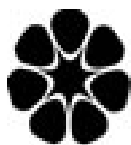




CENTRE FOR DISEASE CONTROL
NORTHERN TERRITORY

Guidelines for the Control of Leprosy in the Northern Territory

October 2002



Northern Territory Government
Department of Health and Community Services

**COMMENTS ARE WELCOME AND SHOULD BE DIRECTED TO THE PROJECT/RESEARCH OFFICER
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Acronyms

<i>AFB</i>	Acid-fast bacilli
<i>BCG</i>	Bacille Calmette-Guerin vaccine
<i>BI</i>	Bacterial Index
<i>MB</i>	Multibacillary
<i>MDT</i>	Multi-drug treatment
<i>MI</i>	Morphological Index
<i>NCS</i>	Nerve Conduction Studies
<i>NFI</i>	Nerve Function Impairment
<i>NT</i>	Northern Territory
<i>PB</i>	Paucibacillary
<i>RFT</i>	Release from treatment
<i>TB</i>	Tuberculosis
<i>VMT-ST</i>	Voluntary Muscle Test- Sensory Test
<i>WHO</i>	World Health Organisation

Preface

The previous edition of “Guidelines for Leprosy Control in the Northern Territory” was published in 1996. Drs John Hargrave, Tania Wallace, and Doug Lush are acknowledged as the authors of those guidelines, on which this document is substantially based. Changed local circumstances and new medical evidence and recommendations since then have been considered in the production of this version.

1. Declining incidence

In 1996 the previously vertical Leprosy Unit was combined with the TB Unit in order to maximise the efficiency of use of staff and resources in Centre for Disease Control (CDC). Declining leprosy detection rates allowed this to occur and 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 Northern Territory. Leprosy now commands an appropriately small proportion of CDC resources, and policies involving CDC staff need to be streamlined compared with the past. Medical evidence shows that some cases are at much higher risk than others of developing nerve function impairment (NFI) after treatment commences, or of relapsing after treatment is completed. Similarly, some types of contacts are at higher risk of eventually developing disease. This knowledge allows CDC staff to target follow up at these groups, and discharge others to the care of the primary health services.

2. WHO recommendations

The WHO Expert Committee on Leprosy modified recommendations for leprosy control in its Seventh Report in 1998. Changes included a purely clinical classification for leprosy (excluding consideration of skin smear results), introduction of a single-dose combination multi-drug treatment (MDT) for single-lesion leprosy, and advocating the reduction of Multibacillary (MB) MDT to 12 months duration.

3. Eradication

Although in the NT the “elimination of leprosy as a public health problem” (defined by WHO as a prevalence of less than 1 per 10,000 population) has been attained, it is no time to be complacent. There is an opportunity to move towards eradication of the disease, at least in terms of indigenous transmission. Recent studies suggest that preventive treatment for close contacts of cases could have a profound effect on future incidence, and answers from a large-scale randomised controlled trial regarding the efficacy of single-dose Rifampicin in India are 2 years away.

4. Early diagnosis

The average delay from the onset to the diagnosis of leprosy increases in settings where it is rare. The hallmark of good leprosy control is early diagnosis. Transmission of infection is interrupted rapidly by treatment. Importantly for the patient, there is also a reduced chance of NFI with early diagnosis, leading in turn to a lower risk of new NFI during treatment, and less disability after treatment completion. These guidelines, together with other resources and advice from the TB/Leprosy Unit, aim to facilitate

primary health personnel to opportunistically diagnose leprosy at the earliest possible point in its presentation.

5. Monitoring NFI after diagnosis

Early diagnosis will reduce the percentage of patients who initially present with established NFI, but alone it is not enough. NFI frequently starts or worsens after MDT treatment commences, and sometimes after treatment completion. The gold standard for detecting neuropathy is Nerve Conduction Studies, but these are clearly not available monthly to detect recent, and thus treatable, deterioration in nerve function. It is imperative that all health workers treating leprosy have the skills to use a simple, rapid, valid, and reliable clinical tool to detect the commonest leprosy-related NFI – the Voluntary Muscle Test–Sensory Test (VMT-ST) (see Appendix 6 p. 44).

The most important changes to note in this revision are:

