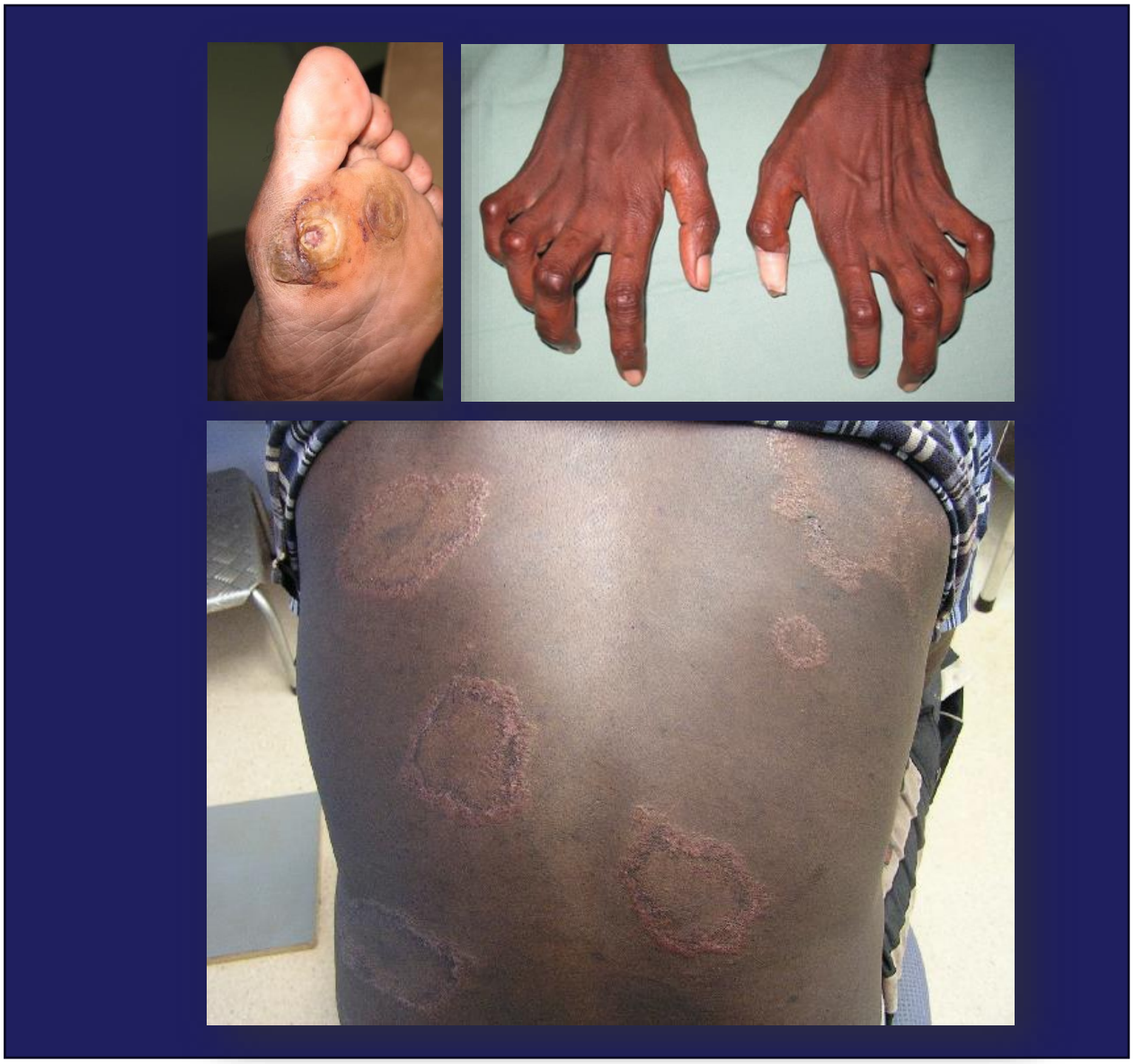
NT Health

Guideline

Due for review: 30/05/2030

Leprosy Management Northern Territory



NORTHERN TERRITORY GOVERNMENT

Contents

Publication overview

- First Edition - 1996
- Second Edition - 2002
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- Fourth Edition - 2018
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2024: Pasqualina Coffey, Elizabeth Stephenson, Sarah Lynar and Vicki Krause are the contributing authors to this edition with input from the Northern Territory Centre for Disease Control Unit, Territory Pathology, Royal Darwin Hospital Infectious Disease Physicians and High Risk Foot Clinic staff. Changing local circumstances, accumulated data, new medical evidence and internationally recognised recommendations have been considered in the production of this current edition.

Photographs in this document come from the Centre for Disease Control collection, and some were previously featured in 'Leprosy in Tropical Australia. A short guide for field staff in the diagnosis, treatment and management of leprosy' (1997).[1]

Many of the photographs were taken by Eileen Jones AM, a leprosy control nurse in the Northern Territory for many years.

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Acronyms

TERM	Definition
AFB	Acid-fast bacilli
BCG	Bacille Calmette-Guérin vaccine
BI	Bacterial index
BB	Mid-borderline (leprosy)
BL	Borderline lepromatous (leprosy)
BT	Borderline tuberculoid (leprosy)
CMI	Cell mediated immunity
DNA	Deoxyribonucleic acid
DOT	Directly observed therapy
ENL	Erythema nodosum leprosum
EHF	Eye Hand Feet score
G2D	Grade 2 Disease
G6PD	Glucose-6-phosphate dehydrogenase deficiency
HIV	Human immunodeficiency virus
HPF	High power field
LL	Polar lepromatous l(leprosy)
MB	Multibacillary (leprosy)
MDT	Multi-drug treatment
MI	Morphological Index
NCS	Nerve conduction studies
NFI	Nerve function impairment
NT	Northern Territory
PB	Paucibacillary (leprosy)
PCR	Polymerase chain reaction
RFT	Release from treatment
RN	Registered nurse
ROM	Rifampicin, ofloxacin, minocycline
RR	Reversal reaction
SLPB	Single lesion paucibacillary
SFG	Solid-Fragment-Granule
TB	Tuberculosis
TT	Polar tuberculoid (leprosy)
VMT-ST	Voluntary Muscle Test-Sensory Test
WHO	World Health Organization

Edition changes

2002 Edition (second edition)

In the 2002 edition the most important changes to note were:

1. a change in the Multi-Drug Treatment (MDT) regimen with rifampicin prescribed monthly rather than daily and the durations fixed at 6 and 24 months for Paucibacillary (PB) and Multibacillary (MB) leprosy, respectively
2. a reduction in the duration of follow-up for cured cases from annual reviews to:
    - MB with a Bacterial Index (BI) ≥4 for 5 years after 24 months of treatment
    - PB who had Nerve Function Impairment (NFI) at time of diagnosis for 18 months beyond 6 months of treatment
    - discharge after treatment completion for all others.
3. a reduction in the duration of follow-up for contacts after diagnosis of an index case to annual reviews for 6 years for MB contacts and a single review for PB contacts
4. the introduction of standardised clinical assessment (Voluntary Muscle Test – Sensory Test VMT-ST) for the common NFI.

2010 Edition (third edition)

In the 2010 edition the most important changes to note were:

1. a reduction in treatment duration to 12 months MDT for MB patients with a BI <4+
2. usage for Northern Territory (NT) treatment purposes of the World Health Organization (WHO) classification for leprosy
3. continuation of previous treatment strategies for single lesion PB patients based on current evidence and despite WHO recommendations to the contrary
4. introduction of photos to help better clinically identify leprosy cases
5. updating of statistics and graphs to reflect the up-to-date NT leprosy situation
6. introduction of a list of differential diagnoses in cases of suspected leprosy
7. revision and restructure of the guidelines to ensure clarity both in terms of clinical presentation, investigation and current treatment
8. adjustment of the recommendations for children with doses only provided for 10–14-year-olds and that for children <10 years old, expert advice be obtained for proportionally reduced doses
9. introduction of special case considerations to aid in the management of leprosy including in the case of co-existent Human Immunodeficiency Virus (HIV) and Tuberculosis (TB) infection, pregnancy, difficulties with certain medications and defaulters
10. recommendations on the usage of thalidomide in the management of the Type 2, Erythema Nodosum Leprosum (ENL) response
11. clarification of optimal current prevention strategies as part of the push to eradicate leprosy from the NT

12. new recommendations regarding follow-up after completion of leprosy treatment.

2018 Edition (fourth edition)

In the 2018 edition the most important changes were:

1. updating of epidemiology and consideration of the WHO Global Leprosy Strategy 2016-2020
2. rearrangement of sections for a more practical flow with descriptions of continuing research together at the end of the document
3. clearer definition of contacts
4. introduction of single dose rifampicin for leprosy contacts
5. updating of monitoring of patients while on treatment, including checklists
6. the WHO in the 2016-2020 guideline does not mention single dose treatment for Single Lesion Paucibacillary Leprosy (SLPB) and our NT recommendations continue to manage single lesion disease in the same way as other paucibacillary cases
7. addition of WHO recommended treatment doses for children under 40kg.

2024 Edition (fifth edition)

In the 2024 edition the most important changes are:

1. updating to include WHO Global Leprosy Strategy 2021-2030
2. updates in laboratory testing and including nasal swabs
3. updated treatment options, to include daily rifampicin for Leprosy treatment
4. update leprosy contacts treatment regimen to include rifampicin and rifapentine
5. updated Bacille Calmette-Guérin (BCG) vaccine guidelines
6. update of ENL grading appendix.

Applicability

This guideline applies to:

- all health staff involved in the care of Leprosy patients including the public health response.

Guideline statement

This guideline provides information regarding diagnosis and case management for Leprosy under the guidance of the NT TB/Leprosy unit.

Policy suite

The guideline forms part of the following policy suite:

- Notification of Communicable Diseases under the Notifiable Disease Act NT Hospitals Policy
- Prevention of Opportunistic Infections in Patients Undergoing Immunosuppression TE, BR, EA Regions Guideline
- Leprosy. Remote Primary Health Care Manuals. Tropical Health Orientation Manual.
- Northern Territory Leprosy Factsheet
- NT Health Non-healing Ulcers Factsheet

Preface

Declining incidence

In 1996 the Leprosy Unit was combined with the TB Unit in order to maximise the efficiency of use of staff and resources in the Centre for Disease Control (CDC).

Declining leprosy detection rates allowed this to occur. We pay tribute to Dr John Hargrave and many co-workers for 40 years of dedication to the detection, treatment, and rehabilitation of persons with leprosy in the NT.

Although of continued importance, leprosy now commands an appropriately small proportion of CDC resources, and policies involving CDC staff have been streamlined compared with the past. Medical evidence shows that some cases are at much higher risk than others of developing NFI after treatment commences, or of relapsing after treatment is completed. Similarly, some contacts are at higher risk of eventually developing disease. This knowledge allows CDC staff to target follow-up of these groups, and discharge others to the care of primary health services.

World Health Organization recommendations

The WHO produced operational guidelines for leprosy control, the *Global Strategy for Further Reducing the Leprosy Burden and Sustaining Leprosy Control Activities* (2006-2010).[2] Changes advocated in these Guidelines included simplification of diagnostic and treatment techniques and the WHO leprosy classification as a purely clinical classification for leprosy that excludes consideration of skin smear results. Other recommendations included single dose combination MDT for SLPB leprosy (which is no longer referred to in the 2016-2020 guideline) and advocating for the reduction of MB MDT to 12 months duration.[3]

The WHO *Global Leprosy Strategy 2016-2020: Accelerating towards a leprosy-free world*[4] involves no new technical tools but emphasised timely detection of new cases, continued effective free chemotherapy, prevention of disability and rehabilitation, prevention of discrimination and promotion of societal inclusion as vital factors in leprosy management. The follow-on document *(Global Leprosy Strategy 2021-2030)*[5] recognises the considerable progress in the past decade and focuses on interrupting transmission and achieving zero autochthonous cases, providing targets for both high and low burden countries. Importantly it redefines the burden of leprosy in terms of socioeconomic and mental health impacts as well as the physical treatment needed.

Leprosy

What is leprosy?

Leprosy, also known as Hansen's disease, is a chronic, granulomatous infection caused by *Mycobacterium leprae*, an Acid-Fast Bacillus (AFB) related to the bacteria causing tuberculosis. It was discovered by the Norwegian, Gerhard A Hansen, in 1873 and principally affects the skin, mucous membranes of the nose, and peripheral nerves. It is a highly variable disease affecting people in different ways according to their immune response and often has a long incubation period.

History

Leprosy, which originates from the Latin word 'leprosus', meaning 'defilement', has been prevalent worldwide since ancient times. Because of the disfigurement it caused and ignorance about how it was spread leprosy was a much-feared disease and those with the disease were often shunned.

Leprosy is classified by the WHO as one of 20 Neglected Tropical Diseases, and its occurrence is historically related to poor socioeconomic conditions.

Leprosy in the NT

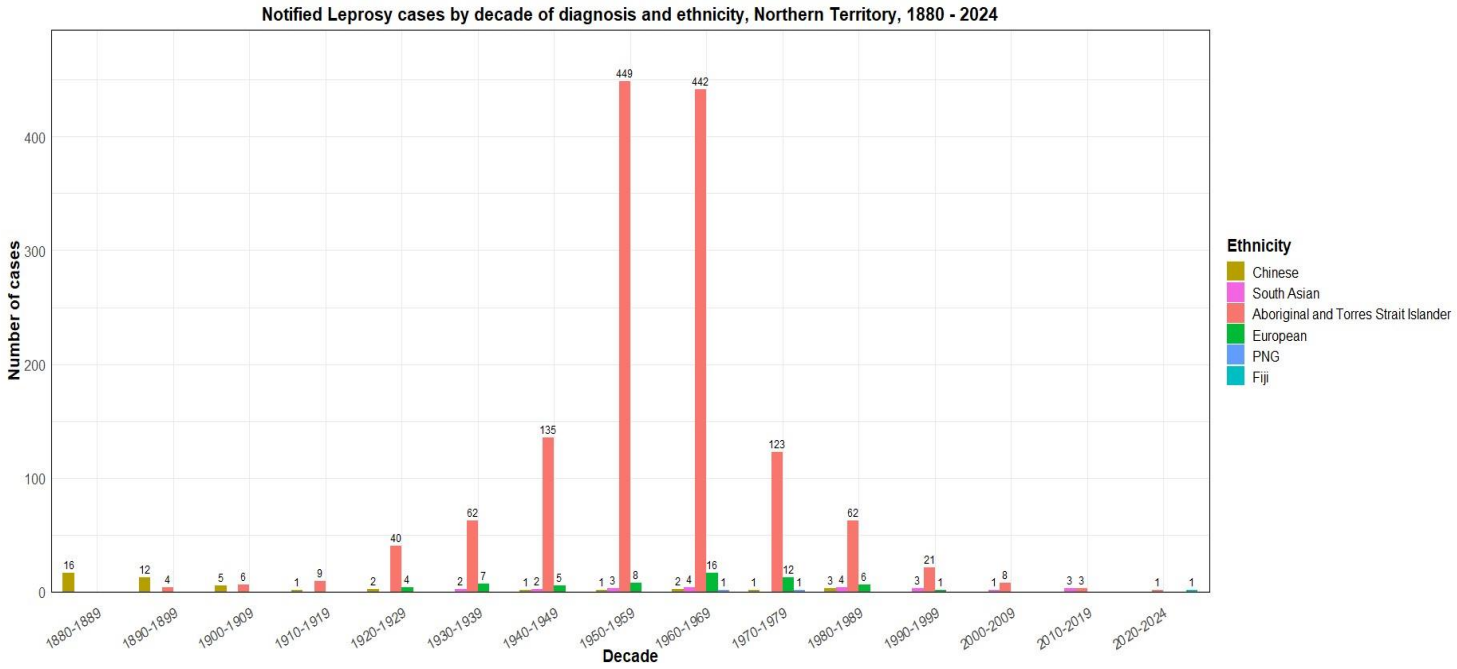
From 1882 to 2024 there have been 1493 leprosy cases notified in the NT with 91% identified as Aboriginal (Figure 1).[6] The first case in the NT was diagnosed in a Chinese-born man in 1882 and the first case in an Aboriginal person was diagnosed in 1890, with a further 4 cases reported by 1900. From 1911-1925 45 Aboriginal, 6 Chinese and 6 'European' cases were diagnosed with leprosy[6] There is no evidence to suggest that leprosy existed in the Aboriginal population prior to this time.

Surveys in the 1950s found up to 10% of NT Top End Aboriginal people had clinical evidence of disease. The peak year was 1961 with 78 new cases of leprosy notified (3.7 cases/1000 population). By 1970 leprosy affected Aboriginal people throughout the northern NT with a few cases as far south as Alice Springs.[6]

Active case finding and treatment were combined with an integrated program of patient education, reconstructive surgery and rehabilitation leading to a significant reduction in leprosy cases in the NT.

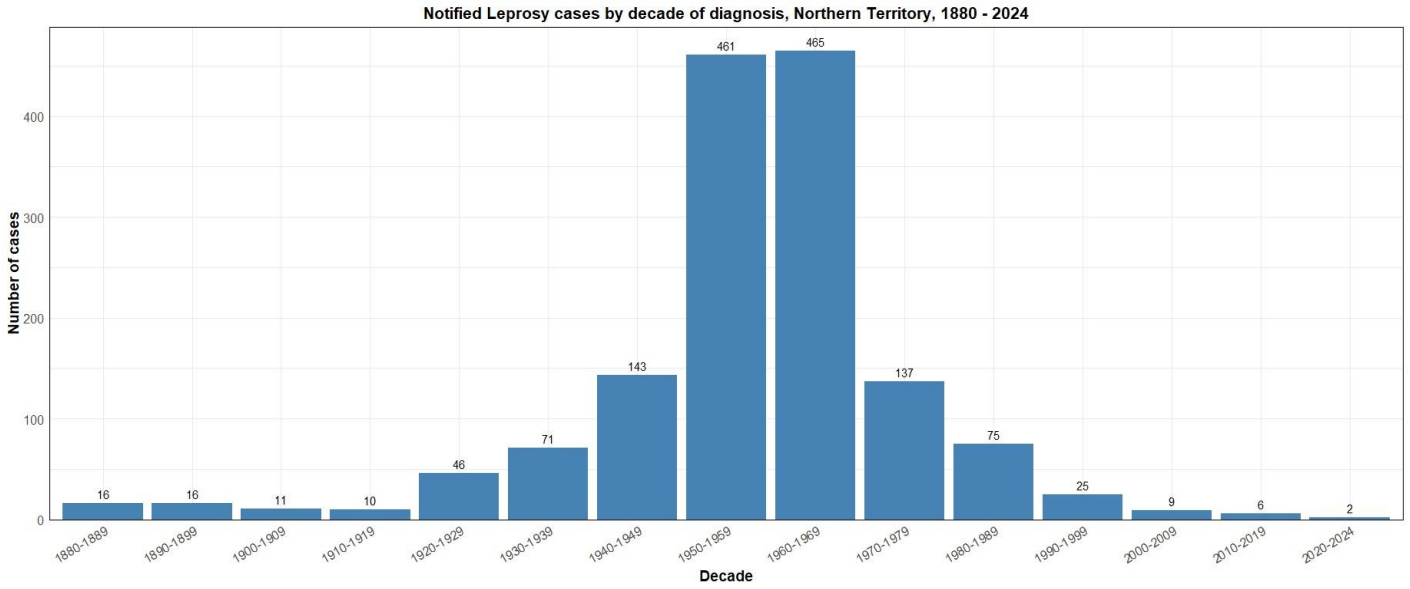
From 1990 to 2024, 42 cases of leprosy (range 0-8 cases per year) were notified; 31(75%) Aboriginal and 10(25%) overseas-born (Philippines [5]; Indonesia [2]; East Timor [1]; Hungary [1]); Papua New Guinea [1]; Fiji [1]), with similar sex distribution and Top End residence predominant.[6-8] In the period 2020 to 2024 there was 1 Indigenous case and 1 overseas-born case.

