Bosnia and Herzegovina	51	X
Botswana	551	X
Brazil	50	
British Virgin Islands	13	
Brunei	83	X
Bulgaria	40	X
Burkina Faso	248	X
Burma (Myanmar)	171	X
Burundi	367	X
Cambodia	500	X
Cameroon	192	X
Canada	5	
Cape Verde	168	X
Cayman Islands	4	
Central African Republic	345	X
Chad	299	X
Chile	15	
China	99	X
Colombia	45	X
Comoros	44	X
Congo	403	X
Cook Islands	16	
Costa Rica	14	
Croatia	40	X
Cuba	9	
Cyprus	5	
Czech Republic	10	
Democratic Republic of Congo	392	X
Denmark	8	

Country	Cases per 100,000/yr 2006	TB Prevalence ≥25/100,000
Djibouti	809	X
Dominica	16	
Dominican Republic	89	X
East Timor	556	X
Ecuador	128	X
Egypt	24	
El Salvador	50	X
Equatorial Guinea	256	X
Eritrea	94	X
Estonia	39	X
Ethiopia	378	X
Fiji	22	
Finland	5	
France	14	
French Polynesia	26	X
Gabon	354	X
Gambia	257	X
Georgia	84	X
Germany	6	
Ghana	203	X
Greece	18	
Grenada	5	
Guam	37	
Guatemala	79	X
Guinea	265	X
Guinea-Bissau	219	X
Guyana	164	X
Haiti	299	X
Honduras	76	X
Hungary	19	
Iceland	4	
India	168	X
Indonesia	234	X
Iran	22	
Iraq	56	X
Ireland	13	
Israel	8	
Italy	7	
Ivory Coast	420	X
Jamaica	7	
Japan	22	
Jordan	5	
Kazakhstan	130	X
Kenya	384	X
Kiribati	372	X
Kuwait	24	
Kyrgyzstan	123	X
Laos	152	X
Latvia	57	X
Lebanon	11	
Lesotho	635	X
Liberia	331	X
Libya	18	
Lithuania	62	X

Country	Cases per 100,000/yr 2006	TB Prevalence ≥25/100,000
Luxembourg	12	
Macedonia	29	X
Madagascar	248	X
Malawi	377	X
Malaysia	103	X
Maldives	45	X
Mali	280	X
Malta	6	
Mauritania	316	X
Mauritius	23	
Mexico	21	
Micronesia	101	X
Moldova	141	X
Monaco	2	
Mongolia	188	X
Montenegro	32	X
Montserrat	9	
Morocco	93	X
Mozambique	443	X
Namibia	767	X
Nauru	106	X
Nepal	176	X
Netherlands	8	
Netherlands Antilles	8	
New Caledonia	27	X
New Zealand	9	
Nicaragua	58	X
Niger	174	X
Nigeria	311	X
Niue	43	X
North Korea	178	X
Northern Mariana Islands	75	X
Norway	6	
Oman	13	
Pakistan	181	X
Palau	51	X
Panama	45	X
Papua New Guinea	250	X
Paraguay	71	X
Peru	162	X
Philippines	287	X
Poland	25	X
Portugal	32	X
Puerto Rico	5	
Qatar	60	X
Romania	128	X
Russia	107	X
Rwanda	397	X
Saint Kitts and Nevis	11	
Saint Lucia	17	
Saint Vincent and Grenadines	30	X

Country	Cases per 100,000/yr 2006	TB Prevalence ≥25/100,000
Samoa	19	
San Marino	6	
Sao Tome and Principe	103	X
Saudi Arabia	44	X
Senegal	270	X
Seychelles	33	X
Sierra Leone	517	X
Singapore	26	X
Slovakia	15	
Slovenia	13	
Solomon Islands	135	X
Somalia	218	X
South Africa	940	X
South Korea	88	X
Spain	30	X
Sri Lanka	60	X
Sudan	242	X
Suriname	64	X
Swaziland	1155	X
Sweden	6	
Switzerland	7	
Syria	32	X
Tajikistan	204	X
Thailand	142	X
Togo	389	X
Tokelau	56	X
Tonga	25	X
Trinidad and Tobago	8	
Tunisia	25	X
Turkey	29	X
Turkmenistan	65	X
Turks and Caicos Islands	17	
Tuvalu	295	X
Uganda	355	X
Ukraine	106	X
United Arab Emirates	16	
United Kingdom	15	
Tanzania	312	X
United States Virgin Islands	10	
United States of America	4	
Uruguay	27	X
Uzbekistan	121	X
Vanuatu	58	X
Venezuela	41	X
Vietnam	173	X
Wallis and Futuna Islands	46	X
West Bank and Gaza Strip	20	X
Yemen	78	X
Zambia	553	X
Zimbabwe	557	X