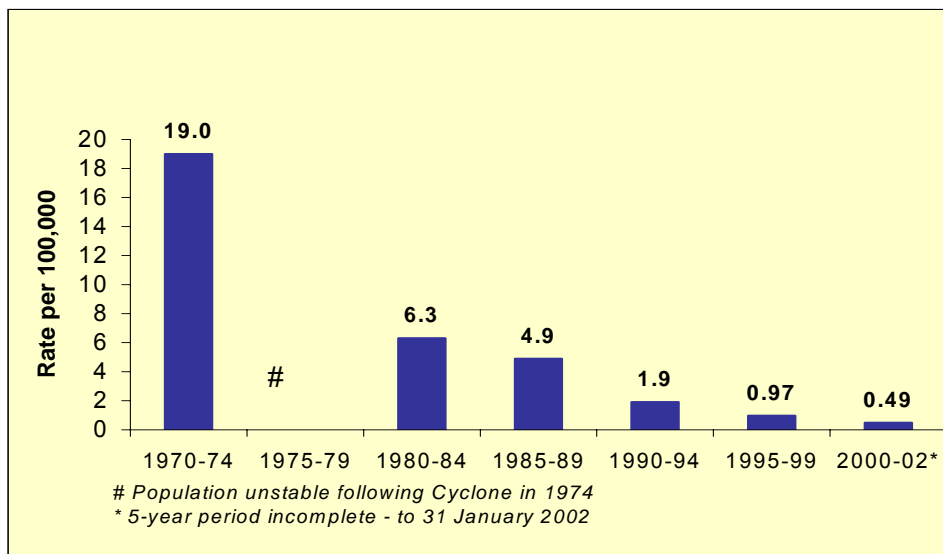
1. A **change in the multidrug therapy regimens** for leprosy to the regimens defined by the WHO Study Group on Chemotherapy of Leprosy in 1994. Rifampicin is now prescribed **monthly** rather than daily and the durations are fixed at 6 and 24 months for PB and MB leprosy respectively (Table 8, p. 16).
2. A **reduction in the duration of follow up** for cured cases following completion of MDT. Follow up for patients who have completed regimens other than MDT is also described (p 31). Previously the practice was annual follow up of all cases for the rest of their lives, but the new recommendations depend on the leprosy classification, the presence of NFI at diagnosis, and the Bacterial Index at diagnosis. MB cases who had a BI ≥ 4 will require 5 years of follow up after 2 years of treatment. PB cases who had NFI at the time of diagnosis will be followed beyond their 6 month course of treatment for 18 months after treatment is completed. All others will be discharged on treatment completion.
3. A **reduction in the duration of follow up** for contacts after the diagnosis of the index case. Previously all contacts were examined annually for 20 years to detect disease early and provide ongoing education. Now, contacts of MB cases will be followed up annually for 6 years, and contacts of PB cases will be examined once.
4. The **introduction of a standardised clinical assessment (VMT-ST or Voluntary Muscle Test-Sensory Test) for the common nerve function impairments** [Section 2.2.2 on p 24 and Appendices 3 & 6] and guidelines for using this to initiate prednisolone therapy for NFI (Table 14, p. 25).

Part 1. Leprosy

1.1 Leprosy in the NT

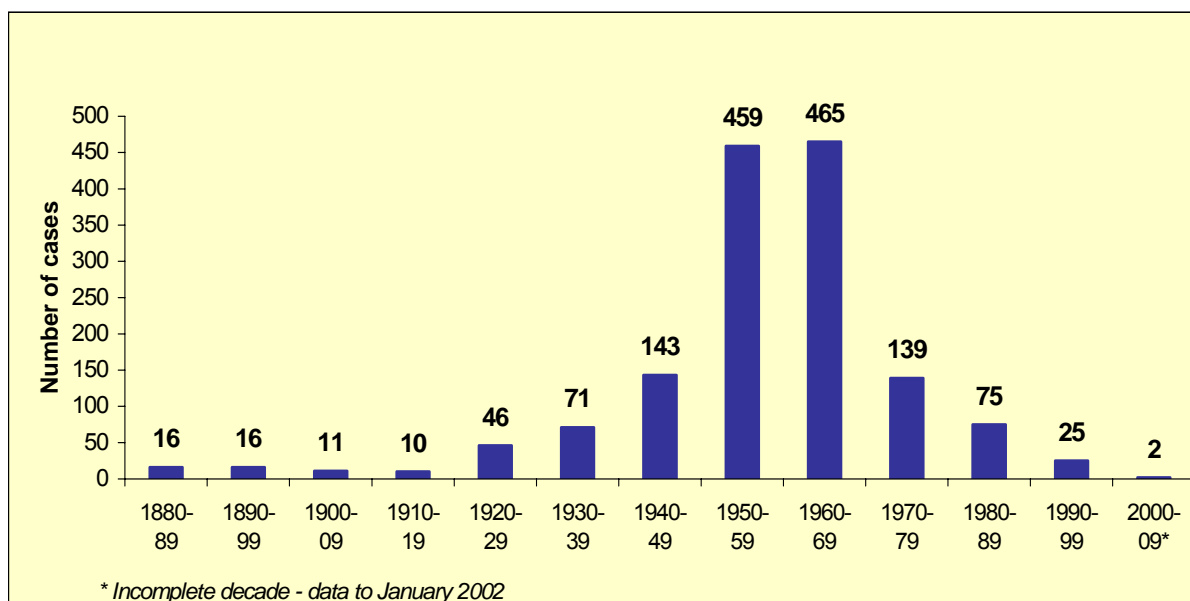
From 1882 to 31 January 2002 there have been 1478 cases of leprosy notified in the NT. Of the total, 1348 (91%) have been Indigenous. The case detection rate for the total population has reduced from 19 per 100,000 per year during the period 1970-74 to 0.97 per 100,000 per year during the period 1995-99 (Figure 1), a decrease of 95%. Over the same interval the rates for Indigenous people have fallen from 56 per 100,000 to 3 per 100,000.