Figure 1. Notified Leprosy cases in the NT since 1880 by ethnicity



Leprosy is now a rare diagnosis in the NT (Figure 2). Contact tracing and opportunistic diagnosis by primary health workers has replaced community surveys as the main case- finding strategy.

Figure 2. Notified leprosy cases in the NT since 1880 by decade of diagnosis



Global incidence

The WHO reports the global registered prevalence of leprosy from 161 countries reporting at the end of 2019 as 202,256 cases.[5] The number of new cases detected globally has been gradually decreasing with reports of 208,641 in 2018[9], 210,671 in 2017[10] and 214,783 in 2016.[11]

During the past 10 years, the global number of new cases detected has continued to decrease with the majority of countries having achieved elimination of leprosy as a public health problem (defined as less

than 1 case per 10,000 population). Of the new cases reported 194,166 (96%) occurred in 23 priority countries, with 79% in India, Brazil and Indonesia.[5] Pockets of endemicity remain in countries reporting less than 1000 new cases per year. It is estimated that 3-4 million people are living with visible impairments or deformities due to leprosy.[5]

In the NT and worldwide, access to information and early diagnosis and treatment with MDT remain key elements in reducing the incidence of disease. The WHO has made MDT drugs free of charge to all leprosy patients worldwide since 1995, providing a simple yet highly effective cure.

Mode of transmission

Transmission of *M. leprae* is assumed to be primarily from untreated MB patients. The route of transmission is not however definitely known. Evidence suggests that the 2 main portals of entry are the skin and the upper respiratory tract. Nasal discharge from untreated patients with active leprosy has been shown to contain large numbers of AFB. Studies have shown experimental transmission of leprosy via aerosols to mice and some evidence of *M. leprae* entering through breaks in the skin barrier.[12] Zoonotic transmission of *M. leprae* by the nine banded armadillo (*Dasypus novecintus*) has been demonstrated but appears very low risk and highly localised.[5] There has been no other evidence of transmission from other animal reservoirs.[13]

Susceptibility to infection

The overwhelming majority of people are not susceptible to leprosy and only a very small proportion of those exposed develop the disease. A number of factors however significantly increase the risk of developing leprosy.

These include older age persons who may reflect both weaker immune systems or the increased likelihood of lifetime exposure, male gender, contact with a MB as opposed to a paucibacillary (PB) case, genetic closeness and increased proximity for a prolonged period to a patient, for example being in the same household.[14] Household contacts of MB patients have been shown to have a relative risk of developing leprosy 5 to 8 times that of the general population and contacts of PB patients a 2 times higher risk.[15]

M. leprae reproduces at a very slow rate and few cases are diagnosed in infants less than 1 year of age. Some cases can arise in people with exposure to contacts many years previously. The maximum incubation period is reported to be greater than 30 years in war veterans known to have been exposed for short periods in endemic areas but otherwise living in non-endemic areas. The average incubation time for tuberculoid and lepromatous cases, is thought to be 2 to 5 years, and 8 to 12 years, respectively.

Contacts who develop leprosy may only have a single skin lesion (indeterminate leprosy), which often self-heals. Where self-healing or treatment does not occur, the disease may progress to active leprosy. Those who develop the disease demonstrate an impaired cell- mediated immune response to *M. leprae* and there is evidence to suggest that there may be a genetic predisposition in the host.

Classification of leprosy

In leprosy there is a continuous spectrum of disease between the 2 polar forms, tuberculoid and lepromatous leprosy, which depends on the ability of the body to mount an immune response to the invading bacilli. It is important to accurately classify cases by both clinical and histological assessment, as their position on this spectrum determines infectivity, prognosis, disease complications and treatment regimens.

Worldwide there are 2 systems used to classify leprosy patients. Proposed in 1966, the Ridley-Jopling classification system is the most comprehensive and accurate and uses clinical and histopathological features and the Bacteriological Index (BI) to identify 5 forms of leprosy. However, it is also relatively complex and therefore is now not commonly used in the field, especially in highly endemic, low resource settings.

A second system, the WHO classification, is based on the number of skins lesions and identifies 2 forms, PB and MB. It is used as the basis of guiding MDT and was developed primarily to allow classification and therefore rapid treatment in the field when skin smears may not be available. Furthermore, it is easy to use and teach and allows general health workers to be confident of their diagnosis and therefore management.

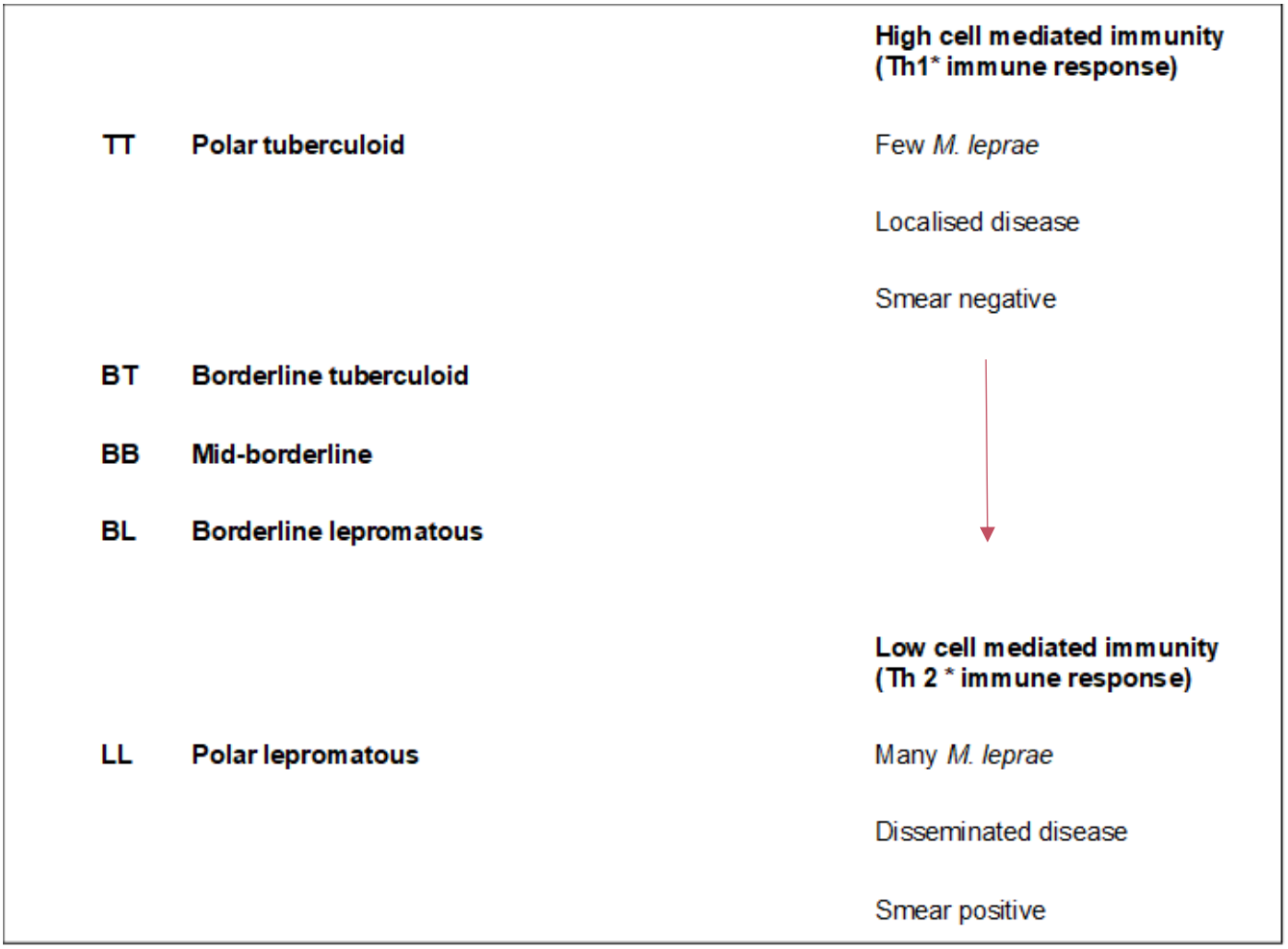
The Ridley-Jopling classification

The Ridley-Jopling classification[16] combines clinical, histopathological, and immunological criteria to identify 5 leprosy forms:

- Tuberculoid (TT)
- Borderline Tuberculoid (BT)
- Mid-Borderline (BB)
- Borderline Lepromatous (BL)
- Lepromatous (LL)

In this classification, there is progression from the mildest (TT) to the disseminated form (LL) of disease as shown in Figure 3.

Figure 3: Ridley-Jopling classification of leprosy



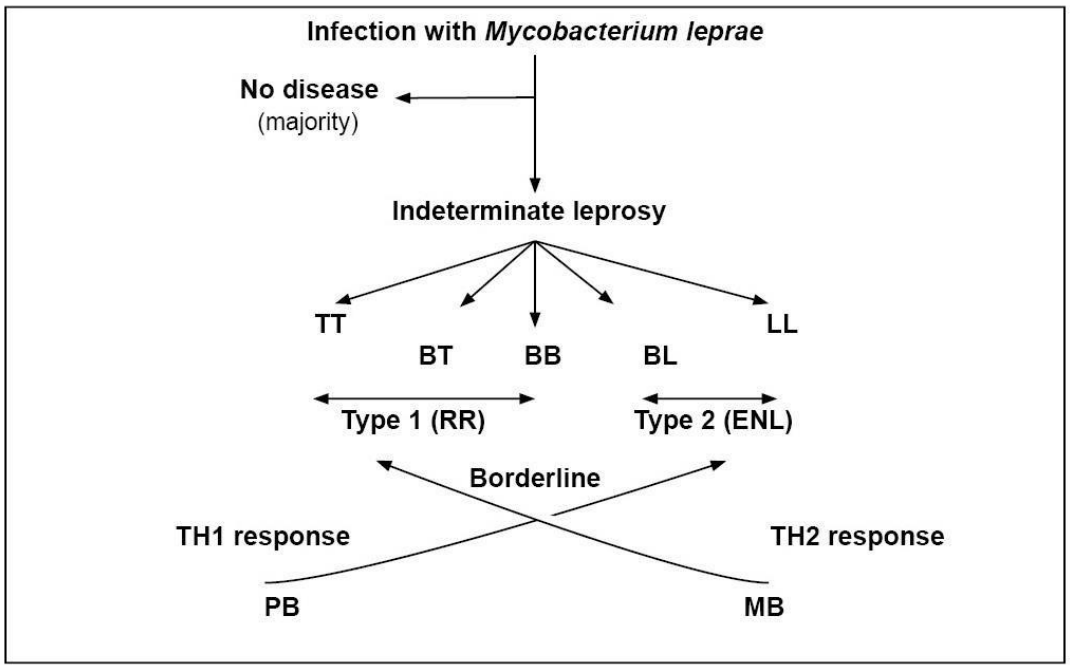
*T helper cells (Th cells) are lymphocytes that help to coordinate the immune system's response to infection by releasing specific types of chemicals called cytokines. There are 2 major types of Th cell responses, Th1 and Th2. Th1 cell cytokines produce a pro-inflammatory response and Th2 cytokines produce an anti-inflammatory response but also promote allergic responses.

The Th1 response produces inflammation to primarily kill intracellular pathogens such as viruses and certain bacteria like listeria and mycobacteria. They do this by activating macrophages and cytotoxic T cells, leading to 'cell mediated immunity'.

The Th2 response counteracts the effects of Th1 cytokines and promotes B-cells to evolve to antibody producing cells (called plasma cells), leading to 'humoral immunity'.

Toward the TT end of the spectrum, leprosy lesions have features of a well-developed Cell Mediated Immunity (CMI) response or a Th1* type response and contain few AFB. Toward the LL end of the spectrum, the immune response displays a Th2* type immune response with a poorly developed CMI and numerous AFB (Figure 4).

Figure 4. Ridley-Jopling classification of leprosy



RR = reversal reaction

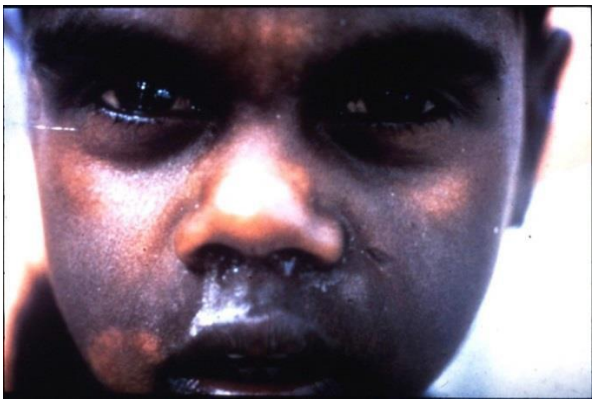
ENL = erythema nodosum leprosum

The borderline area of the spectrum is highly unstable and represents poorly understood immunoregulatory responses; BT and BB (and TT) patients are prone to disfiguring Reversal Reactions (RR) (or Type 1 reactions) while BL (and LL) patients are subject to painful ENL (or Type 2 reactions).

Clinical features of (early) indeterminate leprosy

Indeterminate leprosy represents an early form of the disease before differentiation toward the TT or LL end of the spectrum (Figures 3 and 4). Indeterminate leprosy may present either as an area of numbness on the skin or as a visible skin lesion. The classic early skin lesion (Figure 5) mainly occurs in children and is most commonly found on the face, extensor surfaces of the limbs, buttocks or trunk. Scalp, axillae, groins and lumbar skin tend to be spared, and hair growth and nerve function are unimpaired.

Figure 5. Early leprosy



Source CDC collection

Skin lesions in this form tend to be either single or few in number and appear as small, flat, hypopigmented or coppery with an irregular border. Biopsy may show the perineurovascular infiltrate with only scanty AFB.

The majority of these cases will heal spontaneously and of the remainder, some will persist in the indeterminate form indefinitely, but most will develop into 1 of the forms demonstrated in the Ridley-Jopling classification.

Features of established leprosy

Presentation is often with signs of nerve damage such as weakness or anaesthesia due to a peripheral nerve lesion, or a blister, burn or ulcer in an anaesthetic hand or foot. Borderline patients may present with RR (Type 1 reactions) with nerve pain, sudden palsy, multiple new skin lesions, pain in the eye, or a systemic febrile illness.[17]

Presenting symptoms

For the forms of established leprosy, clinical features are determined by the host response to *M. leprae* and there is a continuous spectrum of disease between the 2 polar forms: TT and LL leprosy (Table 1). The clinical pattern depends on the ability of the body to mount an immune response to the invading bacilli.

Table 1. Characteristics of lesions of polar leprosy

	Tuberculoid (TT)	Lepromatous (LL)
Number of lesions	Very few	Many to hundreds
Distribution	Asymmetrical, anywhere	Symmetrical, avoiding 'spared' areas
Definition and clarity	Defined edge, hypopigmented	Vague edge, slight hypopigmentation
Anaesthesia	Early, marked, defined, localised to skin lesions or major peripheral nerve	Late, initially slight, ill-defined but extensive, over 'cool' body areas
Autonomic loss	Early in skin and nerve lesions	Late, extensive as for anesthesia
Nerve enlargement	Marked, in a few nerves	Slight but widespread
Mucosal and systemic	Absent	Common, severe in Type 2 reactions
Number of *M. leprae*	Not detectable	Numerous in all affected tissues

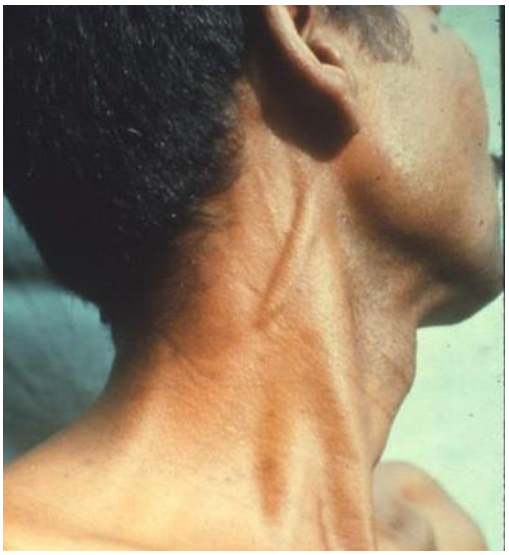
Tuberculoid leprosy (TT)

In the NT, TT has been the commonest form of leprosy in the past, making up more than a third of the cases.[8] These cases have had a well-developed cell-mediated immunity and a very low bacillary load. TT may present as purely neural, with pain or swelling of the affected nerve/s (Figure 6) followed by anaesthesia and possible muscle weakness and wasting.

Alternatively, skin lesions may appear with or without evidence of nerve involvement. These are single or few in number and usually present as hypopigmented (never depigmented), erythematous, coppery patches, with a well-defined, but irregular, and often slightly raised border (Figure 7). The lesions are non-sweating, have decreased hair and decreased sensation.

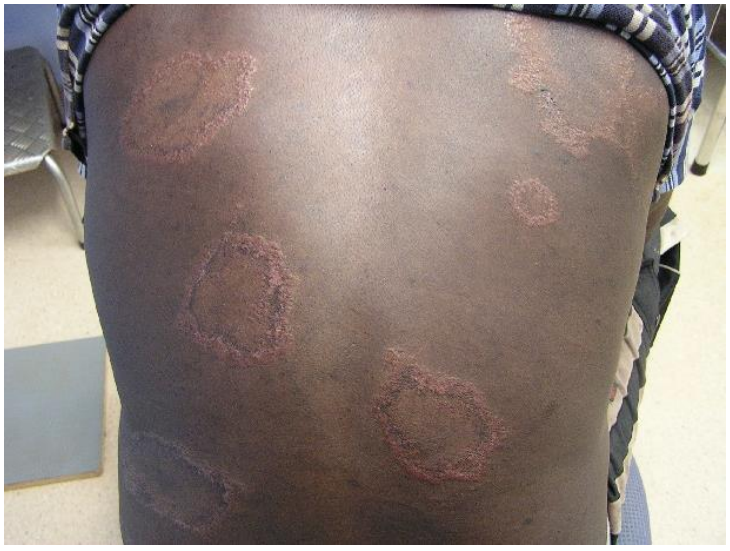
Diagnosis depends on clinical examination and biopsy, as smears are usually negative. Palpation should be undertaken around the lesion for the possible palpation of a thickened nerve trunk. Tissues other than the skin and nerves are not typically affected.

Figure 6. Characteristic nerve enlargement of tuberculoid leprosy (TT)



Source CDC collection

Figure 7. Characteristic lesion of tuberculoid leprosy (TT)



Source CDC collection

Lepromatous leprosy (LL)

Lepromatous leprosy is the more serious and disabling disease on the spectrum. There is loss of leprosy-specific mediated immunity with no check on multiplication and spread of bacilli. There is therefore wide dissemination and a very high bacillary load. The proportion of leprosy on this end of the spectrum has been increasing in the NT in recent years.

Early symptoms

1. **Skin lesions** are usually the first clinical manifestation as early nerve involvement is asymptomatic. These are extensive and can be varied—macular, diffuse papules, nodular or infiltrative. Some may resemble urticaria. There is little depigmentation, and usually no sensory loss in the lesions. In some cases, the skin can be diffusely smooth and shiny (infiltration), with no discrete lesions.
2. **Nasal symptoms** of congestion can occur resulting from infiltration of the mucous membranes of the nose and mouth. Patients may complain of increased nasal discharge and papules and nodules on their lips, tongue, palate or larynx. Epistaxis is common and patients can develop a 'saddle nose deformity' resulting from destruction of the nasal septum and cartilage.
3. **Leg and ankle oedema** due to increased capillary stasis and permeability.