Source: World Health Organization, Global TB Database; www.who.int/tb/country/global_tb_database/en/index.html.

APPENDIX 10 BCG SIDE EFFECTS QUESTIONNAIRE

DISTRICT REPORTING:(Please circle) Darwin Katherine East Arnhem Barkly Alice Springs

PLACE GIVEN (eg ASH): _____

SURNAME: _____ FIRST NAME: _____

SEX: M ☐ F ☐ DOB: ___ / ___ / ___ HRN: _____

DELIVERY: _____ WEEKS: _____ DATE OF BCG: ___ / ___ / ___ BATCH NO: _____

REASON: (Please tick) Aboriginal ☐ Living Overseas > 3 mths ☐ No Reason ☐

Aboriginal Community dweller ☐ Other (eg migrant parent) ☐ _____

1ST PRESENTATION: ___ / ___ / ___ NUMBER OF PRESENTATIONS: _____

TECHNIQUE INFORMATION: Bleb seen ☐ No Bleb seen ☐ Given S.C. ☐

Given I.M. ☐ Overdose ☐ Amount _____ Other _____

Eye splash ☐ Goggles worn Y / N 20 minute eyewash Y / N INH given Y / N

Outcome _____

COMPLICATIONS: (Please tick) AREA INVOLVED

- Left Axillary Node Enlarged ☐ _____
- Left Axillary Suppuration Node ☐ _____
- Left Local Site Abscess ☐ _____
- Left Local Site with Suppuration ☐ _____
- Left Local Site secondary Infection ☐ _____
- Disseminated BCG ☐
- Keloid ☐
- Other (Please state) _____

HOSPITALISED: Yes ☐ No ☐

Dates: Admitted: ___ / ___ / ___ Discharged: ___ / ___ / ___

Admitted: ___ / ___ / ___ Discharged: ___ / ___ / ___

Admitted: ___ / ___ / ___ Discharged: ___ / ___ / ___

Other Diagnosis: Yes ☐ No ☐ Scabies ☐ Skin Sores ☐ Other _____

ACTION TAKEN: (Please tick)

Excision of node ☐ Drainage (needle or surgical) ☐ Excision of local site ☐

Medication only ☐ Medication and other ☐ Observation only ☐ Other _____

SPECIMEN TAKEN: Yes ☐ No ☐

AFB Smear +ve ☐ AFB Culture +ve ☐ *M bovis* ☐ Resistant to INH ☐

Histology Yes ☐ No ☐ Compatible ☐

OUTCOME: Healed ☐ Other_____

APPENDIX 11

Managing IFF in Detention with Sputum Cultures Pending

This procedure is to enable the appropriate follow up for Illegal Foreign Fishermen (IFF) who are transferred to the Northern Immigration Detention Facility from another state with the following investigations carried out and/or pending.

- 3 sputum specimens for AFB have been collected as per the IFF guidelines

  AND
- all 3 are smear negative

  AND
- any sputum culture is pending.

Management

1. Notify CDC of the IFF on transfer – fax CDC screening documentation.
2. Weekly review by visiting GP to monitor for TB signs and symptoms while they remain in detention.
   - history – review for cough, fevers, night sweats, weight loss
   - examination – temperature, pulse, weight
   - please record findings to enable comparison/tracking.
3. If there is:
   - worsening cough features – increase in frequency or productiveness, haemoptysis
   - appearance of fever or night sweats
   - subjective impression by IFF of weight loss
   - temperature elevated above 38°C
   - pulse rate elevated
   - weight loss of >2kg

   THEN
   - collect sputum for AFBs
   - place mask on fisherman while inside
   - contact CDC to discuss.