Figure 1. Mean annual case detection rates for leprosy in the NT by 5-year period, 1970-2002



Leprosy is now a rare diagnosis in the NT (Figure 2) and 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



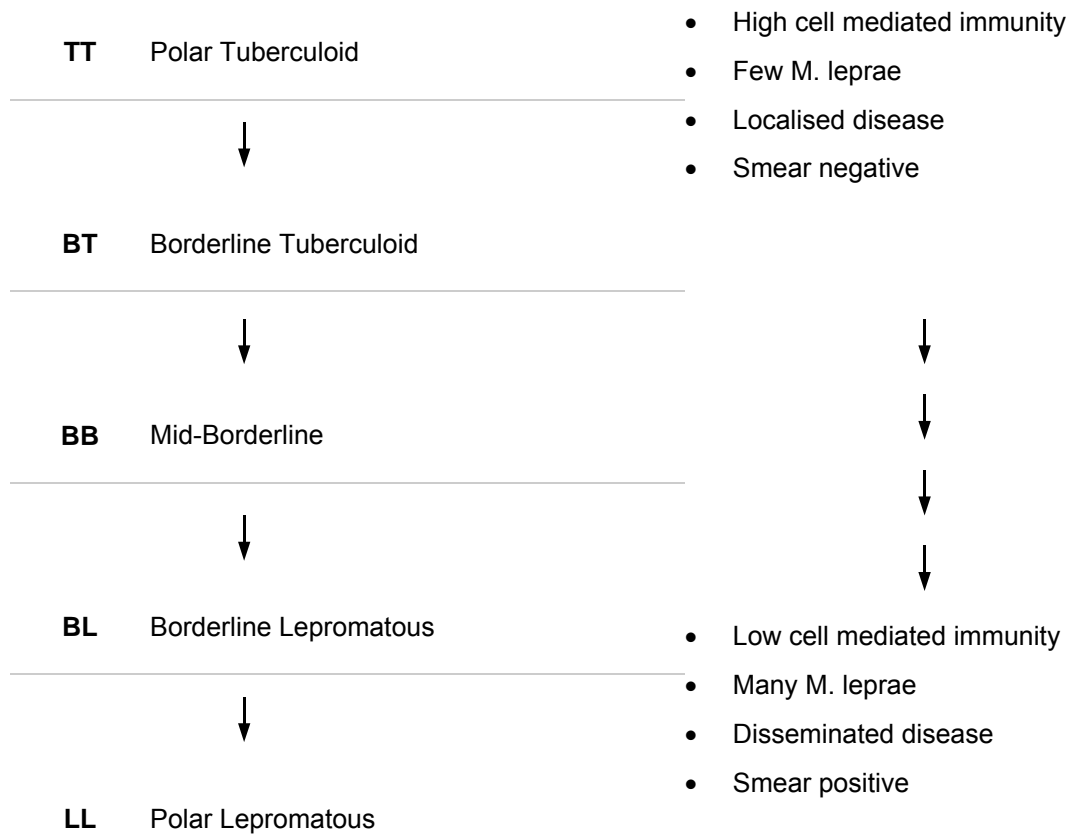
1.2 Classification

Mycobacterium leprae primarily attacks the skin, mucous membranes of the nose, and peripheral nerves. There is a continuous spectrum of disease between the two 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.

1.2.1 The Ridley-Jopling system

In the Ridley and Jopling system, there is a progression from the mildest to the more disseminated form of disease (Figure 3).

Figure 3. Ridley-Jopling classification of leprosy



TT has been the commonest type in the past, making up more than a third of the cases in the NT. These cases have a well developed cell mediated immunity and a very low bacillary load (paucibacillary or PB). There are single or few skin lesions, which are hypopigmented coppery patches, with a well defined, but irregular, and often slightly raised border. The lesions are non-sweating, have decreased hair, and decreased sensation. Peripheral nerve damage usually only occurs in one or two nerves and is asymmetrical, but the damage is severe, with accompanying swelling. Diagnosis depends on clinical examination and biopsy, as smears are usually negative.

LL is less common, but is a more serious and disabling disease. There is loss of leprosy-specific cell mediated immunity, with no check on multiplication and spread of bacilli. There is therefore wide dissemination and a very high bacillary load (multibacillary or MB). The nasal mucosa is involved, rendering the patient highly infectious. The skin lesions are extensive, presenting as erythematous nodules or macules, which 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. The forehead and earlobes become thickened, and the eyebrows become thin, particularly laterally, and are eventually lost (madarosis). There is infiltration of the mucous membranes of the nose and mouth, with atrophic rhinitis. The nasal septum can also be destroyed. Other organs such as the liver, spleen, eyes and testes can be involved. Some patients have gynaecomastia. Amyloidosis is a common problem with late renal complications. Reactional episodes are also common. There is involvement of numerous peripheral nerves which is usually symmetrical, but often not as severe as in tuberculoid leprosy.