Later symptoms

Subsequent to this, disease progression normally occurs with numbness and anaesthesia on the dorsal surfaces of the hands and feet and later on the extensor surfaces of the arms and legs and finally over the trunk. There may also be infiltration of the corneal nerves that may predispose to injury and blindness.

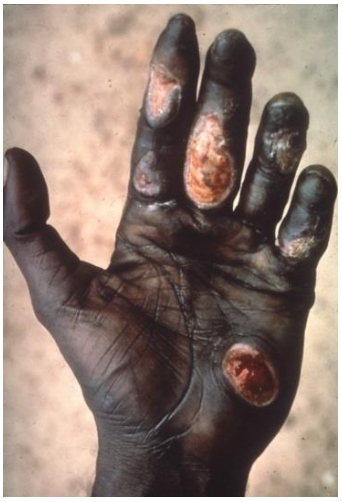
Left untreated the forehead and earlobes become thickened (leonine facies), and the eyebrows become thin, particularly laterally, and are eventually lost (madarosis) (Figure 8). The nose may collapse due to septal perforation and loss of the nasal spine and upper teeth may fall out. Skin becomes thickened with ulcers on the hands and legs (Figure 9) and development of a glove and stocking peripheral neuropathy. Muscle wasting can progress to deformities such as claw hand (ulnar nerve) (Figure 10) and foot drop (common peroneal nerve).

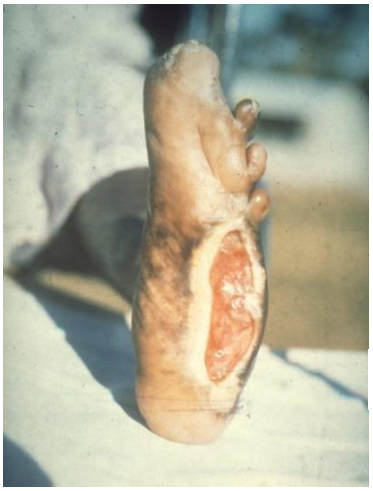
Figure 8. Characteristic lesions of lepromatous leprosy

Source CDC collection

Other organs such as the liver, spleen, eyes (keratitis from leprous deposits) and testes (causing atrophy) can be involved, and patients may develop gynaecomastia. Renal amyloidosis is a common complication particularly in those who develop Type 2 reactions (ENL).

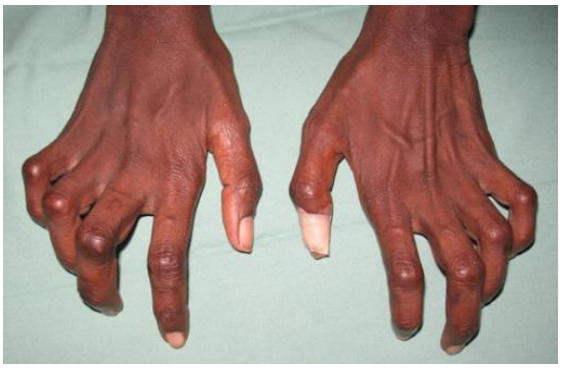
Figure 9. Characteristic anaesthetic hand and foot complications of leprosy





Source CDC collection

Figure 10. Characteristic 'claw hand' complication of leprosy



Source CDC collection

Borderline leprosy (BT, BB, BL)

BT, BB and BL lie in the middle of the polar TT to LL spectrum. This form is seen in those people with limited or variable resistance to *M. leprae*. Skin and nerve involvement is commonly seen, with only rare involvement of other structures.

Skin lesions are intermediate in number between the 2 polar forms. Asymmetrical 'punched out' plaques are characteristic with a distinct, raised inner edge and outer edge that merges with surrounding skin. They may also appear as macules (erythematous or hypopigmented), nodules or irregularly shaped bands.

Borderline disease is unstable, and it can 'upgrade' towards TT with treatment, or 'downgrade' towards LL if left untreated. Neurological symptoms such as paresthesia may precede skin changes by many years in borderline forms of leprosy with the clinical changes lagging behind the immunological and histological changes.

Pure neuritic leprosy

Purely neuritic leprosy presents with asymmetrical involvement of peripheral nerve trunks with no evident skin lesions. It may present with or without tenosynovitis and symmetric polyarthritis, nerve abscesses may occur. Skin smears are negative and nerve biopsy and Polymerase chain reaction (PCR) are usually required for diagnosis. It is more commonly seen in people from India and Nepal.[18] This form of leprosy is no longer recognized by WHO as a distinct subgroup.

WHO classification

The WHO classification[13] used since 1997, is based on the assessment of the number of skin lesions and was designed to simplify and aid diagnosis of leprosy in the field and therefore guide MDT (Table 2). It allows easy assessment by health workers with only basic training, and there is no requirement for skin smears. It is made up of 2 broad categories.[13]

Paucibacillary (PB): a case of leprosy with 1–5 skin lesions and without demonstrated presence of bacilli in a skin smear

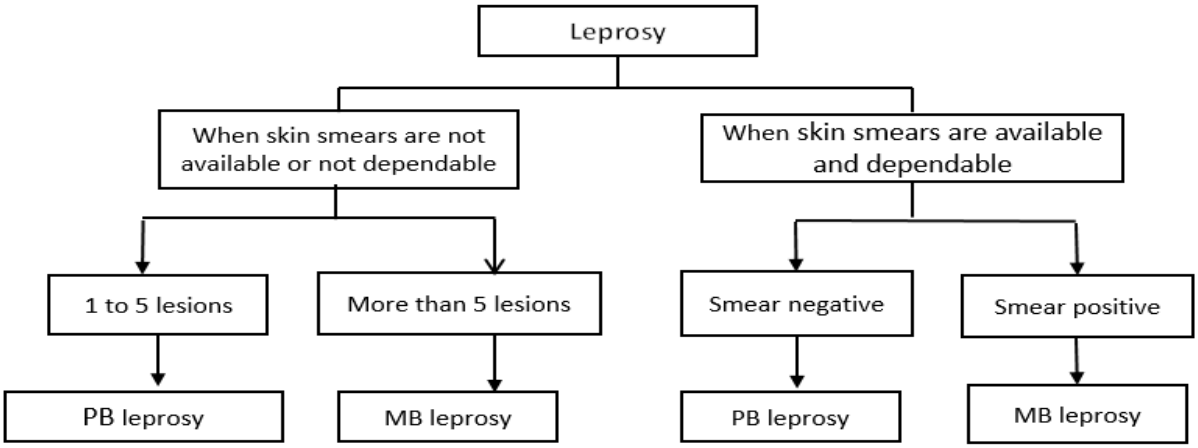
Multibacillary (MB): a case of leprosy with >5 skin lesions; or with any nerve involvement (including pure neuritis or any number of skin lesions and neuritis); or with demonstrated presence of bacilli in a slit-skin smear, irrespective of the number of skin lesions.

Table 2. WHO classification of leprosy and the Ridley-Jopling correlation

Clinical classification	PB	MB
Number of skin lesions	1 to 5 lesions	6 or more lesions
	AND	OR
Skin smears	Negative at all sites	Positive at any site
Distribution	Asymmetrical distribution	More symmetrical distribution
Sensation loss	Definite loss of sensation	Extensive sensation loss
Nerve damage (loss of sensation or muscle weakness)	-	Any neuritis regardless of number of skin lesions
Ridley-Jopling correlation	TT, most BT	Some BT, BB, BL, LL

Figure 11. Classification of leprosy

The following flowchart (Figure 11) based on the WHO classification can also be used to aid classification of leprosy.



In the NT, classification of patients is by the Ridley-Jopling classification (for prognosis) and the WHO classification (for reporting and treatment guidance). Patients in the NT are therefore classified for treatment on the basis of the number of skin lesions, the presence or absence of AFB on skin smears and the histopathological findings (Table 3). Results of skin smears are an important part of the classification process and where there is doubt about the classification based on skin lesion and skin smears, skin histopathology may also be considered in the decision regarding final diagnosis.

In this setting where resources are available, it is important to accurately classify cases by both clinical and histological assessment, as their position on this spectrum determines infectivity, prognosis, disease complications and treatment regimens.

Table 3. Classification of leprosy for treatment in the NT

	PB	MB
Number of skin lesions	1 to 5	6 or more
	AND	**OR**
Skin smears (AFB)	Negative at all sites	Positive at any site
Histopathology (skin)	**Compatible**	**Compatible**

Diagnosis

Definition of a leprosy case in Australia

The National Notifiable Diseases Surveillance System (NNDSS) definition[19] for a confirmed case of leprosy is applied in the NT. A confirmed case requires either laboratory definitive evidence or laboratory suggestive evidence and clinical evidence (Table 4). Only confirmed cases are reported.

Table 4. NNDSS case definition for leprosy

A confirmed case requires either **Laboratory definitive evidence** OR **Laboratory suggestive evidence** AND **clinical evidence**
Laboratory definitive evidence Detection of *M. leprae* by nucleic acid testing from the ear lobe or other relevant specimens.
Laboratory suggestive evidence Demonstration of characteristic acid fast bacilli in slit skin smears and biopsies prepared from the ear lobe or other relevant sites OR Histopathological report from skin or nerve biopsy compatible with leprosy (Hansen's disease) examined by an anatomical pathologist or specialist microbiologist experienced in leprosy diagnosis.
Clinical evidence Compatible nerve conduction studies OR Peripheral nerve enlargement OR Loss of neurological function not attributable to trauma or other disease process OR Hypopigmented or reddish skin lesions with definite loss of sensation.

The WHO case definition[13] for leprosy is a patient having at least one of the following "cardinal signs":

- definite loss of sensation in a pale (hypo-pigmented) or reddish skin patch
- thickened or enlarged peripheral nerve with loss of sensation and/or weakness of the muscles supplied by that nerve
- presence of acid-fast bacilli in a slit-skin smear.

Clinical assessment

A complete history and physical examination in addition to laboratory tests are essential to diagnosis of leprosy. The main components of the clinical assessment are:

- history
- skin and nasal examination
- nerve palpation
- NFI assessment –VMT-ST
- eye examination
- deformity, disability and psychological assessment.

Use the leprosy examination forms (Appendices 1 and 2) for skin at the time of diagnosis and annually, and for nerves, NFI, and eyes monthly while on treatment and at routine follow-up after treatment.

History

While history taking, enquire specifically about the presence and duration of lesions, nerve pain, numbness and tingling, weakness, ulcers and injuries, eye pain and worsening vision. It is also important to determine any underlying disability resulting from their illness on initial consultation. In addition, assess possible previous exposure to leprosy and current contacts.

Skin and nasal examination

The entire skin surface should be examined carefully for lesions that can include macules, papules, plaques, nodules, urticaria-like lesions and smooth infiltrations. This requires a full explanation to the patient as to the importance of a thorough examination and requires privacy. Patches may appear coppery on dark skin and pink on fair skin. Sometimes the only lesions are on the buttocks. Look for loss of sensation, hair, pigmentation and sweating.

The nasal mucosa and septum should be examined, looking for ulcers, nodularity, inflammation and discharge, as well as septal destruction or collapse.

Natural sunlight is the best light for detecting subtle changes, but privacy and patient comfort must be ensured.

Same-sex examiners or the presence of an escort or chaperone may be required. Since loss of sensation in a patch is a cardinal sign, demonstration of this sign must be done systematically to accurately determine its presence (Table 5). Digital photography of skin lesions at the time of diagnosis and on completion of treatment is recommended where possible. Consent should be obtained from the patient for photo documentation and photographs should be included in the patient record for comparison and ongoing management.

Table 5. Method of testing loss of sensation in a patch

Environment	Privacy, relaxed patient, 1 examiner.
Cotton wool	Roll it to a point, touch the skin so the point bends, don't stroke it.
Explain	"I'm going to do this…" and demonstrate touch on your own arm.
Trial test	With patient's eyes open, touch an area of normal skin with cotton wool. Ask them to point to the spot where they felt the touch with their index finger.
Real test	With patient's eyes closed, test normal skin near the patch, then the patch—ask patient to touch each time the spot where they feel the wool.
Interpretation	Loss of sensation if no response. Reduced sensation if they touch >3cm away from the point you touch (misreference). Normal sensation if localised within 3cm.
Errors	Leprosy patch may not be insensitive on the face. Areas of thick skin which are normal may not feel cotton wool (soles, elbows).
Children	Cooperation may be difficult—look for loss of sweating in the patch instead—ask the child to run around in the sun, then examine.

Nerve palpation

The most commonly affected nerves are ulnar, median, radial cutaneous, common peroneal (lateral popliteal) and posterior tibial nerves, the sural nerve, the 5th and 7th cranial nerves, and the greater auricular nerve. Widespread involvement of cutaneous nerves is also common. Patients may present with limb deformities and chronic ulceration and scarring on hands and feet as a result of trauma to areas with loss of sensation. Patients may also present with neuropathic joints, traumatised by repeated injury to a joint with no protective sensation.

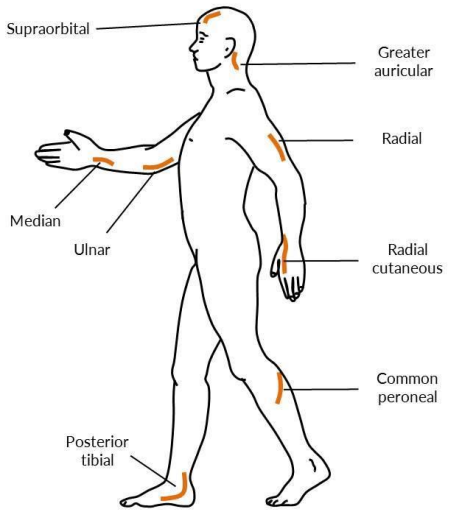
The nerves are affected by leprosy at the most superficial, and thus coolest points in their course, since *M. leprae* prefers to multiply *in vivo* at a temperature of 27-30° Celsius.

Therefore, they are quite easily felt. Learn the size of normal nerves by practising palpation on yourself and friends (Table 6, Figure 12). Examine the nerve on both sides simultaneously to help differentiate whether 1 is abnormal. Use 3 fingers to roll the nerve *gently* against the bone—nerves may be very tender if inflamed.

Table 6. Method of palpation of commonly involved nerves

Supraorbital	Run examiner's thumb-tips just above both eyebrows of the patient – the nerve may be felt 1cm from the inner end of the eyebrow if enlarged.
Greater auricular	Turn the head to 1 side and feel along the opposite sternomastoid muscle.
Ulnar	With patient's arms flexed to 90° feel in the bony groove just inside (medial to) the point of the elbow and follow the nerve up for 10cm.
Median	Feel at the wrist crease next to the palm just on the small finger side of a large tendon (medial to the flexor carpi radialis tendon).
Radial cutaneous	Roll it over the lateral side of the radius near the wrist crease.
Common peroneal	With the patient seated, find the fibular head—2cm down (distally) and 1cm behind it (posteriorly) the nerve is felt winding around the neck of the fibula.
Posterior tibial	Palpate 2cm down and 2cm behind the point of the inner ankle bone (medial malleolus).

Figure 12. Sites of commonly affected nerves



Nerve function assessment (VMT-ST)

See Appendix 1 and 2.

Eye examination

Gerhard Armauer Hansen, who discovered the leprosy bacillus, claimed in 1873, "there is no disease which so frequently gives rise to disorders of the eye, as leprosy does".[20] Today cataracts are the most common cause of blindness in leprosy.[21] Table 7 provides information that underscores the importance

of examining for the common ocular manifestations of leprosy. Eye examination at diagnosis and annually and referral to an ophthalmologist for annual slit-lamp examination to detect silent iritis is recommended including after treatment is completed (see p38).

Table 7. Common ocular manifestations of leprosy

Complication	Description	Mechanism	Class	Signs/Symptoms
Madarosis	Loss of eyebrows and lashes	Bacillary infiltration/destruction of follicles	MB	Observe loss
Corneal hypoaesthesia	Reduced corneal sensation to cotton wool (not anaesthesia)	Trigeminal nerve damage to the small branches innervating cornea	Borderline	Observe spontaneous blinking. Test with cotton wool wisp if less than 3 blinks per minute*
Lagophthalmos	Weakness or paralysis of the orbicularis oculi muscles leading to lid gap	Facial nerve damage to the zygomatic branch with Type 1 reaction in a skin patch overlying the cheekbone	Borderline	Gentle eye closure Eye closure with effort, and against resistance Exposure keratitis (lower half of cornea dry, scarred)*
Iridocyclitis	Inflammation of the iris and ciliary body	Type 2 reaction	MB	Eye pain/ache Photophobia Tenderness Tearing Redness (perilimbal) Small, poorly reactive, ovoid pupil Dull cornea Reduced visual acuity
Scleritis	Inflammation of the sclera near the cornea	Type 2 reaction	MB	Eye pain and tenderness Deep red scleral patch
Dacrocystitis	Infection of the lacrimal sac	Bacillary infiltration in the nasal mucosa (or nasal collapse) blocks the nasolacrimal duct, causing stagnation and infection	MB	Tearing Pus expressed from punctum in lower lid Swelling and tenderness over lacrimal sac (between eye and nose)
Ectropion	Sagging turned out lower lid	Bacillary infiltration and distortion of lid	MB	Tearing Exposure keratitis
Entropion	Lid turned in towards eyeball	Bacillary infiltration and distortion of lid	MB	Tearing Conjunctivitis Scarred cornea from turned in lashes (trichiasis)
Cataract	**Lens opacity**	**Primary age-related (commonest), secondary to chronic iridocyclitis or steroid treatment of NFI**	**All**	**Reduced visual acuity** **Milky opacity in pupil** **Opacity in red reflex**

* See Appendix 1

Deformity, disability and psychological assessment

An assessment of deformity or disability is an important part of the initial clinical assessment. Deformities can result from infection, relapse or Type 1 and Type 2 immune reactions and all can lead to irreversible nerve damage. This in turn can impact upon the patient's psychological and social wellbeing, leading to anxiety or depression that is compounded by the stigmatised view of leprosy in many societies. Signs and symptoms of these disorders should therefore be sought during the history and examination and appropriate referrals made to provide support to the patient.

Investigations

The diagnosis of leprosy is based primarily on demonstrated clinical features and can be confirmed by slit skin smears, skin/nodule or nerve biopsy, or nasal swab.

Specimen collection

Slit skin smears

A slit skin smear may demonstrate the presence of AFB in the skin. AFB are always present in the LL or BL cases, but will not be found in the TT or indeterminate forms.

Indications

1. For diagnosis where there is clinical suspicion of disease.
2. To monitor treatment in lepromatous (MB) cases.
3. Suspicion of relapse after completion of MDT.

Preferred sites (*Sites 1 and 2 are minimum requirements*).

1. Both ear lobes.
2. Suspicious skin patches—2 smears taken from the edge if the lesion is distinct, and from the centre if the lesion is indistinct.
3. Thickened skin on forehead above the medial border of the eyebrows.
4. Knees or elbows.
5. Previously positive sites.

Procedure

1. Wash microscope slide in water and dry with methylated spirits or alcohol wipe.
2. Clean earlobe with alcohol swab and let it dry.
3. Optionally, apply EMLA cream to all sites and allow 30 minutes to anaesthetise the skin.
4. When desired effect achieved (test with sterile needle prick), wipe EMLA from skin (wearing gloves will prevent the examiner's finger tips from becoming numb).
5. Squeeze sample area or roll between index finger and thumb until it becomes bloodless (white). This requires a lot of pressure—initially using 2 hands to squeeze is helpful.
6. Make an incision about 5mm long and 3mm deep with a size 15 Bard Parker scalpel blade.
7. Turn the blade at right angles to the cut and without relaxing finger pressure scrape the incision

with the slanted edge of the scalpel blade several times in 1 direction.