CDC Darwin contact details:
Telephone (08) 8922 8804
Fax (08) 8922 8310

APPENDIX 12 - STANDARD LETTERS

Notice to detain 124

Order to detain a person or suspect person 125

Positive tuberculin skin test letter for patient information 126

Tuberculin skin test positive contact follow up 127

Contact completed 2 years follow up 128

Tuberculin skin test positive (<15 mm) and prior BCG 129

Starting isoniazid 130

LTBI completed isoniazid 131

LTBI refused isoniazid 132

DEPARTMENT OF **HEALTH AND COMMUNITY SERVICES**

Section: Centre for Disease Control
TB Unit

Reference:

Phone: 89228804

Facsimile: 89228310

NORTHERN TERRITORY OF AUSTRALIA

Notifiable Diseases Act

NOTICE TO DETAIN

I hereby notify that you are an infected person within the meaning of the Notifiable Diseases Act.

You are directed in pursuance of section 11(1) of that Act to proceed to Royal Darwin Hospital where you should remain for the purpose of receiving daily medication for the treatment of your pulmonary tuberculosis. You should remain at Royal Darwin Hospital until such time as your attending physician considers you are no longer at risk of spreading this disease.

Under section 11(2) of the Act you are required to comply with this notice. Failure to do so, may make it necessary for me to seek an order under section 13(2) of the Act to detain you at Royal Darwin Hospital to ensure adequate administration of medication.

You are advised that you are entitled to appeal to the Local Court against this notice or a direction contained in it.

Dated this day of 200

Medical Officer of Health

(appointment under the Public Health Act)

DEPARTMENT OF **HEALTH AND COMMUNITY SERVICES**

Section: Centre for Disease Control
TB Unit
Phone: 89228804

Reference:

Facsimile: 89228310

NORTHERN TERRITORY OF AUSTRALIA

Notifiable Diseases Act

ORDER TO DETAIN A PERSON OR SUSPECT PERSON

I, ... the Chief Medical Officer in pursuance of section 13 of the Notifiable Diseases Act, order that -

(Name) .....

being an infected person or suspect person be removed to and detained at a hospital or other place until a medical officer authorises the release of the person on the grounds that that person is not an infected person or is no longer a suspect person.

Dated this day of 200

Chief Medical Officer

DEPARTMENT OF **HEALTH AND COMMUNITY SERVICES**

Centre for Disease Control
TB Unit

Darwin	(08) 8922 8804
Alice Springs	(08) 8951 7548
East Arnhem	(08) 8987 0282
Katherine	(08) 8973 9040
Tennant Creek	(08) 8962 4259

Date: ___ / ___ / ___

Dear _____

You have been found to have a positive tuberculin skin test (Mantoux Test) on screening for tuberculosis. This measured _____. **This DOES NOT mean that you have the disease tuberculosis** and therefore you cannot infect other people. It does indicate that you have come into contact with the germ that causes TB at some time.

Most people who have a positive tuberculin skin test Test DO NOT get the disease tuberculosis (TB). However the positive test does indicate that they have an increased risk or possibility of going on to get the disease. That is why a chest X-ray is taken, a clinical review is given and sometimes preventive medication (isoniazid) is offered.

The TB Clinic reviews all people who have a positive tuberculin skin test result.

To arrange an appointment at the TB Clinic please phone 89228804. Please ask to talk to a nurse if you have any concerns.

Yours sincerely

TB Unit

DEPARTMENT OF **HEALTH AND COMMUNITY SERVICES**

Centre for Disease Control
TB Unit

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East Arnhem	(08) 8987 0282
Katherine	(08) 8973 9040
Tennant Creek	(08) 8962 4259

Date: ___ / ___ / ___

Dear Doctor

RE: _____DOB:

who was referred to the TB Clinic for assessment following a history of exposure to a sputum positive case of pulmonary tuberculosis and a tuberculin skin test result of_____mm on ___/__ /____ with/without prior BCG immunisation.

The risk of a contact developing pulmonary tuberculosis depends on the patient's immune status, but is thought to be about 2 - 5% per year for two years after exposure. If they are well at the end of the two year period they carry a small but real risk of developing tuberculosis at some time during their life, of about 5 - 10% overall.

We follow infected contacts (those with a tuberculin skin test of 10mm) for 2 years with regular reviews, if they are ineligible for treatment of Latent TB infection with isoniazid (to prevent TB disease).