BB, BT, and BL lie in the middle of the spectrum. When there are few skin and peripheral nerve lesions the classification is borderline-tuberculoid (BT) leprosy. When there are many skin and peripheral nerve lesions it is classified as borderline-lepromatous leprosy (BL).

Indeterminate leprosy (I) is an early form of the disease which is manifested by a single or few skin patches which are small, flat, hypopigmented or coppery, and with an irregular border. It occurs mainly in children. The majority of these cases will heal spontaneously. Of the remainder, some will persist in the indeterminate form indefinitely, but most will develop into one of the other forms.

1.2.2 WHO classification

The WHO system has classified cases into three MDT treatment categories since 1997 (Table 1). It has been relying increasingly in recent years on the number of skin lesions since some programs have poor quality smear microscopy services. False-negative smears have been a common reason for misclassification of MB cases as PB, with subsequent relapse after PB-MDT.

Table 1. WHO classification of leprosy (WHO expert committee on leprosy, 1997)

	Single lesion PB	PB	MB
<i>Number of skin lesions</i>	1	2 to 5	6 or more
	AND	AND	OR
<i>Skin smears</i>	Negative at all sites	Negative at all sites	Positive at any site
<i>Ridley-Jopling Correlation</i>	I, TT, some BT	TT, most BT	Some BT, BB, BL, LL

1.2.3 Classification in the NT

In the NT an attempt is made to classify all patients by both the Ridley-Jopling classification (for prognosis) and the WHO classification (for reporting). However, the criteria for assigning a patient to treatment in the NT is based on the WHO system prior to 1997 with 2 categories, PB and MB (Table 2). Evidence supporting the long-term efficacy of new treatment regimens for single-lesion and MB leprosy is considered incomplete at this point in time. Results of skin smears are an important part of the classification process. Where there is doubt about the classification based on skin lesions and skin smears, skin histopathology may be considered in the decision.

Table 2. Classification of leprosy for treatment in the NT

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

1.3 Diagnosis

1.3.1 Case definition

The National Notifiable Diseases Surveillance System (NNDSS) definition for a confirmed case of leprosy is followed in the NT (Table 3). A confirmed case requires definitive laboratory criteria and one or more supportive clinical symptoms and signs. Only confirmed cases are reported nationally.

Table 3. NNDSS case definition for leprosy, 2002

<p>Laboratory evidence – at least one of:</p> <ol style="list-style-type: none"> 1. Demonstration of characteristic acid fast bacilli in split skin smears and/or biopsies prepared from the ear lobe or other relevant sites; OR 2. Histological report from skin or nerve biopsy compatible with leprosy read by a laboratory experienced in leprosy diagnosis. <p style="text-align: center;">AND</p> <p>Clinical evidence – at least one of:</p> <ol style="list-style-type: none"> 1. Compatible nerve conduction studies; OR 2. Peripheral nerve enlargement; OR 3. Loss of neurological function not attributable to trauma or other disease process; OR 4. Hypopigmented or reddish skin lesions with definite loss of sensation.
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Regarding international reporting of Australia's leprosy cases to WHO, a different WHO working definition is used, based on the **three “cardinal signs of leprosy”**. In this context, a case of leprosy is defined as “a person showing one or more of the following features, and who has yet to complete a full course of treatment:

Cardinal signs of leprosy

1. hypo-pigmented or reddish skin lesions with definite loss of sensation
2. OR involvement of the peripheral nerves, as demonstrated by definite thickening with loss of sensation
3. OR Skin smear positive for acid-fast bacilli.

1.3.2 Clinical assessment

The main components of the clinical assessment are the history, skin examination, nerve palpation, nerve function assessment (VMT-ST), and eye examination. Use the leprosy examination forms for skin (Appendix 2) at the time of diagnosis and annually, and for nerves, NFI, and eyes (Appendix 3) monthly while on treatment and at routine follow up after treatment.

History

In the history, enquire specifically about the presence and duration of lesions, nerve pain, numbness and tingling, weakness, ulcers and injuries, eye pain, and worsening vision. Ascertain previous possible exposure to leprosy.

Skin

The entire skin surface should be examined carefully for lesions which can include macules, papules, plaques, nodules, urticaria-like lesions and smooth infiltrations. 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. Natural sunlight is the best light for detecting subtle changes, but ensure privacy and patient comfort. Same-sex examiners or the presence of a friend 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 it's presence (Table 4). Digital photography of skin lesions at the time of diagnosis and on completion of treatment are recommended. Consent should be obtained from the patient.

Nerves

The most commonly affected nerves are: ulnar, median, radial cutaneous, common peroneal (lateral popliteal) and posterior tibial nerves, the sural nerve, the fifth and seventh cranial nerves, and the greater auricular. 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 easily felt. Learn the size of normal nerves by practising palpation on yourself and friends (Table 5). Examine the nerve on both sides simultaneously to help differentiate whether one is abnormal. Use 3 fingers to roll the nerve *gently* against the bone - nerves may be very tender if inflamed.