8. Tissue obtained should be gently smeared on a small area of the slide in a central circle. Samples with obvious blood content are unlikely to be useful so wiping the sample site with a cotton swab while maintaining pressure may enable you to collect a second sample that is not bloody, without a repeated incision.
9. Fix the slide by passing the underside for 2 seconds over a naked flame (a lit match, cigarette lighter, or spirit lamp) until the slide feels slightly warm on the back of your hand.
10. Label slide with site of smear, and patient details, and place in holder.
11. Send to Royal Darwin Hospital (RDH) Microbiology Laboratory requesting AFB for leprosy.
12. A smear from different sites in the same patient is useful for diagnosis.
13. A dry swab should also be taken from the incision site (rub vigorously) for leprosy PCR testing.

Skin or nerve biopsy

Biopsy of affected nerve or skin is sometimes necessary in cases where the diagnosis may be uncertain. This is usually performed by a dermatologist. When a skin biopsy is performed the incision should contain the whole depth of the dermal layer so that AFB in the deeper layers of the dermis will not be missed. They should also be taken from areas of skin with the most active disease.

Method for skin biopsy

1. Clean the site and inject local anaesthetic deep into the subcutaneous tissue around the biopsy site. Do not inject intradermally as it ruins the biopsy.
2. Insert a cotton tie into the end of the site and use this as a retractor (forceps crush the tissues).
3. Excise an elliptical piece of skin approximately 1 centimetre long and down to subcutaneous fat (about 5mm deep) such that the dermis is included (leprous changes may occur in the deep layers of the dermis).
4. Place most of the biopsy tissue into Buffered Formal Saline (10% formalin) and request histopathology with Wade-Fite stain for AFB, and fungal stains. Save a small piece of biopsy as a fresh specimen* and request leprosy PCR and fungal culture. Note: formalin degrades DNA and should not be used.
5. Send all samples to Territory Pathology at RDH.

A nerve biopsy may be indicated where a skin biopsy has not been diagnostic or in cases of purely neuritic leprosy. In this case a thickened area of nerve should be sampled i.e. radial cutaneous nerve at the wrist, or at the ankle the superficial peroneal, sural or posterior tibial nerve. A surgical consultation to obtain the biopsy is required. Specimens should be sent for histology, AFB and PCR.

Nasal swab

Nasal swabs are relatively non-invasive and are now recommended in all patients with suspected leprosy. Nasal mucous membrane swabs can be taken using both a sterile cotton bud and a red flocked swab wiped firmly against the nasal septum bilaterally. Prepare a smear using the sterile cotton bud swab using the same method outlined above under ‘slit skin smear’. This

should be sent to the laboratory labelled 'Nasal swab for leprosy - AFB/bacillary index'. Send the red flocked swab to the laboratory labelled 'Nasal swab for leprosy - PCR'.

Laboratory testing

All specimens should be sent for microscopy/AFB, and all biopsy specimens sent for histology. Bacterial index is useful in determining bacterial load and therefore length of treatment and response to treatment. PCR is useful as part of the diagnostic workup on any specimen type, regardless of whether or not AFBs are seen, if the clinical suspicion is high.

Bacterial index

The BI (Table 8) is a mean score that quantifies bacilli, usually in the skin. Nasal secretions may also be assessed for bacterial index if performed. It is derived by adding the scores from each site and dividing by the number of sites sampled. The grades range from 0+ to 6+, depending on the number of bacilli seen in an average microscopic field using an oil immersion lens or high power field (hpf). In untreated lepromatous leprosy the BI can be 5+ or 6+. It falls with treatment by approximately 0.75- 1.0+ BI units per year, and can therefore be used to gauge response to treatment for MB leprosy, as well as for initial classification or detecting relapse.

The morphological index (MI) is the percentage of solidly stained bacilli of normal size and shape. These bacilli are thought to be the viable, living bacteria that could potentially infect others.

Table 8. Bacterial index definitions for skin smears

Bacterial index	Description
0+	0 bacilli in 100 hpf
1+	1-10 bacilli in 100 hpf
2+	1-10 bacilli in 10 hpf
3+	1-10 bacilli in 1 hpf
4+	10-100 bacilli in 1 hpf
5+	100-1000 bacilli in 1 hpf
6+	>1000 bacilli in 1 hpf

Low BI 0+ - 3+, High BI 4+ - 6+

AFB in skin smears may also be reported as 'fragmented' meaning recently dead, or 'granular' suggesting old, non-viable bacteria. These descriptions are used in the Solid-Fragment-Granule (SFG) reading reported by the laboratory.

The MI falls rapidly to zero after MDT is commenced indicating a bactericidal effect, whilst a high BI can take years to reach zero since it relies on the gradual clearance of debris. The MI is often not used in routine practice due to problems with standardisation and reproducibility.

PCR based assays

PCR based methods are both sensitive and specific for diagnosis, particularly in those with paucibacillary disease (indeterminate and tuberculoid forms of leprosy with limited clinical manifestations) and inconclusive histology.[22] Samples for PCR testing is referred to the Victorian Infectious Diseases Research Laboratory (VIDRL).

Molecular drug susceptibility testing

Molecular Drug Susceptibility Testing (MDST) has also been employed to survey for drug resistance and in patients who fail or relapse after treatment. Resistance to rifampicin, fluoroquinolones and dapsone is detected by targeting the *rpoB*, *gyrA* and *folP1* genes. Phenotypic and molecular susceptibility testing of *M. leprae* is not available in Australia. The WHO's *Anti-microbial resistance surveillance in leprosy* [23] published by WHO provides a list of collaborating reference laboratories for MDST.

Differential diagnosis

The differential diagnosis of leprosy is broad. The consideration of leprosy when skin and nerve pathology is suggested is key to diagnosis and adherence to the clinical criteria for diagnosis will facilitate a correct diagnosis. The following should be considered in differential diagnosis of leprosy.[24]

Commonly occurring conditions

1. **Birth marks (naevus anaemicus)** are well-defined hypopigmented skin patches that are present from birth and are typically single or few in number. Sweating and sensation is normal.
2. **Vitiligo** lesions are white lesions with white hairs caused by depigmentation due to melanocyte damage. Sensation, sweating and skin texture are normal.
3. **Post-inflammatory hypochromia** is a reduction of normal pigment at the site of previous inflammation from wounds or simple inflammatory conditions and may mimic early leprosy.
4. **Scar tissue** due to skin injury may show sensation loss and resemble a patch of PB leprosy.
5. **Litchenoid dermatitis** presents with scaly, itchy hypopigmented lesions with normal sweating and sensation. Sometimes lesions may looks like coins 'nummular-like dermatoses'.
6. **Tinea versicolor** is a fungal infection often co-existing with leprosy and caused by *Malassezia furfur* with well-defined, scaly brown lesions on the trunk, neck and limbs. Diagnosis is based on assessment under Wood's lamp and identifying fungus in skin scrapings.
7. **Tinea corporis** often presents with well defined, round lesions, with a raised and vesicular edge. There may be 2 or more concentric rings and the lesions are usually scaly and itchy. Diagnosis is confirmed by microscopic examination of skin scrapings.
8. **Tinea circinata** presents with round fungal lesions on the face and leg with normal sensation.
9. **Pityriasis rosea** presents with an initial 'herald lesion' followed several weeks later by numerous oval shaped lesions generally only on the trunk. Lesions are normally not itchy and sensation, sweating and peripheral nerves are all normal.
10. **Seborrhoeic dermatitis** lesions are yellow coloured, itchy and show coarse scaling. Sensation is normal and lesions are common on the trunk and may coalesce into larger patches.
11. **Annular psoriasis** is characterised by the presence of grey scaly figurate lesions that usually exhibit a symmetrical distribution. There may be pustules or pitting of the nails.
12. **Lichen planus** presents with skin papules that may coalesce into larger patches or annular

lesions. Can affect any part of the body, but commonly the wrists, lumbar region and ankles.

13. **Granuloma annulare** presents with round ring-like symptomless papules or nodules. Affects mainly children and young adults. A possible variant is the less common granuloma multiform with itchy lesions that eventually self-resolve.

14. **Pityriasis alba** is a mild eczematous condition which leaves slightly scaling hypopigmented macules with an ill-defined border. It can be difficult to distinguish from early leprosy disease.

15. **Discoid eczema** presents as discrete well-defined coin shaped patches of eczema on the skin. Usually the pattern of the lesions is symmetrical and they are very itchy.

16. **Fixed drug eruptions** show well defined violaceous macules. In the active stage the lesions are more erythematous and infiltrated. Lesions subside after the withdrawal of the causative drug and reappear rapidly at the same site with re-administration of the drug.

Less commonly occurring conditions

1. **Systemic lupus erythematosus (SLE)** may be mistaken for leprosy particularly the ring-like skin and mucosal lesions of lupus erythematosus discoides.

2. **Necrobiosis lipoidica** (an uncommon complication of diabetes) causes skin abnormalities on the lower legs that may ulcerate and may be painless.

3. **Porphyria cutanea tarda** (lesions chiefly on the hands and face, where exposed to the light) may pose diagnostic problems.

4. **Sarcoidosis** may show annular lesions, sometimes polycyclic, which may closely resemble tuberculoid leprosy. They can be differentiated by absence of loss of sensation.

5. **Neurofibromatosis (Von Recklinghausen's disease)** has numerous café au lait patches that may be confused with leprosy. In neurofibromatosis Type 1 all children have these patches before 2 years old and 70% have freckles in the axillae. Nearly all also have hamartomas in the iris (Lisch's nodules) and develop neurofibromas. In Type 2 café au lait patches rarely occur and freckles are absent.

6. **Kaposi's sarcoma lesions** are often found on the foot or leg and some as associated with HIV. Lesions are shiny, violaceous and nodular. They can be found particularly in Aboriginal and African patients and mimic lepromatous leprosy.

7. **Lupus vulgaris** (skin tuberculosis) shows brown-yellowish nodules that may coalesce into plaques. Typically lupus vulgaris lesions are accompanied with ulceration and scarring.

8. **Syphilis** infection may lead to a residual light coloured skin lesion. People with leprosy may often have a false positive VDRL screening test for syphilis.

9. **Diffuse cutaneous leishmaniasis** may closely mimic lepromatous leprosy and should be considered in immigrants from or travellers to regions with endemic leishmaniasis. In dermal leishmaniasis however, eyebrows are not affected.

10. **Lymphoma** may present with shiny nodular skin lesions. It occurs more commonly in adult males.

Causes of neuropathy should also be considered in those patients presenting with a peripheral neuropathy. If assessment demonstrates diminished temperature and pain sensation, while sparing vibration, position sense and deep tendon reflexes, which is very unusual, **primary amyloidosis** and **syringomyelia** should be considered. Cases of peripheral neuropathy such as foot drop or muscle wasting of the hand should also warrant the exclusion of leprosy as a diagnosis.

Of note, 2 conditions may co-exist, especially in tropical climates such as the NT. In particular leprosy and fungal lesions may have a similar appearance, and can often occur together, especially in tropical climates. If there is any doubt about the diagnosis a trial of antifungal treatment such as selenium sulphide (Selsun) for tinea versicolor or a topical antifungal such as miconazole for tinea corporis should be commenced. For widespread rash terbinafine oral daily for 2 weeks is recommended. The patient can be reviewed after a month of therapy to assess the response.

Treatment

MDT is the standard for the treatment of leprosy worldwide. Since it was first introduced in 1982, 18 million people have been successfully treated, reducing global leprosy prevalence by 95%, reducing the rates of drug resistance and breaking the cycle of transmission. Recommended regimens for treatment have been based on those recommended in the WHO *Global Leprosy Strategy* (2016-2020)[4] but the NT has included a 24-month treatment option for cases with a high bacillary index (BI). There are ongoing studies of rates of relapse and leprosy reactions.

Review of literature provides differing opinions relating to expected outcomes of the treatment programs.[25-30] In countries with larger numbers of patients being treated it is more acceptable to retreat a relapsed patient than continue to treat all patients with a high bacillary index for a longer period.[27] The advantages of a shortened duration of treatment need to be balanced against the risk of relapse. Patients with a BI ≥4 have been shown to have a higher rate of relapse.[26] The US National Hansen's Disease Program (NHDP) recommends 24 months for MB disease.[30] The 24 month treatment regimen will continue to be offered in the NT to MB patients with a BI ≥4 based on the decreased likelihood of relapse on this regimen.

In the NT Rifampicin dosed daily rather than monthly doses may also be considered as the recommended treatment regimen.

Consideration should be taken of the drug profiles, side effects and monitoring requirements (Appendices 3, 4). It is recommended that if the classification of a case is in doubt, or the skin smear is positive, that the patient be treated as having MB leprosy.

NT CDC leprosy treatment recommendations

Paucibacillary leprosy (PB)

The NT CDC recommended treatment for those 15 years and above is dapsone 100mg daily (self-administered) plus rifampicin 600mg monthly†‡ for 6 months for all types of PB leprosy (Table 9).

See Appendix 4 for drug profiles and side effects.

Multibacillary leprosy (MB)

NT CDC recommended treatment for those 15 years and above (Table 10):

1. Low BI (<4+) MB leprosy patients should be adequately treated with 12 months treatment but still require vigilant follow-up.
2. High BI (≥4+) MB leprosy patients should have treatment for at least 24 months.

Although the WHO currently recommends 12 months of treatment for all MB leprosy, the NT recommendation is for 24 months treatment for MB patients with a BI of ≥4+. MB patients with a BI of 4+ or greater have a higher rate of relapse.[26] Patients with a high bacillary index are more likely to have smears that remain positive at the end of treatment[26] and should continue to be reviewed in case of relapse.

Table 9. NT first line MDT regimen with adult (≥15 years old) doses

	PB*	MB—Low BI <4+	MB—High BI ≥4+
Duration	6 months	12 months	24 months
Dapsone	100mg daily self-administered	100mg daily self-administered	100mg daily self-administered
Rifampicin	600mg monthly† DOT‡ ° or daily self-administered as directed the by NT TB/Leprosy unit	600mg monthly† DOT‡ ° or daily self- administered as directed the by NT TB/Leprosy unit	600mg monthly† DOT‡ ° or daily self- administered as directed the by NT TB/Leprosy unit
Clofazimine	50mg daily self-administered plus 300mg monthly† DOT‡	50mg daily self-administered plus 300mg monthly† DOT‡	50mg daily self-administered plus 300mg monthly† DOT‡

* Any single lesion paucibacillary leprosy (SLPB) is included here as it is not treated differently from PB leprosy

† In practice, 4-weekly dosing and review may be easier to implement for the health service and easier for the patient to remember (on the same day of the week throughout the course)

‡ DOT, directly observed treatment, means dose ingestion is observed and recorded by a health worker

Special case considerations

Treatment of children with leprosy

The WHO recommends fixed doses for children from 10-14 years. These doses are also recommended for use in the NT in consultation with appropriate specialists (Table 10).

Table 10. WHO and NT recommended doses for 10–14-year-old children

	PB including SLPB	MB—Low BI <4+	MB—High BI ≥4+
Duration	6 months	12 months	24 months
Dapsone	50mg daily self-administered	50mg daily self-administered	50mg daily self-administered
Rifampicin	450mg monthly* DOT†	450mg monthly* DOT†	450mg monthly* DOT†
Clofazimine	50mg every other day self-administered 150mg monthly* DOT†	50mg every other day self-administered 150mg monthly* DOT†	50mg every other day self-administered 150mg monthly* DOT†

In practice, 4-weekly dosing and review may be easier to implement for the health service and easier for the patient to remember (on the same day of the week throughout the course)

† DOT, directly observed treatment, means dose ingestion is observed and recorded by a health worker

Children, especially those under the age of 10 years, should with the assistance of expert specialist advice, receive proportionately reduced doses of the above drugs to minimize adverse drug reactions. Clofazimine is available only in a 50mg capsule formulation and smaller calculated daily doses may be given for example as 50mg on alternate days, or 50mg twice a week. Doses for children weighing less than 40kg should be discussed with a TB medical officer/infectious diseases physician/paediatrician (Table 11).

Table 11. Doses for children weighing 40kg or less (WHO)

	Weight 20-40kg	Weight <20 kg
Dapsone	25mg (1/2 tablet) daily	2mg/kg daily
Clofazimine	50mg twice weekly PLUS Monthly dose (DOT)*	1mg/kg daily PLUS 6mg/kg monthly (DOT)
Rifampicin	300mg monthly (DOT)	10mg/kg monthly (DOT)

* Discuss monthly dose with TB medical officer/infectious diseases physician/paediatrician

Pregnancy

Leprosy is exacerbated during pregnancy and therefore continuation of patients on standard MDT is essential. The medications are excreted in breast milk. There are however, no reports of any adverse effects except for mild transient skin discoloration of the infant due to Clofazimine.

Co-existent leprosy with active TB disease

Screening for leprosy should be considered in all cases of active TB infection. Patients diagnosed with both leprosy and TB require both full TB and leprosy treatment (see *Guidelines for the Control of Tuberculosis in the Northern Territory*, 2016).[31] Currently only rifampicin is common to both regimens and should be given in the dose required to treat TB. Second-line regimens for leprosy that contain minocycline or ofloxacin may be necessary if there are severe side-effects caused by a drug in the first-line regimens.[32] Information about drugs used and monitoring recommendations are provided in Appendices 3 and 4.

Co-existent leprosy with latent tuberculosis infection (LTBI)

Leprosy treatment should be the priority however if LTBI is present and active TB is excluded then LTBI can be opportunistically treated. Treatment completed with a MDT leprosy regimen containing rifampicin, ***however given daily***, for at least 4 months will provide prophylactic treatment for LTBI avoiding the requirement for isoniazid treatment.

Co-existent infection with human immunodeficiency virus (HIV)

The concern that HIV infection would increase susceptibility to leprosy has not been realised and evidence suggests it does not alter the clinical features of leprosy. Patients may have co-infection with leprosy and HIV and current evidence suggests that no modification is required of the standard MDT for leprosy or the antiretroviral regimen for HIV management. Care of the patient should be by specialists familiar with both diseases.

Inability or refusal to take one of the first line drugs

Alternative treatment regimens should only be used where severe side effects or contra- indications exist. In this circumstance there should be consultation with a specialist leprosy service. Current WHO recommended alternative treatment regimens for patients unable to take rifampicin (or there is resistance), include at least two of clarithromycin, minocycline or a quinolone, plus clofazimine daily for 6 months, followed by clofazimine plus one of these drugs for an additional 18 months. If ofloxacin resistance is also present, a fluroquinolone should not be used as part of second-line treatment.[13] Instead, 6 months of clarithromycin, minocycline and clofazimine followed by clarithromycin or minocycline plus clofazimine for an additional 18 months is recommended. Evidence on the potential benefits and harms of alternative drug regimens is poor.[13]

Treatment monitoring and adherence (case holding)

Medication should initially be dispensed weekly until full adherence with and understanding of the regimen is assured, and then a 4-weekly cycle of DOT and examination is established. Failure to attend a single 4-weekly DOT requires an immediate effort to trace the patient and find an explanation.

Sometimes this situation arises because the patient is ill at home with a leprosy reaction, a drug side effect, or inter-current illness. The patient who suffers a leprosy reaction may lose confidence in the treatment regimen unless it is carefully explained beforehand that this might occur and does not imply bacteriological worsening of the illness or failure of treatment See Appendix 5 for a checklist of issues to discuss with the patient.