Your patient falls into this category, so will be reviewed by the TB Clinic over the next 2 years. If this patient should develop a productive cough for 3 weeks or more, fever and night sweats for no obvious reason, or unexplained weight loss, please think of TB and refer to the TB Clinic for investigation.

If at any time in the future they have any need for prolonged therapy with corticosteroids then it is very important they are referred to the TB Clinic for prior review.

Yours sincerely

TB Unit

DEPARTMENT OF **HEALTH AND COMMUNITY SERVICES**

Centre for Disease Control
TB Unit

Darwin	(08) 8922 8804
Alice Springs	(08) 8951 7548
East Arnhem	(08) 8987 0282
Katherine	(08) 8973 9040
Tennant Creek	(08) 8962 4259

Date: ___ / ___ / ___

Dear Doctor

RE:_____DOB:

This patient has been assessed at the TB Clinic following contact with a case of active tuberculosis. Tuberculin skin testiing revealed ____mm induration on __/__/____, with/ without previous BCG vaccination.

As the patient had evidence of infection with *Mycobacterium tuberculosis* but no clinical or radiographic evidence of active disease he/she has been reviewed at the clinic at regular intervals for 2 years, according to our protocol for those with evidence of infection due to recent contact. He/she was not eligible for isoniazid for treatment of latent TB infection (prevention treatment) or refused isoniazid.

After 2 years of follow-up there has been no evidence of active tuberculosis and they have been discharged from the clinic.

The likelihood of this patient developing active disease in the future is small but not negligible (_____% lifetime risk*). They have been advised of this risk and told to seek medical attention promptly in the event of suggestive symptoms such as protracted fever, sweats, cough, haemoptysis or unexplained weight loss.

If at anytime in the future they have any need for prolonged therapy with immunosuppressive medications such as systemic corticosteroids, or develop co-morbidities associated with immunosuppression such as chronic renal insufficiency, then it is very important that they are referred to the TB Clinic for review.

Yours faithfully

TB Unit

* Horsburgh CR. Priorities for the treatment of latent tuberculosis infection in the United States. *N Engl J Med* 2004; 350: 2060- 2067.

DEPARTMENT OF **HEALTH AND COMMUNITY SERVICES**

Centre for Disease Control
TB Unit

Darwin	(08) 8922 8804
Alice Springs	(08) 8951 7548
East Arnhem	(08) 8987 0282
Katherine	(08) 8973 9040
Tennant Creek	(08) 8962 4259

Date: ___ / ___ / ___

Dear Doctor

RE: _____DOB:

who has been investigated at the TB/Chest Clinic following the finding of a Mantoux test (tuberculin skin test) result on __/__/____of_____mm with history of past BCG.

A chest X-ray was taken and this was normal. They have therefore been reassured that they are not suffering tuberculosis disease, but that they may have been exposed to tuberculosis disease, and have asymptomatic latent TB infection (LTBI). They have not been offered routine LTBI treatment (for prevention of TB disease) because when a past BCG has been given, the criteria for giving preventive treatment is a Mantoux test result 15mm or greater with a history of past BCG.

It has been explained to them that should they develop a productive cough for longer then 3 weeks, fever and night sweats for no obvious reason, or unexplained weight loss then their investigations should include a search for tuberculosis disease. Also, should prolonged corticosteroid therapy be required for treatment of asthma, etc a course of preventive isoniazid treatment should be considered.

They have been discharged from the Clinic.

Thank you for continuing their care.

Yours sincerely

TB Unit

DEPARTMENT OF **HEALTH AND COMMUNITY SERVICES**

Centre for Disease Control
TB Unit

Darwin	(08) 8922 8804
Alice Springs	(08) 8951 7548
East Arnhem	(08) 8987 0282
Katherine	(08) 8973 9040
Tennant Creek	(08) 8962 4259

Date: ___ / ___ / ___

Dear Doctor

Your patient has been screened for tuberculosis on __/__/____ and was found to be Mantoux test (tuberculin skin test) positive (_____mm). She/he has accepted the offer of treatment of latent TB infection (LTBI) with isoniazid for 9 months.