Table 4. Method of testing loss of sensation in a patch

Environment	Privacy, relaxed patient, one 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	<ul style="list-style-type: none"> ▪ 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

Table 5. 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 one 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	2cm down and 2cm behind the point of the inner ankle bone (medial malleolus)

Nerve function assessment

This is discussed in section 2.2 on page 24.

Eyes

Gerhard Armauer Hansen discovered the leprosy bacillus and claimed in 1873, “there is no disease which so frequently gives rise to disorders of the eye, as leprosy does”. Whether or not this remains true today, it underscores the importance of examining for the common ocular manifestations of leprosy in a suspected case (Table 6).

Table 6. Common ocular manifestations of leprosy

Complication	Description	Mechanism	Class.	Signs/Symptoms
Madarosis	Loss of eyebrows & lashes	Bacillary infiltration/destruction of follicles	MB	
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 (See p. 44)
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) (See p. 44)
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 & 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

1.3.3 Skin smears

Indications

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

Preferred sites

1. Both ear lobes
 2. Suspicious skin patches – 2 smears - 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
- (Sites 1 and 2 are minimum requirements)

Procedure

1. Wash microscope slide in water and dry with methylated spirits.
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 1-2 mm deep with a no. 15 scalpel blade.
7. Scrape one side of the incision with the slanted edge of the scalpel blade.
8. Tissue obtained should be spread on a small area of the slide in a central circle.
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 cardboard holder.
11. Send to Royal Darwin Hospital Microbiology Laboratory.
12. A smear from different sites in the same patient is useful for diagnosis.

Nasal mucous membrane smears can also be taken, using a sterile cotton wool bud, and wiping firmly in the nasal passage. The smear is then prepared in the same way as for skin smears as outlined above from points 8 to 11. The results of slit skin smears are reported as the number of AFB seen in the microscope's oil immersion or high-power fields (hpf), and this is represented by the logarithmic Bacterial Index (BI) (Table 7).

The SFG reading (Solid-Fragment-Granule) records 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. The Morphological index (MI) is the percentage of solid bacilli seen. The MI falls rapidly to zero after MDT is commenced indicating a bactericidal effect, but a high BI may take years to reach zero since it relies on gradual clearance of debris. The mean BI reduction with successful treatment is around 0.75 BI units per year.

Table 7. Bacterial index definitions

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

1.3.4 Biopsies

Biopsies are used in combination with clinical signs to diagnose and classify leprosy cases. Biopsies can be taken from a number of sites including the earlobe, forehead, skin patches, and peripheral nerves in some circumstances.

The method for skin biopsies is:

1. Clean 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 one centimetre long and the full skin thickness (about 5mm deep).
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 fungal culture.
5. Send all samples to Royal Darwin Hospital Microbiology Laboratory.

1.3.5 Differential diagnosis

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 miconazole for other fungal infections should be commenced. The patient can be reviewed after 2 months of therapy to assess the response, and the need for further investigation.

1.4 Treatment

Multi-drug therapy (MDT) of diagnosed cases is the key to achieving cure in the individual and breaking the cycle of transmission. Recommended regimens for treatment have been based on those of the WHO Study Group on the Chemotherapy of Leprosy in 1994. If a patient has a positive skin smear, regardless of clinical classification, or if the classification is in doubt, treatment should be MDT for multibacillary disease.

1.4.1 Regimens

Table 8. First line MDT regimen with adult doses

	PB	MB
<i>Duration</i>	6 months	24 months
<i>Dapsone</i>	100mg daily self-administered	100mg daily self-administered
<i>Rifampicin</i>	600mg monthly# DOT*	600mg monthly# DOT*
<i>Clofazimine</i>	-	50mg daily self-administered + 300mg 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)

Patients diagnosed with both leprosy and TB require both full TB and leprosy treatment. The rifampicin should be given in the dose required to treat TB. Second-line regimens for leprosy which contain Minocycline or Ofloxacin may be necessary if there are severe side-effects caused by a drug in the first-line regimens. Information about all drugs used is provided in Appendix 4.

The WHO recommends fixed doses for children in age categories 0-9 years and 10-14 years (Table 9).

In the NT however, doses for children should be calculated based on body weight to minimise adverse drug reactions in the youngest and smallest children in each of these categories (Appendix 4). Since Clofazimine is available only in a 50mg capsule formulation, smaller calculated daily doses may be given for example as 50mg on alternate days, or 50mg twice a week.

Table 9. WHO recommended doses for children

	0-9 years	10-14 years
<i>Dapsone daily</i>	25mg	50mg
<i>Rifampicin monthly</i>	300mg	450mg
<i>Clofazimine daily (MB)</i>	50mg twice a week	50mg alternate days
<i>Clofazimine monthly (MB)</i>	100mg	150mg

1.4.2 Pre-treatment investigations

1. FBE, UEC, LFT, HIV ab.
2. G6PD.
3. Mantoux and CXR to exclude co-existent TB.

1.4.3 Case Holding

Medication should initially be dispensed weekly until full concordance with and understanding of the regimen is assured, and then a 4-weekly cycle of directly observed treatment and examination is established. Failure to attend a single 4-weekly directly observed treatment 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 intercurrent 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. 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 – all on a 4-weekly basis. Review should occur 3-monthly by a local medical officer, and 6-monthly by TB/leprosy unit staff. Adherence should be documented on the leprosy treatment card (see Appendix 5).