For each case a local member of the health staff should be identified to accept responsibility for providing medication, assessing adherence, monitoring nerve function, and tracing absentees. For regional or remote patients review should occur 4 weekly by a local medical officer and 6-monthly by TB/leprosy Unit staff. For patients in NT urban locations TB/Leprosy Unit staff review 4 weekly.

Adherence should be documented on the leprosy treatment card (see Appendix 6).

Treatment completion

Treatment completed within standard duration[13] (treatment for a cure) is defined as:

- **MB leprosy (BI ≥4+)**—24 months of doses (or 24 x 4-weekly cycles) within 36 months
- **MB leprosy (BI <4+)**—12 months of doses (or 12 x 4-weekly cycles) within 18 months
- **PB leprosy**—6 months of doses (or 6 x 4-weekly cycles) within 9 months.

Those who do not adequately complete treatment need to be fully re-evaluated. Re- treatment regimens will depend on clinical and bacteriological examination.

Defaulters

Leprosy treatment defaulters represent a challenge to manage due to the requirement for many months of treatment and for extended time period follow-up. Usage of the treatment regimens (referred to in 4.2.6) can be considered where refusal is of certain regimen medications.

In extreme defaulters with PB disease a single dose rifampicin, ofloxacin and minocycline treatment as given previously for single lesion PB[32] cases may be considered but is not ideal. For all cases especially, MB cases, every effort should be made to treat and follow-up the patient according to the treatment guidelines due to significant concerns regarding long- term relapses.

Patient Monitoring

Treatment plan while on MDT

Pre-treatment investigations

1. FBE, UEC, LFT, hepatitis B and C and HIV serology.
2. G6PD.
3. Mantoux and CXR to exclude co-existent TB or LTBI.
4. Baseline & at 1 month ECG to exclude prolonged QTc.

See Appendix 5 for a checklist for patients commencing treatment.

Follow-up consultations

1. Document BI of skin smears/biopsies.
2. Discuss importance of medication adherence and the planned regimen.
3. Discuss drug side-effects and when to report to medical staff.
4. Discuss the need to seek medical advice about deteriorating nerve function.
5. Assess skin and nerve function impairment at each visit using the leprosy examination forms (Appendix 2 and 3).
6. Ophthalmology review at initial visit then annually.
7. Photography of skin lesions (with consent)—to be recorded in patient record.
8. Monitoring of electrolytes, liver function (Table 12).
9. Repeat slit skin smears (Table 12).

Table 12. Follow-up of leprosy cases while on treatment

Frequency	Initial	1m	3m	6m	12m	18m	24m
FBE, platelets, LFT*	√	√	√	√	√	√	√
Skin check	√	Monthly while on treatment					
VMT-ST	√	Monthly while on treatment					
Slit skin smear							
Initial skin smear BI<4	√	-	-	-	-		
Initial skin smear BI ≥4	√		√	√	Yearly until completion of treatment		

* Repeat monthly if abnormal

Follow-up of leprosy cases after MDT completion

Follow-up after completion of a course of leprosy treatment is essential to ensure:

- early detection of disease relapse
- early detection of new NFI.

The highest incidence of relapse has been reported among MB cases that had a high pre- treatment BI (≥4+).[25,26] Cases with bacterial loads less than 4 (BI <4) before treatment have a much lower rate of relapse after MDT completion.

The recommended duration of follow-up by CDC after leprosy cases have completed anti- mycobacterial treatment will depend on the type of treatment received. Patients are therefore categorised by their disease classification, treatment type and duration (Table 13).

1. MDT regimens where rifampicin was used for:
    - at least a 6-month (PB) period in daily or monthly administration in combination with dapsone
    - 12 or 24-month (MB) period in daily or monthly administration in combination with dapsone and clofazimine.
2. Treatment regimens predating MDT eg:
    - treatment with 3 months of daily rifampicin and long term dapsone
    - treatment with long term dapsone alone.

Recent cases that received the MDT regimens should be followed-up according to Part A of Table 13.

Part B of Table 13 should be used for cases who were treated initially with dapsone and then later with rifampicin and/or clofazimine, but in whom the total duration of combined treatment was less than 6 months (PB) or 12 or 24 months (MB). Patients who received dapsone monotherapy alone have a high risk of relapse and their follow-up is as per Part C of Table 14.

In addition to relapse, there is also the risk of new NFI, especially in the first 2 years after treatment commences. Useful predictors of new NFI in the first 2 years after MDT starts are classification (MB or PB) and/or the presence of NFI at the time of diagnosis of leprosy.[33]

As 95% of NFI is likely to occur within 2 years[33,34] PB cases with NFI at diagnosis require VMT-ST monitoring every 3 months for 2 years and PB cases without NFI at diagnosis require annual monitoring for 2 years. MB cases will benefit from VMT-ST monitoring monthly throughout the 12 or 24-month period of treatment and should then be followed up for 2 to 5 years after treatment.

For all cases, it is important to remind patients during each examination about the signs that should prompt presentation to the health services between routine reviews. Scheduled follow-up examinations by CDC staff are also an ideal time to enquire if other household members have signs or symptoms of leprosy.

Table 13. Follow-up of leprosy cases after treatment completion

A. Treatment with WHO-MDT*					
Classification	PB (after 6 months of MDT)		MB (after 12 or 24 months of MDT)		
Risk factors	NFI at diagnosis		BI		NFI at diagnosis
	No	Yes	0 to 3+	4+ to 6+	Yes
CDC follow-up after completion of treatment	Annually for 2 years after MDT completed	3 monthly until 2 years after MDT completed	Annually for 2 years after MDT completed	3 monthly for 2 years then annually until 5 years after MDT completed	3 monthly for 2 years then annually until 5 years after MDT completed
Type of follow-up	Clinical†	Clinical†	Clinical†	Clinical† Smear‡ Eyes§	Clinical† Smear‡ Eyes§

B. Treatment with 3 months of daily rifampicin and long term dapsone		
Bacterial index on skin smear at diagnosis	0 to 3+	4+ to 6+
CDC follow-up after completion of treatment	Discharge after a final examination	Annually for 15 years
Type of follow-up	Clinical† Smear (if MB) ‡	Clinical† Smear‡ Eyes§

C. Treatment with long term dapsone alone		
Bacterial index on skin smear at diagnosis	0 to 3+	4+ to 6+
CDC follow-up after completion of treatment	Discharge after a final examination	Annually for 30 years
Type of follow-up	Clinical# Smear (if MB)†	Clinical# Smear† Eyes§

* WHO-MDT is a multiple drug regimen where rifampicin and dapsone are used in combination (sometimes with clofazimine if MB leprosy), given for at least a 6 month (PB) or 12-24 month (MB) period. Rifampicin may be given monthly or daily.

† Clinical means skin, nerve, and nerve function impairment (VMT-ST) assessments, including visual acuity.

‡ Take follow-up smears from 2 sites with the highest BI at the time of diagnosis

§ Eyes means annual slit-lamp examination by an ophthalmologist to detect silent iritis

Screening and contact tracing

High risk group screening

Opportunistic screening for leprosy by primary health care staff should be undertaken whenever those people in high-risk groups present for medical care or examination.

The main high-risk groups are Aboriginal and migrant populations. These populations are also the high-risk groups for TB, so leprosy screening should be considered whenever screening for TB.

TB screening includes:

- review of asylum seekers, newly resettled humanitarian migrants and detained fisherman
- review of patients on Immigration Department TB Health Undertakings (TBUs)
- community TB screening programs.

Patients with crusted scabies should be examined for signs and symptoms of leprosy. Patients with unexplained peripheral neuropathy should have leprosy considered.

Screening should include a full examination of the skin, including eyebrows, nerve examination including abnormalities in extremities due to denervation (see Appendix 2 and 3).

Contact tracing

M. leprae transmission is considered to be via nasal secretions or skin. The risk to contacts of leprosy patients of developing disease varies according to the 'closeness' of the contact (bedroom, household, neighbour, social), the type of index case (MB/PB) and the contact age.

Of all new leprosy cases in highly or moderately endemic areas, only around 30% have a history of having been a household contact of a previous case.[15] This percentage is likely to be much higher where leprosy is now rare and there is a delay in presentation, as in the NT. However most secondary cases are likely to occur within 5 years of the diagnosis of the primary case.[15]

In the NT contacts are defined as those living in the same household for at least 3 months and can be extended to include neighbours and social contacts. The WHO defines a contact as having close proximity to a leprosy patient for a prolonged duration, which is typically 20 hours per week for at least three months in a year.[35] In our low burden setting wider inclusion is encouraged especially when contact occurs in institutional settings such as jails.

If the index case is a child, this would indicate recent infection and screening of wider community should be considered. A checklist is provided in Annex 6 of the *Global Leprosy Strategy 2016-2020. Monitoring and Evaluation Guide*[4]

Importantly, if the index case is a school going child, disclosing his/her diagnosis and labelling him/her as a cause of potential spread to others may lead to stigma and discrimination. Hence, it is not advisable to trace classmates and teachers in the school.[35]

There are few health staff experienced with leprosy management, so most need to be trained in detecting the early signs and symptoms of leprosy. Patients who are suspected of having leprosy should be reviewed by the most experienced local staff who will in turn liaise with the CDC TB/Leprosy Unit.

How to conduct leprosy contact tracing

1. Household, family, and close social contacts should be identified and examined for signs of leprosy. Those at highest risk of disease are shared-bedroom contacts, and children who share the household with the index case.
2. Results should be documented in the local records, and the central leprosy database.
3. New cases should be referred to the TB/leprosy Unit.
4. Contacts of MB cases need to be reviewed annually with a clinical examination for 5 years (Table 14).
5. Contacts of PB cases are at lower risk of developing disease. They should be examined once to exclude disease, provided advice about symptoms and signs and a search for a source of infection for the diagnosed PB case should be carried out.

Table 14. Follow-up of contacts of leprosy cases

Classification of the index	PB	MB
Years of annual CDC follow-up after index diagnosis	0*	5
Type of follow-up	Skin and nerve examination†	Skin and nerve examination†

* Discharge if initial examination is negative
† Perform VMT-ST or skin smear only if indicated by skin and nerve examination

Chemoprophylaxis

Chemoprophylaxis with a single dose of rifampicin (SDR) has been shown to reduce the incidence of leprosy among contacts.[36] Results from a single-centre randomised controlled trial in a high incidence setting showed that when SDR was given to contacts of newly diagnosed leprosy patients it reduced their risk of developing leprosy by 57% in the first two years.[37] This protective effect was strongest in the least high-risk contacts (eg distant contacts rather than household contacts) and the number needed to treat among contacts to prevent one case was 256.[37]

SDR should be given to household contacts only after the index case has taken treatment for at least four weeks. This mitigates the small chance that infection happens during the initial weeks of treatment. The broader use of SDR may be considered for other family and close social contacts depending on clinical context. Single dose rifapentine is likely to be non-inferior to rifampicin and possibly superior, and is a viable alternative when available[38] (same dosing regimen).

Table 15 Recommended rifampicin/rifapentine doses for leprosy prophylaxis

>35kg	600mg
20-35kg	450mg
<20kg	10-15mg/kg

A checklist, including inclusion and exclusion criteria, for contacts taking prophylactic rifampicin/rifapentine is provided at Appendix 7.

Immunoprophylaxis

Bacille Calmette-Guérin (BCG) vaccine

BCG vaccine has been widely used in the NT since 1960 and more than 90% of Aboriginal people have been vaccinated. International trials have demonstrated a protective efficacy of BCG of between 20% and 80%,[1] and it is a recommended leprosy (and in certain population age groups for TB) control strategy in the NT.

Until 2016 the policy* in the NT was that BCG was recommended at birth for:

- all Aboriginal neonates
- non-Aboriginal neonates who lived in Aboriginal communities or in countries for more than 3 months with a high prevalence of tuberculosis.

From 2020 the policy in the NT was changed to:

- children younger than 5 years with a high probability of traveling to countries with high TB incidence (defined as an annual incidence of >40 cases per 100 000 population) based on an individual risk assessment
- newborn babies whose parents have leprosy, or who have an immediate family history of leprosy
- children under 5 years of age considered by the TB Unit to be at ongoing high risk of TB exposure in Australia.

Nerve function impairment and lepra reactions

Classification of nerve function impairment (NFI)

NFI is a clinically detectable loss of motor, sensory, or autonomic peripheral nerve function that necessitates intervention. M. leprae is the only bacterial agent known to specifically infect peripheral nerves. It is the resulting NFI and associated deformities and disability that has made leprosy such a feared disease. In field cohort studies 33-56% of newly diagnosed patients have nerve damage39,40 and in a Bangladeshi study 25% of MB patients developed nerve damage during treatment.41 The main processes associated with NFI include silent neuropathy and Type 1 and Type 2 reactions.

Silent neuropathy

NFI may occur in association with symptoms of neuritis (point pain and tenderness in nerve trunks, or distal pain, hyperaesthesia and tingling in the sensory areas supplied by the n e r v e) or it may occur insidiously without symptoms (termed 'silent' neuropathy). **Silent neuropathy is impairment of nerve function without any nerve pain, nerve tenderness, or symptoms of reaction.** Up to 86% of all NFI occurs silently,[41] which mandates regular testing of motor and sensory function by VMT- ST whether or not the patient complains of symptoms. When the directly observed component of MDT is administered monthly (or 4-weekly) by a health worker, such an assessment should be performed.

Lepra reactions

Lepra reactions are immunologically mediated episodes of acute or subacute inflammation and are classified as either Type 1 (RR) or Type 2 (ENL) reactions (Table 16).[42] MB leprosy patients are at higher risk of reactions than PB leprosy patients and in patients who present initially with NFI.[43]

Type 1 (reversal or upgrading) reactions are a delayed hypersensitivity response to

M. leprae antigens occurring in BL, BB or BT cases. They are characterised by acute neuritis and/or acutely inflamed skin lesions. Usually with onset there is an associated change in Ridley-Jopling classification towards the tuberculoid end of the spectrum. There is nerve tenderness with loss of sensory and motor functions. Redness and swelling in pre-existing skin lesions occur, and lesions which have not been visible may appear. Fever, malaise and peripheral oedema are additional features if the reaction is severe. Onset may be spontaneous though it is commonest after starting treatment.

Type 2 (ENL) reactions are an immune complex response that develops due to an imbalance of the humoral immune system. They are the most serious complication of leprosy and occur in about 15% of patients with multibacillary disease (LL and BL).[42] Reactions may occur spontaneously or while on treatment. There is a sudden appearance of superficial or deep crops of new, tender, subcutaneous nodules on the back, the dorsum of the hands or the extensor aspects of the forearms and thighs that generally last for about 3 days. The whole episode usually lasts 2 weeks though may be prolonged or recurrent over several years. Patients with ENL are likely to have an impaired quality of life and may face significant socioeconomic consequences. Patients need to be warned that this be a chronic complication.

ENL is commonly associated with systemic systems including:

- high fever peaking in the evenings
- neuritis
- leucocytosis
- orchitis
- nephritis
- periostitis including joint inflammation
- iridocyclitis (eye inflammation).

Type 1 and Type 2 reactions may coexist in a case of BL. The introduction of WHO-MB-MDT has seen a reduction in the frequency and severity of ENL due to the anti-inflammatory effect of the clofazimine component.

Table 16. Comparison of the features of Type 1 and Type 2 reactions

	Type 1	Type 2
Classification	BT, BB, BL	LL (occasionally BL, BB)
Immunology	Changing cell mediated immunity	Immune-complex deposition, elevated TNF-alpha levels, dysfunctional cell mediated immunity
Classification change	Upgrading (usually) toward TT	No change
Timing	First months of MDT	May be years after treatment
Recurrent	Usually not	Often
Duration	Several months	2 weeks
Sites of inflammation	Nerves, skin lesions	Skin nodules, iris, testes, joints, nerves, soles, lymph nodes
Key feature	Typical features of inflammation: swelling, redness, heat, pain, loss of function	Erythema nodosum (inflamed nodules); pain, fever, peripheral oedema, inflammation of joints and digits

The differential diagnosis of the skin lesions of Type 1 or Type 2 reactions is active leprosy. In the context of drug resistance, leprosy may progress with the appearance of new lesions despite MDT. Also, following the completion of treatment and apparent cure, new leprosy lesions can be associated with a relapse (see Table 21).

Table 17. Comparison of the features of new leprosy nodules and Type 2 reactions

	New leprosy nodules	Type 2 reaction
Onset	Gradual	Sudden
Number	1 at a time	Nodules appear in crops
Tenderness	-	+
Bacterial index	High in the nodule	High or low
SFG reading*	Often solids	Mainly granules
Resolution	After months of MDT	Successive waves of nodules subside after 2 weeks, with or without treatment

SFG, Solid-Fragmented-Granular reading—the proportions of solid, fragmented or granular appearing AFB in a skin smear. 'Solids' are presumed to be viable bacilli; 'fragmented' and 'granular' are recently and remotely dead, respectively.

Disability grading

NFI and its secondary consequences are described in a 'disability grading' (0, 1, or 2) for the purposes of reporting to the WHO, and for monitoring program objectives (Table 18). The highest value for any body part is taken as the overall disability grading for the patient; eg if hands, feet, and left eye are graded 0, but the right eye is graded 2, then the overall grading for the patient is 2. It is sometimes expressed as an Eye-Hand-Foot (EHF) score where each hand, foot, and eye is graded 0, 1 or 2, and these grades are summed bilaterally for a maximum score of 12.[34]

Table 18. WHO grading of leprosy related disability[4]

Grading*	Hands and Feet	Eyes
0	No anaesthesia, no visible deformity or damage	No eye problems due to leprosy; no evidence of visual loss
1	Anaesthesia present, but no visible deformity or damage†	
2	Visible deformity or damage present‡	Severe visual impairment (visual acuity worse than 6/60; unable to count fingers at 6 meters) or lagophthalmos or iridocyclitis or corneal opacities

* The highest value of the leprosy disability grade for any part is taken as the overall disability grading of the patient
† Includes muscle weakness
‡ Includes ulceration, shortening, disorganisation, stiffness, loss of part or all of the hand or foot

However, disability grades or eye, hand, feet, (EHF) scores are not sensitive enough to be useful in monitoring the progress of subtle impairment in an individual patient. For this purpose, the VMT-ST is required (Appendices 1 and 2), and together with the indications for prednisolone and other therapies, decisions about the requirement for prednisolone therapy can be made.

Detection of neuropathy

Nerve conduction studies (NCS)

Advanced neuropathy is already present before signs and symptoms of NFI appear. Nerve conduction studies are able to detect this neuropathy before it is clinically apparent. This is a time consuming and uncomfortable procedure and should only be requested in consultation with the TB/Leprosy Unit.

The indications are:

- to assist (where necessary) in the diagnosis of a suspected leprosy case
- as soon as possible after diagnosis to establish a baseline assessment of the extent and severity of nerve damage
- ideally at yearly intervals while taking MDT
- when new symptoms of neuritis, or findings of NFI, appear after MDT completion.

Voluntary muscle test-sensory test (VMT-ST)

In between the sensitive assessments that NCS provide, a VMT-ST should be performed to detect NFI as a baseline at diagnosis, monthly while on MDT, and at each review after release from treatment for the prescribed durations of follow-up (see Table 14). With practice (for both health worker and the patient), this should take around 10 minutes to complete thoroughly. See Appendix 1 for the method.

The advantage of a standardised form of documentation is that an examiner can make a direct comparison with an earlier examination (even if performed by another person) in trying to assess whether new NFI has occurred or not. Use of a ballpoint pen for sensory testing is not as sensitive for protective light-touch thresholds as nylon monofilaments, but they are universally available when the latter are not. With appropriate training, their use produces reliable results between different observers.