The Mantoux test is an indicator to help identify people who have been infected with *Mycobacterium tuberculosis*. Many people are infected with *Mycobacterium tuberculosis* but on average, only a small percentage (5-10%) over a lifetime go on to develop the disease tuberculosis. Some persons have an even higher risk of developing TB disease including those who:

1. are documented as “new Mantoux test converters” over the past 2 years
2. are a recent contact of a case of pulmonary tuberculosis
3. have CXR evidence of old disease and were never treated
4. receive prolonged immunosuppressive medication, eg. corticosteroids, or have co-morbidities such as chronic renal insufficiency or diabetes mellitus
5. are HIV positive
6. are children.

A 9 month course of preventive therapy with isoniazid has been shown to reduce the possibility of going on to develop the disease by up to 92%. Generally isoniazid LTBI treatment as a TB control/preventive measure is only offered to Mantoux test positive patients who do not drink alcohol regularly, have no evidence of liver disease, and are not pregnant or immediately post-partum.

Your patient will be followed monthly at TB Clinic for compliance, evidence of side effects and renewal of isoniazid prescription. Baseline liver function tests were done and were normal. It is important that patients on LTBI treatment with any suspected isoniazid side effects (especially hepatitis symptoms), stop medication at once and notify the TB Unit for further evaluation.

Should you have any queries please feel free to call the TB Clinic on 89228804.

Yours sincerely

TB Unit

DEPARTMENT OF **HEALTH AND COMMUNITY SERVICES**

Centre for Disease Control
TB Unit

Darwin	(08) 8922 8804
Alice Springs	(08) 8951 7548
East Arnhem	(08) 8987 0282
Katherine	(08) 8973 9040
Tennant Creek	(08) 8962 4259

Date: ___ / ___ / ___

Dear Doctor

RE: _____DOB:

This patient was referred to the TB Clinic following a Mantoux test (tuberculin skin test) result of ____mm on ___/__/___.

A chest X-ray and clinical assessment was performed and tuberculosis disease was excluded. He/she was therefore diagnosed with asymptomatic latent TB infection (LTBI), and as there were no contra-indications, treatment with isoniazid to prevent TB disease was offered.

Your patient accepted this treatment and a 9 month course of isoniazid and pyridoxine has now been completed (date ___/__/___).

In an individual with asymptomatic infection (positive Mantoux test) the rate of developing tuberculosis disease later in life is estimated to be between 5-10% of cases. This risk of developing disease is reduced by up to 92% by completing a nine month course of isoniazid therapy.

He/she is now being discharged from the TB Clinic but has been advised that if a productive cough lasting for longer than 3 weeks, fever or night sweats or unexplained weight loss develops a medical assessment should include ruling out of tuberculosis.

Thank you for your continuing care.

Yours sincerely

TB Unit

DEPARTMENT OF **HEALTH AND COMMUNITY SERVICES**

Centre for Disease Control
TB Unit

Darwin	(08) 8922 8804
Alice Springs	(08) 8951 7548
East Arnhem	(08) 8987 0282
Katherine	(08) 8973 9040
Tennant Creek	(08) 8962 4259

Date: ___ / ___ / ___

Dear Doctor

RE:_____DOB:

She/he was referred to the TB Clinic following a Mantoux test (tuberculin skin test) result on __/__/___of_____mm (with/without prior BCG).

A chest X-ray was normal. As they have NO evidence of tuberculosis disease, they have been diagnosed as having latent TB infection (LTBI).

The risk of developing tuberculosis disease in a patient who is suffering an LTBI is estimated at between 5-10%, half of whom will develop disease in the first few years after exposure, the other half doing so at some time in their remaining years. Consequently, if patients have no contra-indications they are offered a 9 month course of isoniazid preventive treatment, which reduces their risk of developing disease by up to 92%.

Your patient was offered this course but declined to take it. They have been advised that should they develop a productive cough lasting longer than 3 weeks, fevers or sweats without an obvious cause, or unexplained weight loss then they should attend for medical review, including investigations for tuberculosis disease. Also, should prolonged corticosteroid therapy be required for treatment of asthma etc, a course of preventive isoniazid treatment should be reconsidered regardless of age.

She/he has been discharged from the Clinic but of course we will be happy to see her/him again if requested.

Yours sincerely

TB Unit