Completed treatment for a cure is defined as:

- MB leprosy - 24 months of doses (or 24 four-weekly cycles) within 36 months.
- PB leprosy - 6 months of doses (or 6 four-weekly cycles) within 9 months.

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

1.5 Prevention

1.5.1 Early case detection and MDT

Opportunistic examination by primary health care personnel in the context of a high index of suspicion for leprosy is important. The focus should be on people in the “high risk” groups, and those who have lived for long periods in areas where leprosy is endemic. There are some health staff who have much experience with leprosy, but others need to be trained in detecting the early signs and symptoms. Cases, and people who are suspected of having leprosy should be reviewed by the most experienced local staff who will in turn liaise with the TB/Leprosy Unit.

Contact tracing

- 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.
- Results should be documented in the local records, and the central leprosy data base.
- New cases should be referred to the TB/leprosy Unit.
- Contacts of MB cases need to be reviewed annually with a clinical examination for 6 years (Table 10). One study has shown that 95% of secondary cases occurred within 6 years of the diagnosis of the primary cases.
- Contacts of PB cases are at lower risk of developing disease. They should be examined once to exclude disease, provide advice about symptoms and signs, and search for a source of infection for the diagnosed PB case.

Table 10. Follow up of contacts of leprosy cases

Classification of the index	PB	MB
Years of annual CDC follow up after index diagnosis	0 [^]	6
Type of follow up	Skin and nerve examination*	Skin and nerve examination*

[^]Discharge if initial examination is negative
^{*}Do VMT-ST or Skin smear only if indicated by skin and nerve examination

Screening of other high risk groups

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, which includes,

- TB school screening of ten year olds (which targets migrant and Aboriginal children);
- review of asylum seekers and detained fishermen;
- review of patients on Immigration Department TB Undertakings (TBUs); and
- community TB screening programs.

Health education

This aims to provide health staff with the knowledge and ability to diagnose patients with leprosy, provide ongoing care and management of patients, and to form a working relationship with the TB/Leprosy Unit. This should be achieved through,

- the Health Worker curriculum;
- in the orientation package for health and allied health staff; and
- with ongoing education sessions for health staff in the NT.

There needs to be awareness of leprosy amongst people "at risk" for disease. This includes the Aboriginal and migrant populations, and specifically family and household contacts of active cases of leprosy.

1.5.2 Improving the environment

Leprosy has long been considered a 'disease of poverty' but there is little evidence confirming the precise mechanisms through which poverty exerts its effects. In Malawi, persons living in the worst standard of housing had double the risk of leprosy compared with those living in the best category of dwelling. Other diseases with respiratory transmission such as TB and meningococcal disease are associated with overcrowding, and this factor probably also increases the risk of acquiring leprosy. Advocacy to improve housing quality, ventilation, water supply, nutrition, and to alleviate overcrowding, particularly in pockets of relatively high incidence, is considered important for leprosy control.

1.5.3 BCG

BCG at birth

BCG 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 30% and 80%, and it is a recommended leprosy (and TB) control strategy in the Northern Territory.

The current policy in the NT (1 June 2001) is that BCG is recommended at birth for:

1. All indigenous neonates
2. Non-indigenous neonates who will live in indigenous communities
3. Non-indigenous neonates born to mothers who have been treated for leprosy

BCG in leprosy contacts

Studies in Venezuela, Myanmar, and Malawi have shown that the protective effect of BCG against leprosy increases from around 50% to over 70% with repeated vaccination. In Brazil, Cuba and Venezuela, contacts of known leprosy cases are repeatedly vaccinated with BCG as part of the national leprosy control strategies.

However, the WHO currently recommends BCG vaccination *only* at birth and does not endorse the use of booster vaccinations. Repeating BCG vaccination for contacts of leprosy cases would be complicated by the need to ascertain HIV sero-status prior to vaccination to avoid the risk of disseminated BCG disease. Latent TB infection would also need to be excluded, since tuberculin reactions of more than 5mm are a contraindication for BCG in Australia. Therefore, BCG is not routinely recommended in the NT for contacts of leprosy patients.

1.5.4 Preventive Treatment

Medication can be given before the onset of disease to persons exposed to *Mycobacterium leprae* to prevent disease. A meta-analysis of 14 older trials demonstrated that preventive treatment (using dapsone in 13 and rifampicin in one) provided 60% protection against leprosy. However, the Dapsone regimens are not practical since they take years to complete. In India, a randomised placebo-controlled trial is currently underway to examine the effect of a single dose of rifampicin (10mg/kg) in household contacts, with 5 years of follow up. If the efficacy, safety, and long-term effect of this regimen proves similar or superior to long courses of dapsone, it should be considered for implementation among leprosy contacts in Australia.