Treatment of nerve function impairment (NFI) and lepra reactions

Nerve damage occurs before diagnosis, during and after drug treatment and may also occur as silent neuropathy without signs of inflammation. Treatment of reactions is aimed at controlling acute inflammation, reducing pain and reversing eye and nerve damage. During treatment for lepra reactions MDT should be continued.

Clinical suspicion of reactional states should lead to urgent specialist review and advice should be sought regarding anti-inflammatory and immunomodulating drugs due to the potential for permanent disabilities. Disabilities are a consequence of neural damage with decreased peripheral nerve function because of motor and sensory loss.

Many, but not all studies have reported beneficial responses of NFI in reactions and silent neuropathy with prednisolone. Studies show that improvement occurs in 60-80% of patients with neuropathy, mostly within the first 3 months of a course, especially within the first few days, but further gains can be made at a slower rate for several more months.[45,46] However, some studies have shown no benefit at 12 months compared to placebo.

Acute primary NFI (first attack and those less than 6 months in duration) have a better prognosis with treatment than chronic or recurrent forms, but improvement may still be seen in up to 50% of the latter episodes.[7,46] Variability in response to corticosteroid treatment relates to severity and duration of NFI.[46]

The major modes of action of corticosteroids are:

1. reduction of oedema in nerves and skin (improvement may be seen within days because of alleviation of raised intra-neural pressure and ischaemia)
2. suppression of *M. leprae*-specific T-cell inflammation. In Type 1 reactions, serial skin biopsies have shown a slow decrease in Th1*cytokines (interferon-gamma, interleukin-12, and inducible nitric oxide synthase) and cellularity in lesions. BL patients however may still have considerable inflammation in lesions at 180 days, despite a course of treatment.
3. reduction of post-inflammatory scarring within lesions.

Indications for prednisolone

Table 19. Indications for prednisolone

1	Recent NFI at diagnosis	At the time of diagnosis of leprosy, NFI is detected that the patient tells you is <12 months old.
2	New NFI during or after MDT	NFI with or without symptoms of neuritis or reaction, detected on a monthly VMT-ST during treatment or on annual VMT-ST after MDT completion that had not been recorded on the previous assessment. This includes: new loss of sensation in 2 or more points on the sensory chart; and new weakness, paralysis or increasing lid gap on the motor record.
3	Type 1 reaction	Any degree of severity, with or without neuritis or new NFI. If present at diagnosis, start prednisolone with MDT.
4	Type 2 reaction	Moderate or severe ENL (not mild), or, ENL with neuritis or new NFI.
5	Progressive subclinical neuropathy	Deteriorating nerve conduction studies where worsening NFI has not been detected on VMT-ST.

NB. **Advancing secondary consequences of NFI**, eg enlarging ulcer, worsening contracture, increased clawing, digital shortening, or deteriorating vision are **not alone** an indication of worsening NFI or an indication for prednisolone treatment. They may instead reflect old irreversible NFI that is being inadequately managed in terms of appropriate footwear and self-care. However, coexisting new NFI should be excluded.

Prednisolone regimens

There is no firm consensus about the optimum regimen of corticosteroids and no randomised controlled trials have been reported comparing regimens of differing dose and duration. However, severe reactions need to be treated with a course of steroids, usually lasting 3-6 months. Patients with recurrent reactions should be treated with high dose clofazimine (300mg daily for 3 months; tapering to a monthly maintenance dose of 100mg daily, until no further reaction episodes occur).[13]

Whenever prednisolone is being used precautions and prior screening for opportunistic infections must be carried out (see below).

There is consensus about the general principles of treatment with prednisolone, which should ideally be tailored to the response of the individual.

Therefore:

1. A starting dose is usually 1mg/kg (60mg for adults) for a severe reaction with symptoms of neuritis. For silent neuropathy or mild reactions, a dose of 40mg may be sufficient since rapid symptom amelioration is not required. The initial dose in either situation can be increased if symptoms or NFI fail to improve after 2 weeks.
2. When the symptoms are controlled and NFI improves, tapering can commence.
3. Dose reduction can occur at a rate equivalent to 5mg every 1 to 2 weeks. This may need to be slowed, or the dose increased again if symptoms recur or NFI deteriorates.
4. Generally, in Type 1 reactions, BL cases will require longer treatment than BT.
5. Change to alternate daily dosing will minimise the cushingoid effects of therapy, particularly where prolonged courses are anticipated. This is appropriate when a daily dose of 20mg has been attained.
6. Morning dosing is less suppressive of adrenal function than evening doses.
7. Once physiological values of corticosteroid have been reached (the equivalent of 7.5mg prednisolone per day), tapering should occur slowly to allow recovery of the hypothalamic-pituitary-adrenal axis.
8. During and after cessation of a prolonged course of prednisolone, supplementary doses may be required for up to 12 months in the event of serious injury, infection or operation. The patient should be advised to specifically mention the course of prednisolone to future medical caregivers.
9. During reactions, **continue MDT without interruption** along with prednisolone.
10. Adjuncts to prednisolone for neuritis symptoms are rest of the affected part (bed rest, sling, splint, crutches) and application of a protective dressing/bandage if required.
11. A regimen that uses multiples of prednisolone 25mg tablets for as long as possible (rather than 5mg tablets) will reduce the overall number of tablets per dose and improve patient acceptability (Table 20).

Precautions with prednisolone usage

- Nerve abscess (requires surgery and appropriate referral prior to prednisolone use).
- Untreated infections (TB, strongyloidiasis, amoebiasis, osteomyelitis, infected ulcers, scabies) need to be referred to a specialist and treated prior to prednisolone use.5,1
- Other conditions to consider when prescribing prednisolone are diabetes, osteoporosis, mental disturbance, dyspepsia, Cushing's syndrome, growth suppression, intra-uterine growth retardation and Addison's disease.

In addition, if prolonged use:

- avoid live vaccines during and for 3 months after therapy
- increase dose during acute stress (intercurrent illness, surgery)

- high calcium intake (1200mg/day); restrict sodium intake; add potassium supplements if necessary.

Screening prior to the commencement of prednisolone

1. Mantoux or IGRA test, clinical review and chest x-ray for TB infection (latent or active).
2. Blood glucose, electrolytes, urea and creatinine, FBE, LFT, HIV, hepatitis B, hepatitis C and melioidosis serology. Where tests are abnormal refer to physician, infectious diseases physician or liver clinic doctors as appropriate.
3. Serology for Strongyloides stercoralis. If serology positive or eosinophilia, collect stool (single stool minimum, 3 preferred) and send for ova/cysts/parasites, writing 'immunosuppressed, ?strongyloides'. See *Prevention of Opportunistic Infections in Patients Undergoing Immunosuppression TE, BR, EA Regions Guideline*.[47]
4. Visual acuity and check history of glaucoma.
5. Pregnancy test in reproductive age females.
6. Bone density assessment in postmenopausal women and elderly men.
7. History or risk factors for peptic ulceration.
8. History of psychiatric disorders.
9. Blood pressure and cardiac examination.
10. Weight.
11. Skin examination for scabies.
12. Review of immunisation history (see Australian Immunisation Handbook for recommendations for immunosuppression).[48]

Table 20. Example of 9 month tapering course of prednisolone for Type 1 reaction in leprosy

Week No.	Number of prednisolone tablets		Equivalent daily dose
	25mg tablets	5mg tablets	
1-2	2 OD*		50mg
3-4	1.5 OD	1 OD	42.5mg
5-6	1.5 OD		37.5mg
7-8	1 OD	1 OD	30mg
9-10	1 OD		25mg
11-14	1.5 AD†		18.75mg
15-18	1 AD		12.5mg
19-22		4 AD	10mg
23-26		3 AD	7.5mg
27-30		2 AD	5mg
31-34		1 AD	2.5mg
35-38		0.5 AD	1.25mg

* OD, once daily

† AD, alternate days. Transition to AD dosing may be done by gradually increasing to the dose shown on 1 day, and tapering the dose on the alternate days to zero

Therapy complications and their management

Type 2 reactions (ENL) are less frequently complicated by neuritis and NFI than Type 1 reactions. In LL, NFI may be largely secondary to bacillary infiltration rather than inflammation and commencing MDT alone may produce improvement.

Assessment of ENL severity is useful to guide appropriate treatment, predict prognosis and monitor progress (see Appendix 8). A severity score of 8 or less indicates mild ENL, and when comparing scores, the minimal important difference is 5.

Mild ENL, not accompanied by neuritis or new NFI, can be managed with bed rest and simple analgesics (aspirin, NSAIDs).[44] If there is worsening of the severity, ENL should be reclassified and managed accordingly.

Moderate and severe attacks of ENL or ENL with neuritis should be treated with prednisolone, initially with moderate doses of 30-40mg prednisolone per day (for an adult).[45] The tendency for ENL to recur means the duration of treatment should be as short as possible to avoid steroid-dependence (eg 2-8 weeks). Recurrent ENL requires an increase of the daily MDT clofazimine dose to 300mg (not for longer than 3 months—see drug information in Appendix 4) to allow prednisolone to be withdrawn. The clofazimine dose is then tapered over several months by 100mg increments to 100mg daily, which is maintained until the completion of MDT.

Iridocyclitis complicating ENL should be treated with corticosteroid eye-drops and a mydriatic and reviewed by an ophthalmologist.

Thalidomide usage

Thalidomide can be used to treat ENL and is rapidly effective in severe and recurrent forms. It controls and prevents neuritis, relieves pain and improves nerve function effectively. Thalidomide use allows a reduction in prednisolone requirements to avoid steroid dependency and furthermore, studies have shown thalidomide to be very effective as a monotherapy.

The WHO Expert Committee on Leprosy (1997) advised that thalidomide is the drug of choice for steroid unresponsive ENL in males and for females of non-reproductive age under expert supervision and with extreme caution due to the risk of teratogenicity in the first trimester of pregnancy. In the United States of America and Brazil it is licensed for steroid dependent leprosy or when steroids are contraindicated in men and women. It is licensed by the Australian Therapeutic Goods Administration for the treatment of ENL[49] though treatment should be under specialist hospital care only and clinicians require training and registration as a thalidomide prescriber. Women should use double contraception and report immediately if there is a delay in menstruation.

Prevention of NFI, deformity and handicap

Early case detection of leprosy

An important indicator in assessing the quality of a leprosy control program is the proportion of newly diagnosed cases who have Grade 2 disability.[6] Global leprosy programs have a target of less than 1 case with Grade 2 disability per million population by the year 2020.[5] To achieve this, effective education strategies to raise the awareness of leprosy among health workers and those at-risk in the community are required. In low burden countries like Australia where the majority of cases are diagnosed by self-reporting and late case detection the disability proportion may be high.

Having NFI at the time of diagnosis is a risk factor for a poor ultimate disability outcome (measured by the EHF score 5 years after completion of MDT). Those who first develop impairment after treatment commences have a better prognosis. Furthermore, patients who have longstanding NFI at the time of

diagnosis (NFI for longer than 6 months) have a 15-fold higher incidence of **further episodes** of acute NFI than those who do not.[34] Early case detection of leprosy and treatment with MDT rapidly stops multiplication of *M. leprae*. Combined, these are the most important steps to prevent NFI.

Early detection and treatment of NFI

Effective and rapid management of lepra reactions is essential. It is imperative that:

- patients are taught to recognize early signs and symptoms of reactions and to report promptly for treatment
- health workers are able to diagnose and treat reactions and refer patients when necessary
- adequate stocks of prednisolone are available and means of accessing thalidomide quickly is determined by a central pharmacy.

The fact that the likelihood of full recovery of nerve function with prednisolone is much higher in acute or recent NFI (<6 months duration) than in older NFI, coupled with the fact that up to 80% of all NFI occurs imperceptibly (silent neuropathy), mandates a system of regular clinical screening for NFI even though a patient is asymptomatic.

Self-care of established complications

Impairments such as anaesthesia, weakness, and loss of sweating may have been present for too long to be reversible with prednisolone or other therapies when discovered. In 20-30% of acute cases the impairments may simply be refractory to therapy. Self-care routines when supported by access to appropriate medical, surgical and rehabilitation services can prevent the secondary consequences of these impairments.

Impairments from peripheral neuropathy (lack of sensation, muscle weakness and loss of sweating) can have a significant impact on the extremities. While the hands may be affected, the feet are at greater risk to due to the increased forces of weight-bearing and footwear. In cases of persistent paraesthesia and weakness on screening, early referral to hand therapy or podiatry is recommended to prevent further deformity, prevent wounds and maintain function. General education should also be provided to patients regarding safety in personal care (e.g. temperature of hot water while showering or cooking safety) to help prevent burns and other injuries secondary to peripheral neuropathy.

Outlined below are some simple steps that can be taken daily to significantly reduce the risk of foot problems.

Self-management of anaesthetic feet

CHECK feet daily

- Look for ulcers, cuts, bruises, new calluses and other signs of injury or damage, including between toes and on lower legs. A mirror may be helpful for examining the bottom of feet.
- Be aware that visible injuries may not cause pain due to loss of sensation in the feet or hands. These injuries still need attention even if they are not currently causing pain.
- Individuals with vision or mobility impairment are advised to seek support from a carer or health care professional. Regular podiatrist appointments can be helpful for ongoing foot care management.
- If any areas of concern are noted, immediate follow up with a medical officer or health

care professional (e.g. a podiatrist or clinic nurse) as soon as possible to ensure early treatment for the best-possible outcome.

WASH feet daily- keeping feet clean will help reduce the risk of infection-causing bacteria.

- Clean daily using soap/body wash and warm (not hot) water, including between toes and around toenails.
- Dry feet well, including between toes.
- If reaching the feet is difficult, please discuss options with a carer or health care professional.

General recommendations for care of feet

- *Moisturise*—keep skin soft and supple by applying moisturiser to the tops and bottoms of feet and lower limbs daily. Avoid between the toes as this may lead to infection and do not moisturise close to broken skin or wounds.
- *Toenail maintenance*—long or ingrown toenails can cut into the skin of feet, potentially causing infection and ulcers. Toenails should be cut straight across and filed gently. If required, seek assistance from a carer or podiatrist.
- *Corns and Calluses*—these can be a sign of pressure being applied to these areas of the feet and are worth mentioning to your GP or podiatrist. There are many do-it-yourself removal methods that can cause wounds, so please avoid these and only have treatment by a qualified podiatrist or other health care professional proficient in debridement.
- *Footwear*—protect feet with well-fitting footwear, both indoors and outdoors.
    - This is important as injuries can easily occur by stepping on something hard or sharp without realising (due to loss of sensation in the feet).
    - Wear clean socks to protect skin from rubbing. Avoid sock seams where possible.
    - Shoes should fit well and not be too tight, as blisters or other pressure lesions may result.
    - Speak to a podiatrist to see if specialised insoles or custom-fitted footwear is required.
    - Check inside shoes before putting them on, checking for small pebbles or rough stitching. Check feet for any blisters or rubbing from new shoes.
- **Avoid exposure to heat/cold**—remember that the nerves in feet may be less efficient at communicating temperature and pain messages than before, so take precautions.
- Avoid exposure to hot pavements, sunburn, heaters, hot or very cold water.

For any active ulcerations/wounds or complex neuropathy-related foot problems please contact the RDH Podiatry/High Risk Foot Clinic on 892 28241 or email PodiatryService.DoH@nt.gov.au. In Alice Springs, please contact ASH.Podiatry@nt.gov.au.

Other complications

Joint contractures can occur when muscles are paralysed, and active and passive exercises should be taught to prevent this result. Involvement of specialist physiotherapy, occupational therapy and/or orthopaedic care may be required.

Eye damage occurs because eyes are vulnerable due to corneal sensory loss (trigeminal neuropathy) or lagophthalmos (facial neuropathy). Eyes should be inspected in a mirror daily for redness. Redness or visual deterioration should be assessed promptly by health staff. Use of lubricating eye drops, or ointment should be encouraged where there is weakness in lid closure. Sunglasses are recommended to protect eyes from sun and dust. Regular ophthalmology review is recommended as per Table 14.

Illustrated resources are available that are excellent and provide more detailed prevention of disability advice for the various impairments. Doctor Grace Warren's manual, *The care of neuropathic* limbs[50] is available in the Department of Health library in Darwin.

The International Federation of Anti-Leprosy Associations' 'How to prevent disability in Leprosy' is also a useful resource.

Referral to specialist vision services should be considered for patients presenting with significant visual changes to support safety in navigating their environment (i.e. orientation training) and daily activities; for example, Vision Australia or Guide Dogs NT/Australia.

Relapse of leprosy

Relapse of leprosy in previously treated patients may occur, especially in patients who have not been treated with a WHO multi-drug regimen. In the MDT era a cure is defined by the completion of an MDT regimen within a fixed time period. Therefore, a relapse is defined as the appearance of new signs of disease in person who has previously completed a course of treatment and been declared 'cured'. By contrast, a new case of leprosy is a person with leprosy who has never previously been treated.

Treated PB cases presenting with new activity

When previously treated PB cases present with fresh activity in old lesions or the appearance of new lesions, either relapse or a Type 1 reaction may be the cause. Furthermore, a relapse may also present as a Type 1 reaction. Although the clinical features described in Table 21 are of some use in differentiating between the 2, there is still considerable overlap.

The most useful criterion is the timing of the new signs. Those which occur within 6 months of completion of MDT are very likely to be due to Type 1 reaction, whereas those occurring more than 1 year after completion are more likely to be caused by a relapse.

Histological findings are not a useful adjunct. Granulomas in a biopsy do not prove evidence of a relapse since they are still present in 40% of cases 2 years after the start of MDT. A lymphocytic infiltrate can also be present in the absence of viable bacilli, being maintained by antigens of dead bacilli.

It is reported that approximately 50% of patients presenting with new activity post-MDT will have skin biopsies compatible with active (relapsed) leprosy, and half will have histopathology consistent with Type 1 reaction.

A course of prednisolone 40mg/day for 4 weeks should be given and if signs and symptoms clear, a Type 1 reaction is the likely diagnosis. If not, relapse is more likely and the new activity should be classified as PB or MB in the usual way and re-treated with MDT.

Treated MB cases presenting with new activity

Relapsed MB patients should be retreated with triple therapy regardless of any change in classification. There are almost as many combinations of criteria for MB relapse as there are studies on the relapse of leprosy after MB treatment.

Diagnosis of MB relapse requires an increase in BI of 2+ at that site confirmed by 2 sets of skin smears 6 months apart.

Table 21. Clinically distinguishing relapse from a late Type 1 reaction

	Relapse	Type 1 reaction
Speed of onset	Slow	Sudden
Timing of onset	>2 (PB) or 5 (MB) years after end of treatment	<2 (PB) or 5 (MB) years after end of treatment
New lesions	+	-
Reappearance of old lesions	+	+
Bacterial index	Increasing	Stable or decreasing
Neuritis	In previously unaffected nerves	Only in previously affected nerves
Fever, oedema	-	+

Prevention

In 2000 the WHO declared global elimination of leprosy as a public health problem, defined as a registered prevalence of less than 1 case per 10 000 population.4 In 2021, the goal is elimination of leprosy, defined as no new autochthonous cases as a result of interruption of transmission.5 The current Global Leprosy Strategy (2021-2030) has 4 pillars:

- implement integrated, country-owned zero leprosy roadmaps in all endemic countries
- scale up leprosy prevention alongside integrated active case detection
- manage leprosy and its complications and prevent new disability
- combat stigma and ensure human rights are respected.

Preventing exposure to the disease remains a key strategy. It can be approached through improving education of health staff, environmental factors and by chemoprophylaxis of contacts when appropriate.

Health education

Health staff need to be aware of the population of people who are at greatest risk of leprosy. This includes the Aboriginal and migrant populations and specifically family and household contacts of active cases of leprosy.