Unlike the tuberculin test for latent TB infection, there is no single method with sufficient sensitivity, specificity or convenience currently available to diagnose subclinical leprosy infection. Therefore if preventive treatment is implemented in the future, it should be given to contacts of leprosy patients who are epidemiologically likely to have been infected, and who have a relatively high risk of developing disease. 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 or PB), and the age of the contact.

In Malawi, household contact with a recent or past **MB** case was associated with a 5-fold increased risk compared with the general population. Forty-eight percent of these contacts slept in the same room, and their risk was 8-fold that of the non-contact individuals. However, children aged between 5 and 9 years who shared a bedroom with an MB case had 37 times the risk compared with children of the same age without contact with a case. For household and bedroom contacts of **PB** cases, the risk was twice as high as the non-contact group. Thus household contacts of MB cases, particularly children and those who have shared a bedroom with the index case will be the highest priority recipients of preventive treatment.

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. This percentage is likely to be much higher where leprosy is now rare, as in the NT. Thus, if a single-dose regimen for household contacts is eventually proven to be efficacious, its use here will be a major boost to the prospects of eradication of indigenous (not imported) leprosy.

Part 2. Nerve function impairment

2.1 Classification of Nerve Function Impairment

NFI is a clinically detectable loss of motor, sensory, or autonomic peripheral nerve function. *Mycobacterium leprae* is the only bacterial agent known to specifically infect peripheral nerves. It is the resulting NFI and associated deformities and disability which has made leprosy such a feared disease. The main processes associated with NFI include silent neuropathy, and Type 1 and Type 2 reactions.

2.1.1 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 nerve) 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 80% of all NFI occurs silently, 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.

2.1.2 Reactions

Neuritis and NFI may also occur suddenly and floridly in association with leprosy reactions of which there are two major types (Table 11).

Type 1 (reversal, or upgrading) reaction is a delayed-type hypersensitivity response to *M. leprae* antigens occurring in BL, BB or BT cases. Usually there is an associated change in Ridley-Jopling classification towards the tuberculoid end of the spectrum, eg. BL to BT as cell-mediated immunity improves. Redness and swelling in pre-existing skin lesions occurs, and lesions which have not been visible may appear. Fever, malaise, peripheral oedema, and symptomatic neuritis are additional features if the reaction is severe.

Type 2 (Erythema Nodosum Leprosum or ENL) reaction is an immune complex disorder due to an imbalance of the humoral immune system. It occurs in approximately 10% of LL cases and less commonly in BL cases. Large numbers of *M. leprae* in the body excite an ineffectual antibody response in the context of weak or absent *M. leprae*-specific cell-mediated immunity. There is a sudden appearance of new, tender, subcutaneous nodules on the dorsum of the hands or the extensor aspects of the forearms and thighs. They appear in crops, each of which last about 3 days, and the whole episode usually lasts 2 weeks. High fever peaking in the evenings can be accompanied by inflammation in the eye (iridocyclitis), joints, testes, and nerves. Note that Type 1 and Type 2 reactions may coexist in a BL case. 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 11. Comparison of the features of Type 1 and Type 2 reactions

	Type 1	Type 2
<i>Classification</i>	BT, BB, BL	LL (occasionally BL, BB)
<i>Immunology</i>	Changing CMI	Immune-complex deposition, elevated TNF-alpha levels, dysfunctional CMI
<i>Classification change</i>	Upgrading (usually) toward TT	No change
<i>Timing</i>	First months of MDT	May be years after treatment
<i>Recurrent</i>	Usually not	Often
<i>Duration</i>	Several months	2 weeks
<i>Sites of inflammation</i>	Nerves, skin lesions	Skin nodules, iris, testes, joints, nerves, soles, lymph nodes

Table 12. Comparison of the features of New leprosy nodules and Type 2 reactions

	New leprosy nodules	Type 2 reaction
<i>Onset</i>	Gradual	Sudden
<i>Number</i>	One at a time	Nodules appear in crops
<i>Tenderness</i>	-	+
<i>Bacterial Index</i>	High in the nodule	High or low
<i>SFG reading*</i>	Often solids	Mainly granules
<i>Resolution</i>	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.

The differential diagnosis of the skin lesions of Type 1 or Type 2 reactions is active leprosy (Table 12). 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 p 32).

2.1.3 Disability grading

NFI and its secondary consequences are described in a 'disability grading' (0, 1, or 2) for the purposes of reporting to WHO, and for monitoring program objectives. 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 a Hand-Foot-Eye (HFE) 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.

Table 13. WHO grading of leprosy related disability¹

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**	Eye problems due to leprosy but vision not severely affected as a result (visual acuity 6/60 or better; can count fingers at 6 metres)
2	Visible deformity or damage*** present	Severe visual impairment (visual acuity worse than 6/60; unable to count fingers at 6 metres) 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 HFE 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 3 and 6), and together with the indications for Prednisolone (Section 2.3.1), decisions about the requirement for Prednisolone therapy can be made.