In addition, ongoing provision and updating of knowledge to health staff is needed to enable them to diagnose patients with leprosy, provide ongoing care and management of patients and to form a working relationship with the TB/Leprosy Unit.

Education can also support health staff to provide counselling to new cases and their contacts. Effective counselling is an integral intervention that can empower patients to accept treatment, understand early warnings of reactions, and facilitate contact surveillance.

This should be achieved through:

- the Aboriginal Health Practitioner curriculum
- orientation of health and allied health staff
- ongoing education sessions for health staff in the NT.

Environmental factors

Leprosy has long been considered a ‘disease of poverty’. One study from Malawi, showed persons living in the worst standard of housing had double the risk of leprosy compared to those living in the best category of dwelling.[15]

Other diseases with respiratory transmission such as TB are associated with overcrowding and overcrowding probably also increases the risk of acquiring leprosy. Advocacy to improve housing quality, ventilation, water supply, and nutrition and to alleviate overcrowding, particularly in pockets of relatively high incidence is considered vital for leprosy control.

Research

Research into the optimal length of treatment for single lesion PB and MB continues.[8]

Studies of use of single dose rifampicin chemoprophylaxis with immunoprophylaxis with BCG for contacts are still being followed, though demonstration of initial benefits[51] have not carried through in longer term follow up[52]

Other research priorities for leprosy outlined by the WHO include[13]:

- Diagnostic tests (e.g. PCR tests using tissue samples, biomarkers) assessed in larger, well-designed studies.
- Benefits and harms of shorted MDT regimens for PB and MB leprosy.
- Efficacy of different second-line regimens.
- Prevention through chemoprophylaxis with vaccines and alternatives to SDR.

Other resources

- McDougall AC, Yuasa Y. A new atlas of leprosy: a pictorial manual to assist frontline health workers and volunteers in the detection, diagnosis and treatment of clinical leprosy. Sasakawa Memorial Health Foundation, Tokyo, 2019
- Hargrave JC, Jones ER. Leprosy in Tropical Australia. Northern Territory Department of Health. 1997. (Available from Department of Health Library or Centre for Disease Control Darwin).
- Infolep. Leprosy Information Services. 2021, InfoNTD. https://www.leprosy-information.org/key-topics-leprosy
- World Health Organization. Regional Office for South-East Asia. Guidelines for the diagnosis, treatment and prevention of leprosy. World Health Organization. Regional Office for South-East Asia. 2018. https://apps.who.int/iris/handle/10665/274127
- World Health Organization. Towards Zero Leprosy. Global Leprosy (Hansen's Disease) Strategy 2021-2030. World Health Organization, Geneva. 2021
- World Health Organization. (2020). Leprosy/Hansen disease: Contact tracing and post-exposure prophylaxis. World Health Organization. Regional Office for South-East Asia. https://apps.who.int/iris/handle/10665/336679.
- World Health Organization. Leprosy/Hansen Disease: Management of reactions and prevention of disabilities. Technical guidance. New Delhi: World Health Organization, Regional Office for South-East Asia; 2017.
- World Health Organization. A guide for surveillance of antimicrobial resistance in leprosy: 2017 update. http://apps.who.int/iris/handle/10665/259357
- The International Federation of Anti-Leprosy Associations (ILEP) publications
- Learning Guide One: How to diagnose and treat leprosy. 2001.
- Learning Guide Two: How to recognise and manage leprosy reactions. 2002.
- Learning Guide Three: How to do a skin smear examination for leprosy. 2003.
- Learning Guide Four: How to prevent disability in leprosy. 2006.

Appendix 1. Method of performing a VMT-ST

Available from the NT Health Public Health Response staff only website.

Neuritis check

Sensation or strength change in the past 6 months Y

N Pain or tenderness Y

N

If answering 'yes' detail below

Neuritis check

1. Ask client about the duration of any NFI, and point pain within nerves or distally in area of sensory supply in the palms and soles.
2. Palpate leprosy-prone nerves for tenderness.
3. Describe abnormal findings.

Motor Test

1. Lid Gap [Zygomatic branch of facial N.] – client closes eyelids lightly as if asleep - examiner measures any lid gap in millimetres with a ruler.
2. Little finger out (abduction) [ulnar N.] – client spreads all fingers wide with palm facing up (paralysis if no movement) – examiner presses outside of base of small finger back towards the ring finger with client resisting (weakness if finger cannot hold against pressure).
3. Thumb up and across (opposition) [median N.] – client rests back of hand on table, lifts thumb up to sky at 90 degrees to table (paralysis if no movement) – examiner presses base of thumb back towards table with client resisting (weakness if thumb yields to pressure).
4. Foot up (dorsiflexion) [common peroneal N.] – client raises foot towards the sky with heel on the ground (paralysis if no movement) – examiner presses top of foot towards ground with client resisting (weakness if foot forced down).

Strength and blink

	Right		Left	
	Yes	No	Yes	No
Blink problems?				
Light closure lid gap	mm		mm	
little finger out	S	W P	S	W P
Thumb up and across	S	W P	S	W P
Foot up	S	W P	S	W P

Circle appropriate letter for strong (S), Weak (W) and paralysed (P) for items 2-4

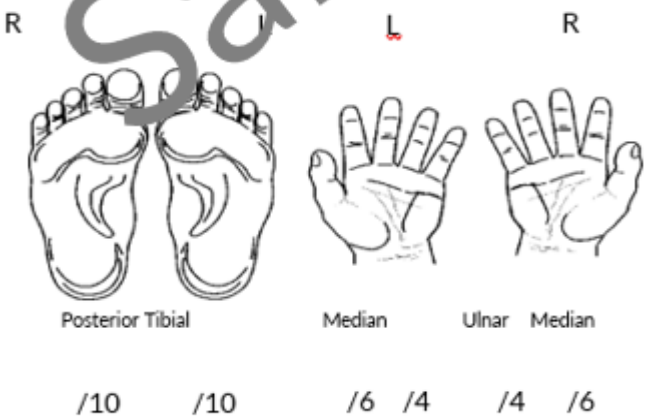
Sensation

Sensation tested by light skin denting with biro tip not dot

Key √ = Feels within 3 cm X = Does not feel

C = Clawed Wound or open ulcer

_____= Shortening level



/10 /10 /6 /4 /4 /6

Sensory Test

1. Corneal anaesthesia (trigeminal N.) – observe client's rate of blinking – if less than twice per minute, reduced sensation is probably present. Test the suspected side first – with the client looking ahead, bring a wisp of clean cotton wool in from the side to touch the centre of the cornea – lack of blink implies anaesthesia (document result in "Strength and Blink" section).
2. Deformities (secondary to primary impairments) – chart any visible deformity in hands or feet ("C" adjacent to clawed finger or toe, indicate ulcers or digital shortening as shown) – ulcer size can be measured in 2 directions in mm to assess future response to treatment.
3. Light touch sensation (ulnar, median, posterior tibial NN.) – using a ball-point pen, with client's eyes open, allow the weight of the pen to depress normal skin on a point on the forearm to demonstrate normal sensation of this stimulus – repeat with client's eyes closed and ask client to touch the point with their index finger – repeat for 10 points shown on each palm and sole – tick points which are accurately felt within 3 cm, cross points which are not accurately felt and score the points felt for each nerve distribution.

Appendix 2. Leprosy Examination form–nerves (VMT-ST)

Available from the NT Health Public Health Response staff only website.

Leprosy Examination—nerves, nerve function impairment (VMT-ST), eyes

Date	Surname	Other name	HRN

Strength and blink	Right	Left
Blink problems?	es No	es No
Light closure lid gap	mm	mm
Little finger out	S W P	S W P
Thumb up and across	S W P	S W P
Foot up	S W P	S W P
SWP = Strong/Weak/Paralysed		

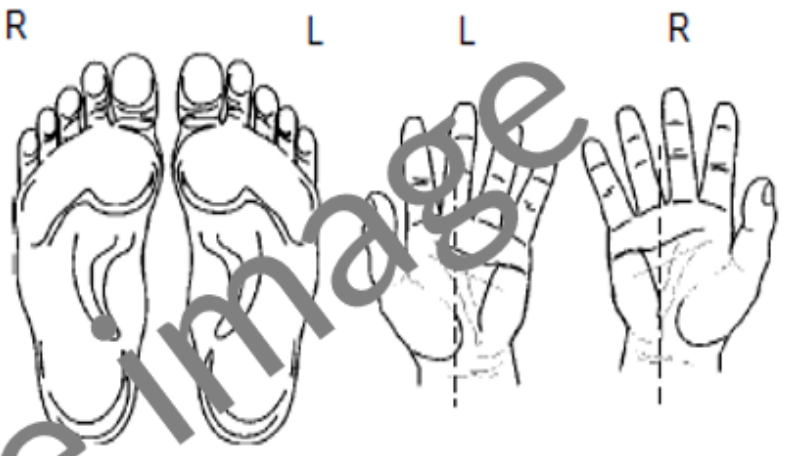
Nerve size	Right	Left
Supraorbital	N + ++	N + ++
Greater auricular	N + ++	N + ++
Median	N + ++	N + ++
Ulnar	N + ++	N + ++
Radial cutaneous	N + ++	N + ++
Lateral popliteal	N + ++	N + ++
Posterior tibial	N + ++	N + ++
Key: N=Normal: += Enlarged ++=Very enlarged		

Sensation tested by light skin denting with biro tip at dot

Key √ = Feels within 3 cm X = Does not feel

C = Clawed = Wound or open crack

___ = Shortening level



/10	/10	/6	/4	/4	/6

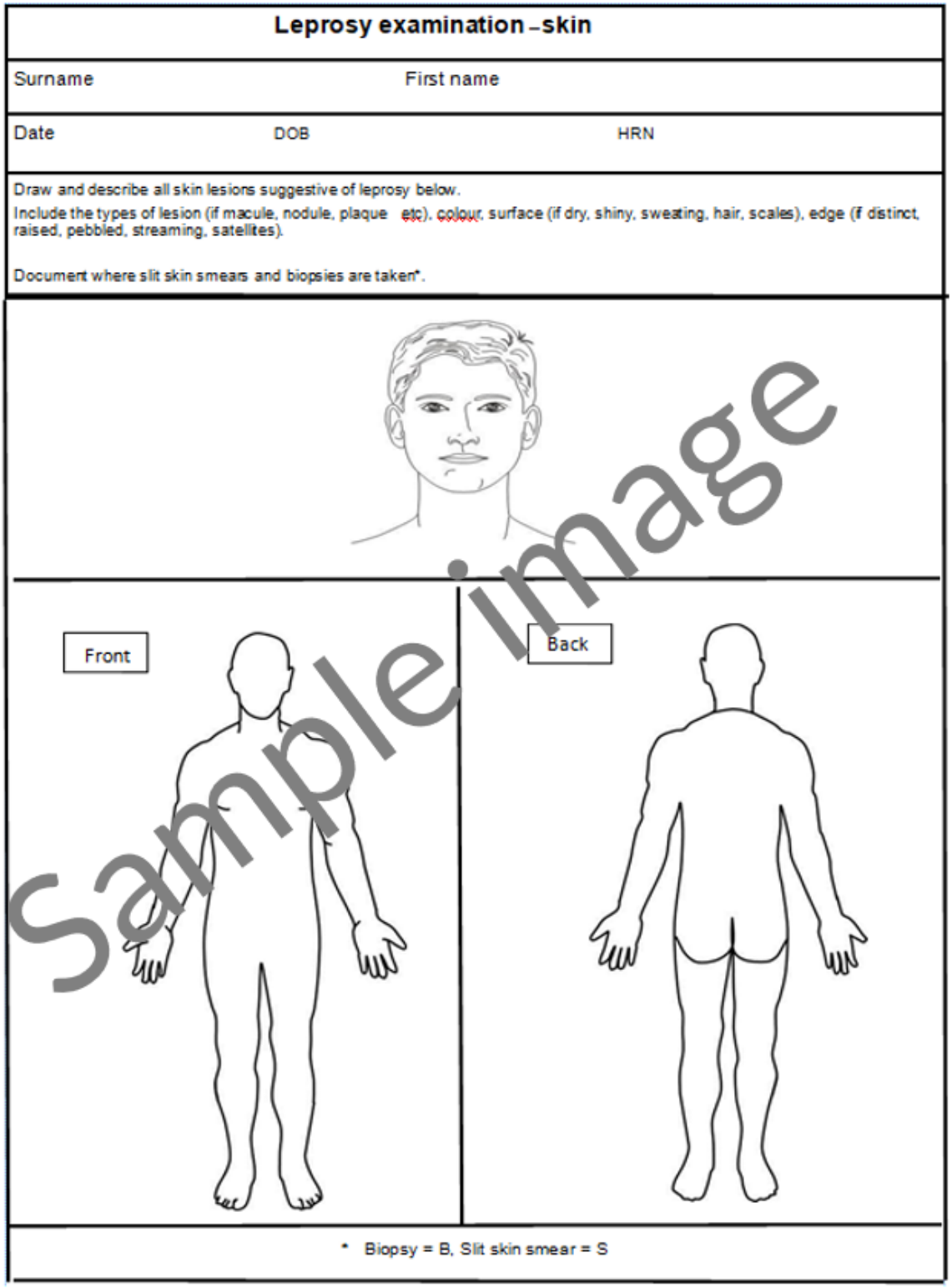
Neuritis check		
Sensation or strength change in the last 6 months	Yes	No
Nerve pain or tenderness	Yes	No
If answering 'yes' give details		

Visual acuity		
	Right	Left
Uncorrected	6/	6/
Corrected	6/	6/
Assessor		

Comments

Appendix 3: Leprosy examination form–skin

Available from the NT Health Public Health Response staff only website.



Leprosy examination –skin

Surname First name

Date DOB HRN

Draw and describe all skin lesions suggestive of leprosy below.
Include the types of lesion (if macule, nodule, plaque etc), colour, surface (if dry, shiny, sweating, hair, scales), edge (if distinct, raised, pebbled, streaming, satellites).

Document where slit skin smears and biopsies are taken*.

Front

Back

* Biopsy = B, Slit skin smear = S

Appendix 4. Drug profiles

Dapsone			
Formulation	**Dose**	**Precautions**	**Adverse reactions**
50mg, 100mg tablet	1-2mg/kg/day Usual adult dose 100mg/day	• Avoid if sulphone allergy, severe anaemia, G6PD deficiency, porphyria. • Folic acid supplement 5mg/day in pregnancy. • Probenecid, trimethoprim increase levels. • Rifampicin reduces levels.	• haemolysis if G6PD deficient and dose >50mg/day • haemolysis/ Methaemoglobinaemia in most subjects at dose of >200mg/day • GI irritation, nausea, vomiting, anorexia • fixed drug eruption • 'dapsone syndrome' – hypersensitivity rash, fever, jaundice, eosinophilia in first 6 weeks of therapy • exfoliative dermatitis • maculopapular rash • headache • nervousness • insomnia • blurred vision • peripheral neuropathy • psychosis • fever • hepatitis • agranulocytosis (rare) • aplastic anaemia.

Clofazimine			
Formulation	**Dose**	**Precautions**	**Adverse reactions**
50mg, 100mg capsules	Children 1mg/kg/day. Adults 0.8-1.6mg/kg/day. Usual adult dose 50-100mg/day (up to 300mg/day for Type 2 reaction) Give after meals.	• Slow elimination with half-life of 70 days. • Close supervision with doses higher than 100mg/day for 3 months. • Do not discontinue in pregnancy. • Hepatic or renal impairment.	• reversible (over months to years) red to brown discoloration of skin (especially sun-exposed areas), hair, cornea, conjunctiva, tears, sweat, sputum, breast milk, urine, faeces • skin discoloration in breast-fed neonates whose mothers take clofazimine • dry skin, ichthyosis, pruritis • dry eyes • GI symptoms of abdominal pain, nausea, vomiting, weight loss, anorexia, diarrhoea, sub-acute bowel obstruction (especially with doses of 300mg/day for >3months) due to crystal deposition in small bowel wall and mesenteric lymph nodes • crystal deposition in liver and spleen

Rifampicin			
Formulation	**Dose**	**Precautions**	**Adverse reactions**
150mg, 300mg tablet/ capsule. 100mg/5mL liquid.	10mg/kg/day. Usual adult dose 450-600mg/day	• Monitor LFT in elderly and those with hepatic dysfunction • Increased doses of oral contraceptives, corticosteroids, anticoagulants and oral hypoglycaemic agents may be required	• red discoloration of urine/tears/contact lenses • GI irritation • liver enzyme induction/ Hepatitis • dermatitis • fever • collapse/shock • influenza-like syndrome • haemolytic anemia • thrombocytopenia • renal failure

Clarithromycin Pregnancy (B3) Lactation (safe)			
Formulation	**Dose**	**Precautions**	**Adverse reactions**
250mg, 500mg tablets	500mg	**Contraindications:** • known hypersensitivity or adverse reaction to macrolide antibiotic drugs • concurrent use of pimozide, ergotamine or dihydroergotamine **Precautions** • renal failure, reduce dose if Cr Cl • <30 mL/minute • concurrent colchicine use **Increases levels of:** • Theophylline • Warfarin • Anticonvulsants • Benzodiazepines • Disopyramide • Digoxin • Tacrolimus • Cyclosporin • Rifabutin • Cilostazol • Methylprednisolon • Quinidine • Colchicine • Sildenafil • Vinblastine **Decreases levels of:** • Zidovudine **Clarithromycin levels increased by:** • Fluconazole Fluoxetine • HIV protease inhibitors such as Ritonavir and Atazanavir*	**Common** • altered taste (3-9%) • nausea or vomiting (3-6%) • diarrhoea (3-6%) • abdominal pain (2%) • headache (2-9%) **Serious** • prolonged QT interval • hepatitis, liver failure • anaphylaxis • Stevens-Johnson syndrome • toxic epidermal necrolysis • blood dyscrasias • psychosis • pseudomembranous colitis **Rhabdomyolysis** reported when taken with statins

* Further information and updates can be obtained from MIMS or product information.

Minocycline			
Formulation	**Dose**	**Precautions**	**Adverse reactions**
50mg tablet, 100mg capsule	100mg/month with rifampicin and ofloxacin for MB 100mg/day with clofazimine and ofloxacin for MB Avoid dosing with iron salts, milk and antacids	• Avoid in tetracycline allergy, severe renal impairment, pregnancy, early childhood • Monitor LFT	• photosensitivity • oesophagitis • abnormal osteogenesis • tooth staining • hypoplasia dental enamel • dizziness, vertigo • GI irritation • enteritis—coagulase-positive Staphylococci, Clostridium difficile • morbilliform rash • urticaria • fixed drug eruption • cheilosis • glossitis
Ofloxacin			
Formulation	**Dose**	**Precautions**	**Adverse reactions**
200mg tablet	400mg/month or 400mg/day depending on regimen Take with full glass of water, avoid dosing with antacids, iron, sucralfate	• Avoid in quinolone allergy, pregnancy, children <18yrs • Reduce dose in hepatic and renal impairment • Increases effect of warfarin	• nausea, diarrhoea, dyspepsia • headache • restlessness • rash, pruritis • dizziness • arthropathy in young animals • crystalluria • seizures (in epilepsy, or in combination with NSAIDs)

Prednisolone			
Formulation	**Dose**	**Precautions**	**Adverse reactions**
1mg, 5mg, 25mg tablets 5mg/ml liquid	0.5-1mg/kg/day initially, reducing gradually See p49	• Avoid if untreated viral, bacterial, fungal infections • Monitor weight, BP, electrolytes, glucose • Avoid live vaccines • Pregnancy—avoid if possible • Rifampicin increases metabolism	• oedema • weight gain • hypertension • glucose intolerance • peptic ulceration • osteoporosis • proximal myopathy • aseptic necrosis femoral head • hypercorticalism (moon face, acne, bruising, striae, truncal obesity, muscle wasting, amenorrhoea and hirsutism in females) • growth retardation in children • exacerbation psoriasis (withdrawal) • adrenal insufficiency (sudden withdrawal) • posterior subcapsular cataracts • glaucoma • insomnia • depression, psychosis • raised intracranial pressure in children • hypercoagulability of blood • delayed tissue healing • activation of latent infections (TB, strongyloidiasis) • increased susceptibility to infections (>20mg/day immunosuppressive) • fetal adrenal developmental impairment, cleft palate

Appendix 5. Checklists for patients commencing treatment

Available from the NT Health Public Health Response staff only website.

☐	Complete notification for leprosy and enter on Leprosy Register and the Northern Territory Notifiable Diseases Data base
☐	Fill in Leprosy Treatment Card
☐	Counsel the patient with regard to the need for regular treatment the appointments and reviews that will be done by the clinic possible complications of leprosy Side effects of the medication The need to contact the clinic for advice between appointments about complications or drug side effects
☐	Complete baseline examination and tests (checklist over page)

☐ Voluntary Muscle Test-Sensory Test – baseline VMT-ST) (monthly)
Date:_____Normal/Abnormal

☐ Skin examination – baseline ☐clear ☐lesions ☐crusted scabies ☐ other (monthly) co[illegible]ts_
_____

☐ Slit skin smears - baseline Date_____Result_____ [illegible]illary Index Result
_____

☐ Nasal swab PCR Date_____Result _____

☐ Slit skin site swab PCR Date_____Resu[illegible]

☐ Biopsy Yes/No Date_____Result _____

☐ Nerve conduction studies (NCS) Yes/No Date _____

☐ Treatment of nerve impairment required [illegible]s/No

☐ Referral/s required (eg Seat clinic, Neurology, [illegible]CS, [illegible]atology) Yes/No
Where referred _____

☐ Visual acuity baseline (& monthly) Res[illegible]t L_____R ___

☐ ECG (to exclude prolonged QT [illegible] Result _____

☐ FBC [illegible]mal/Ab[illegible]rma[illegible]
Monthly Yes[illegible]o

☐ LFT [illegible]ormal/Abnormal
M[illegible]thly Yes/No

☐ U[illegible] Yes/No Normal/Abnormal
Monthly Yes/No

☐ Hepatitis screen Positive/Negative

☐ HIV Positive/Negative

☐ HTLV-1 (in ATSI) Positive/Negative

☐ G6PD Normal/Abnormal
Mantoux test Date_____Result_____mm or
Quantiferon Gold Date_____Result _____

☐ CXR (all cases) Yes/No Result_____ Sputum AFB Yes/No Result _

☐ Baseline weight_____kg

☐ Review potential drug interactions Done/Not done/NA

☐ Family planning discussion (females) Done/Not done/NA

☐ Fact sheet given Given/Not given

☐ Notification form Done/Not done

Appendix 6. Leprosy treatment card

Available from the NT Health Public Health Response staff only website.

LEPROSY TREATMENT CARD
NT Department of Health

HRN	Leprosy Reg No E_____	CCIS Case ID

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_____

Classification Ridley-Jopling (please circle)

I TT BT BB BL LL Other

Annual weights

Week	Date	Weight (kg)
Year 0		
Year 1		
Year 2		

Classification NT

PB MB

WHO disability grading at diagnosis

0 1 2

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

CXR_____
Mx_____
HIV_____

Type of treatment
(please tick)
Initial
Defaulter
Relapse
Resistance

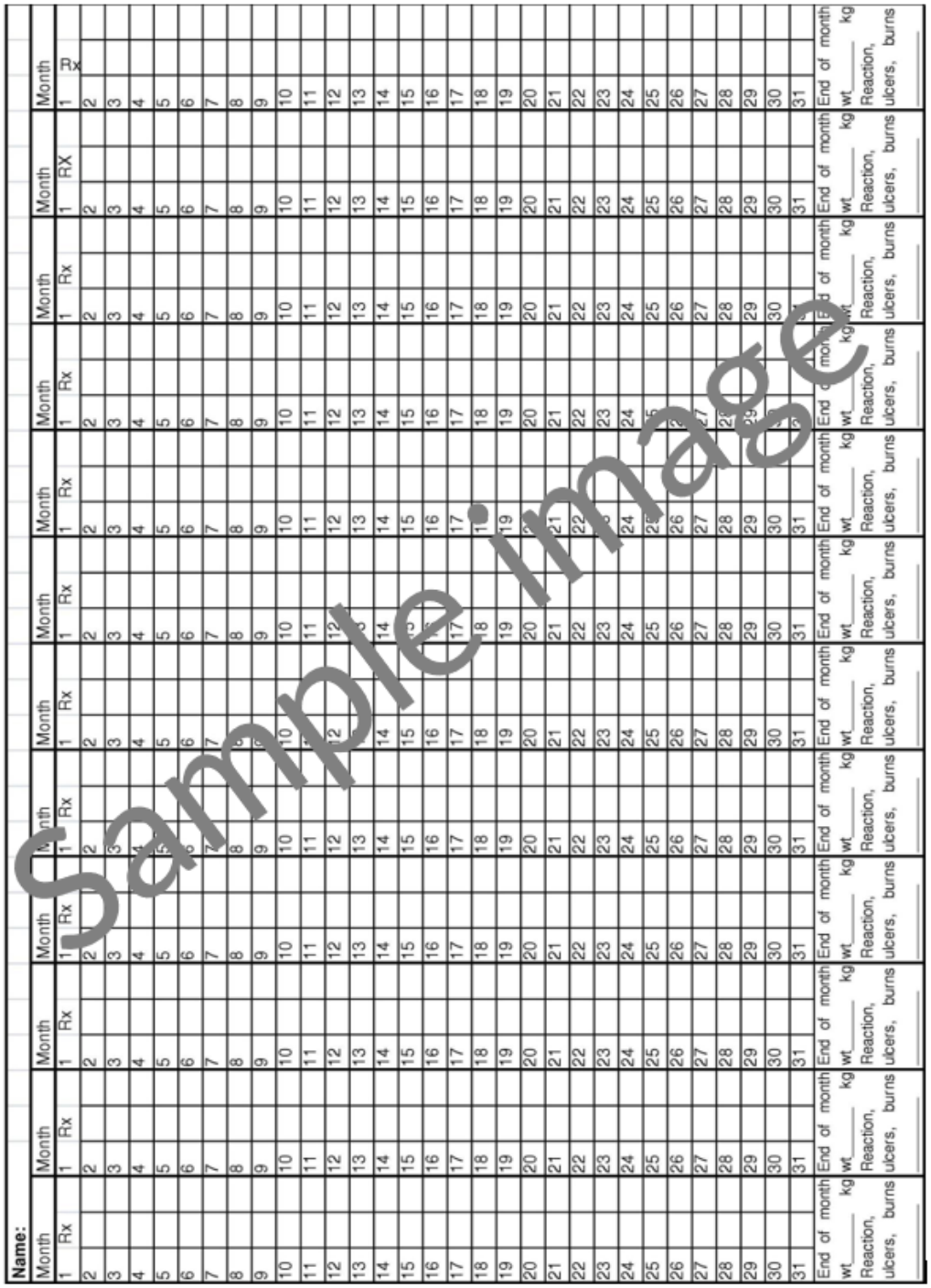
Reason treatment stopped
(please tick 1)
Completed
Transferred out
Lost
Died

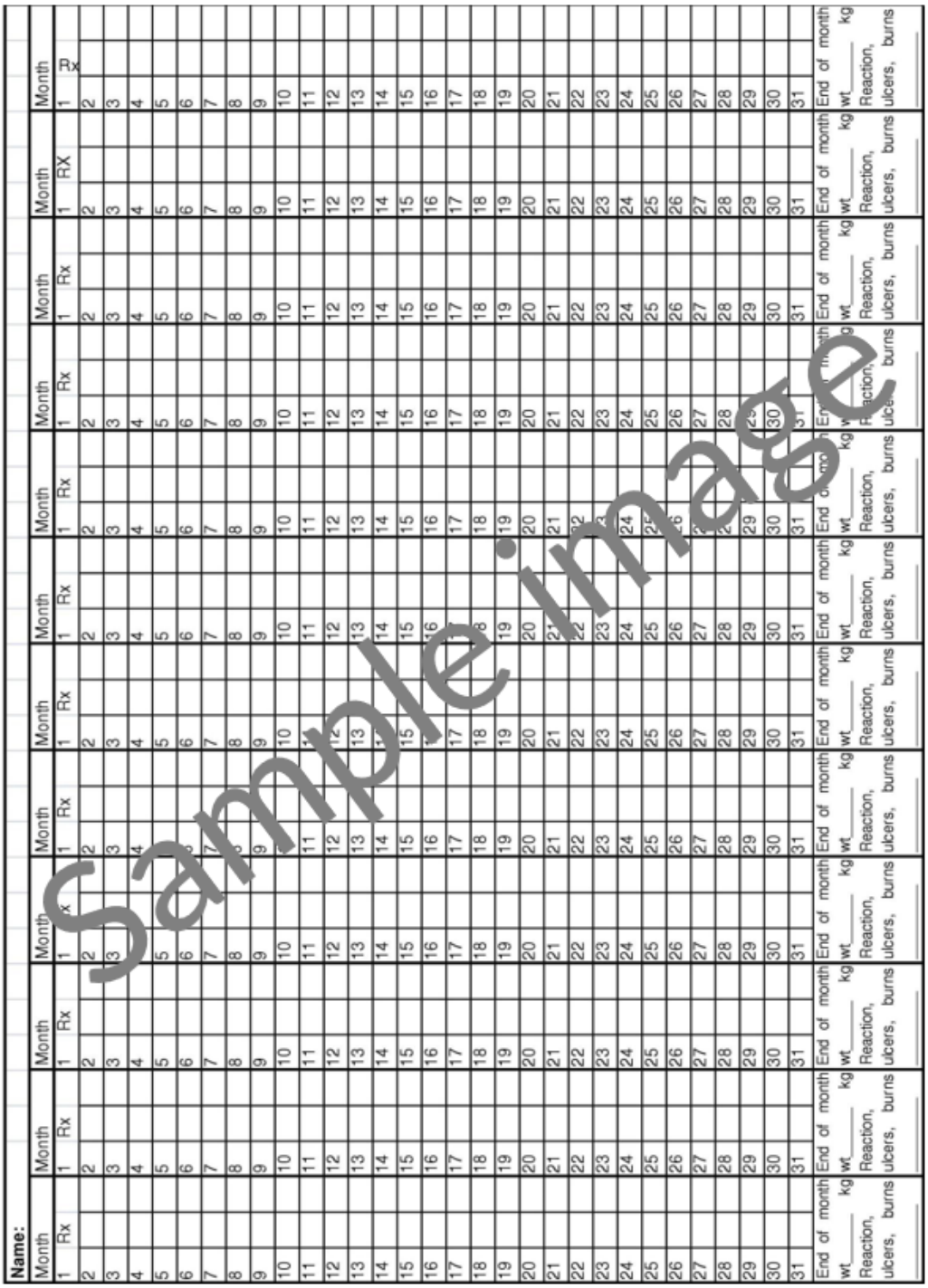
Initial AFB smear result / /
Site_____ 1_____
Site_____ 2_____
Site_____ 3_____
Site_____ 4_____
Site_____ 5_____
Site_____ 6_____

TREATMENT
Daily
From / /
To / /
Dapsone_____
Rifampicin_____
Clofazimine_____
Other_____

Baseline at diagnosis Date / /
FBE result_____
LFT result_____
G6PD result_____
UEC_____
Visual acuity R eye_____
Visual acuity L eye_____

Monthly
From / /
To / /
Dapsone_____
Rifampicin_____
Clofazimine_____
Other_____





Name				
Treatment				
Drug	Dose (mg)	Frequency	Commenced	Completed
Drug toxicities (please circle)	yes		no	
If yes, list drugs and side effects				
End of treatment review	/ /			
Completion AFB result				
Comments				
Defaulter action If client misses 1 treatment If client misses more than 1 treatment	Home visit Report case to supervisory centre			
Defaulter Multibacillary (BI ≥4+) Multibacillary (BI ≤4+) Paucibacillary	24 months treatment must be completed within 36 months 12 months treatment must be completed within 18 months 6 months treatment must be completed within 9 months			

Appendix 7. Leprosy contact – rifampicin/rifapentine prophylaxis

Available from the NT Health Public Health Response staff only website.

First Name:_____Surname: _____

DOB:____/____/____HRN: _____ Gender: Female / Male

Address: _____

Date of contact screening:_____/_____/_____

Type of contact (circle): relative/friend/social/other _____

Inclusion criteria for prophylaxis:

1) Person has been living/working/socialising >3 months with index case, prior to treatment. Y / N

2) Age >2 years. Y / N

3) Signs and/or symptoms of **leprosy excluded** by clinical assessment Y / N

Exclusion considerations:

1)	Pregnancy (delay until delivery)	Y / N
2)	Rifampicin/rifapentine therapy for any reason in the last 2 yrs—discuss with TB MO	Y / N
3)	History of liver disorders—discuss with TB MO	Y / N
4)	History of renal disorders—discuss with TB MO	Y / N
5)	Presence of acute febrile illness (delay until recovery)	Y / N
6)	Potential for drug interactions assessed—discuss with TB MO/pharmacist (document)_____	Y / N

Eligible for chemoprophylaxis: **Y / N**

Recommended Rifampicin/Rifapentine dosage	
> 35kg	= 600mg
20kg – 35kg	= 450mg
< 20kg	= 10-15mg/kg

Weight:_____kg

Contraception discussion (7 days of additional contraception after dose is required for eligible women) Y / NA

Prescription written by: _____

Date dose given_____/____/____Drug and dosage given:_____

Name of staff member giving chemoprophylaxis: _____

Signature:_____Date:____/____/_____

Appendix 8. ENLIST ENL Severity Scale and User Guide[53]

Pain rating: Visual Analogue Scale (ensure line is 100mm long)

How severe is your pain today? Mark the line below with an X to indicate how bad you feel your pain is today.

No pain .....**Worst possible pain**

ITEM		SCORES				
		0	1	2	3	SCORE
1	**VAS – Pain (mm)**	0	1-39	40-69	70-100	
2	**Fever** (in °C)	None (37.5 or less)	No fever now but history of fever in last 7 days	37.6-38.5	38.6 or higher	
3	**Number of ENL skin lesions**	None	1-10	11-20	21 or more	
4	**Inflammation of ENL skin lesions**	Non tender	Redness	Painful	Complex	
5	**Extent of ENL skin lesions**	0	1-2 regions	3-4 regions	5-7 regions	
6	**Peripheral oedema**	None	1 site of Hands or Feet or Face	2 sites	All three sites (Hands and Feet and Face)	
7	**Bone pain**	None	Present on examination but does **not** limit activity	Sleep or activity disturbed	Incapacitating	
8	**Inflammation of Joints and/or digits due to ENL**	None	Present on examination but does **not** limit activity	Sleep or activity disturbed	Incapacitating	
9	**Lymphadenopathy due to ENL**	None	Enlarged	Pain or tenderness	Pain or tenderness in 2 or more groups	
10	**Nerve tenderness due to ENL**	None	Absent if attention distracted	Present even if attention distracted	Patient withdraws limb on examination	
	TOTAL					

User Guide for ENLIST ENL Severity Scale

The score for each item should be **added** together to obtain the ENLIST ENL Severity Scale score.

Mild ENL is categorised as an ENLIST ENL Severity Scale of **8 or less**.

The **Minimal Important Difference** of the ENLIST ENL Severity Scare is **5**.

SCALE ITEM	NOTES
1. VAS Pain	Instruct the patient to point to the position on the line to indicate how much pain they are **currently** feeling. The far left end indicates 'No pain' and the far right end indicates 'Worst possible pain'. Take the measurement (in **mm**) using a ruler from the **LEFT** end of the line to the centre of the cross. **Ensure that the line when reproduced from this document is 100 mm long**.
2. Fever	Take temperature (in **°C**) using a thermometer. If the temperature is **GREATER** than 37.5°C the patient has a fever. If it is less than or equal to 37.5°C the patient scores 0 for this item UNLESS they give a history of having had a fever in the last 7 days in which case they score 1. The cause of the fever does not need to be established.
3. Number of ENL skin lesions	***Note: only skin lesions due to ENL are to be considered for this item.***
4. Inflammation of ENL skin lesions	***Note: only skin lesions due to ENL are to be considered for this item.*** The term complex refers to the following type of skin lesions: vesicular, bullous, pustular, erythema multiform-like, panniculitis, necrotic, ulcerated. ***If the participant fulfils criteria for more than one score then the highest scoring criteria should be used***. For example if there are red ENL skin lesions and some are ulcerated or vesicular or pustular then the patient scores 3 because "complex" lesions are present.
5. Extent of ENL skin Lesions	***Note: only skin lesions due to ENL are to be considered for this item.*** The separate regions are: a) Head and neck b) Left upper limb c) Right upper limb d) Torso –front (including genitals) e) Torso back (including buttocks) f) Left lower limb g) Right lower limb
6. Peripheral oedema due to ENL	The three sites to be considered are the face, hands and feet. Both feet count as one site. Both hands count as one site. Oedema thought to be due to treatment such as corticosteroids or thalidomide should not be counted.

7. Bone pain	Bone pain is distinct from pain or tenderness of the joints. It is most usually elicited by palpation of the subcutaneous border of the tibia.
8. Inflammation of joints and/or digits due to ENL	***Note: only joint inflammation due to ENL are to be considered for this item.*** Inflammation of the joint will be present if there is any of the following: pain or tenderness, redness, swelling or heat. It them must be determined if any of these are sufficiently severe to meet the criteria of the scores. If more than one joint is affected the most severely affected joint is used to determine the score.
9. Lymphadenopathy due to ENL	The lymph node groups to be examined are: a) Head and neck (including the supraclavicular fossae) b) Axillary c) Inguinal ***Note: Lymph node groups on the different sides of the body are separate for example: left axillary and right axillary. Therefore there are 6 lymph node groups for the purposes of the scale.***
10. Nerve tenderness due to ENL	Any peripheral or cutaneous nerve tenderness due to ENL is to be considered. If the participant fulfils criteria for more than one nerve then the highest scoring nerve should be used. ***The most severely affected nerve should be used. Where the examiner suspects that neuropathic pain is being elicited then this should be disregarded.***

Definitions of "complex" skin lesions

Bulla is defined as a visible accumulation of fluid within or beneath the epidermis more than 0.5cm

Erythema multiform-like lesions are atypical ENL lesions resembling those of erythema multiform and include macular, papular or urticarial lesions, as well as the classical iris or 'target lesions'.

Panniculitis inflammation of the subcutaneous adipose tissue.

Pustule an accumulation of free pus.

Target lesions are defined as less than 3 cm in diameter and have three or more zones, usually a central area of dusky erythema or purpura, a middle paler zone of oedema and an outer ring of erythema with a well-defined edge.

Ulceration a break in the epithelial surface (the epidermis in the skin).

Vesicle is defined as a visible accumulation of fluid within or beneath the epidermis 0.5cm or less in diameter.

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National Safety and Quality Health Service standards

National Safety and Quality Health Service standards							
Clinical Governance	Partnering with Consumers	Preventing and Controlling Healthcare Associated Infection	Medication Safety	Comprehensive Care	Communicating for Safety	Blood Management	Recognising & Responding to Acute Deterioration
☐	☐	☐	☐	☒	☐	☐	☐