2.2 Detection of neuropathy

2.2.1 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 carried out by one specialist physician in Darwin, and in relation to leprosy, should be ordered only in consultation with the TB/leprosy Unit.

¹WHO Expert Committee on Leprosy, Seventh Report. Geneva 1998.

The indications are:

1. To assist (where necessary) in the diagnosis of suspected leprosy cases.
2. As soon as possible after diagnosis to establish a baseline assessment of the extent and severity of nerve damage.
3. Ideally at yearly intervals while taking MDT.
4. When new - symptoms of neuritis, or findings of NFI - appear after MDT completion.

2.2.2 Voluntary Motor 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 p 30). With practice (both health worker and the patient), this should take around 10 minutes to complete thoroughly. See Appendix 6 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 ball-point 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.

2.3 Treatment of Nerve Function Impairment

Many studies have reported beneficial responses of NFI in reactions and silent neuropathy with Prednisolone but the results vary. Taken together, improvement occurs in 60-80% of those studied. Most of the improvement occurs in the first 3 months of a course of Prednisolone, but further gains can be made at a slower rate for several more months. Acute primary NFI (first attack and less than 6 months in duration) has a better prognosis with treatment than chronic or recurrent forms, but improvement may still be seen in up to 50% of the latter episodes. The corollaries of these figures are the observations that up to a third of those treated have no benefit, and that some who do not receive treatment spontaneously recover function.

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 ischemia).
2. Suppression of *M. leprae*-specific T-cell inflammation. In Type 1 reactions, serial skin biopsies have shown a slow decrease in Th1 profile 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.

2.3.1 Indications for Prednisolone

Table 14. Indications for Prednisolone

1	Recent NFI at diagnosis	At the time of diagnosis of leprosy, NFI is detected which 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, which had not been recorded on the previous assessment. This includes: <ul style="list-style-type: none"> • New loss of sensation in 2 or more points on the sensory chart • 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 which is being inadequately managed in terms of appropriate footwear and self-care. However, coexisting new NFI should be excluded.

2.3.2 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. WHO recommends a standardised 12-week course for outpatient use for Type 1 reactions where therapy is generally initiated by experienced leprosy field staff who are not doctors or nurses (Prednisolone 40mg, 30mg, 20mg, 15mg, 10mg, and 5mg daily, in this order, each dose for 2 weeks). Some have expressed concern that the doses may be insufficient to be maximally beneficial, and the relatively short duration could allow recurrences of NFI.

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

1. The starting dose should be about 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 care-givers.

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 local warmth and protection around the nerve with a cotton wool bandage.
11. 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. If ENL is mild and not accompanied by neuritis or new NFI, bed rest and Aspirin are recommended. Moderate and severe attacks of ENL or ENL with neuritis should be treated with Prednisolone. The tendency for ENL to recur means the duration of treatment should be as short as possible to avoid steroid-dependence (eg. 2 to 8 weeks). Recurrent ENL requires an increase of the daily MDT Clofazimine dose to 300mg (for not 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 reduces TNF-alpha levels and increases CD8 T cell numbers in ENL and is rapidly effective in severe and recurrent forms. It's use allows a reduction in Prednisolone requirements but it is not approved for use in Australia due to it's teratogenicity.
12. A regimen which 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 15).

Table 15. Example of 9 month tapering course of Prednisolone for Type 1 reaction in BL leprosy

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

* OD, Once daily

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

2.3.3 Precautions with Prednisolone use

Contraindications to Prednisolone for NFI

1. Nerve abscess (requires surgery)
2. Untreated infections (TB, strongyloidiasis, amoebiasis, osteomyelitis, infected ulcers)

Screening prior to the commencement of Prednisolone

1. Mantoux test and chest x-ray for latent and active TB.
2. Stool microscopy and culture (one specimen), and serology for *Strongyloides stercoralis*. If serology and stool negative, no further action. If serology and/or stool positive, give single dose Ivermectin 200mcg/kg, and recheck serology for fall in titre and stool for clearance of parasite.
3. Blood glucose, Electrolytes, Urea & Creatinine, FBE, LFT, HIV antibody.
4. Visual acuities 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.

Precautions during prolonged treatment

1. Avoid live vaccines during and for 3 months after therapy
2. Increase dose during acute stress (intercurrent illness, surgery), eg. double maintenance dose
3. High calcium intake (1200mg/day); restrict sodium intake; add potassium supplements if necessary

2.4 Prevention of NFI, deformity and handicap

2.4.1 Early case detection of leprosy

Arguably the most important indicator in assessing the quality of a leprosy control program is the proportion of newly diagnosed cases who have Grade 2 disability. Programs with effective education strategies to raise the awareness of leprosy among health workers and at-risk sections of the community will have a new case disability Grade 2 proportions of around 5%, while programs with late case detection may have proportions in excess of 50%.

It is known that NFI existing 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) compared with those who first develop impairment after treatment commences. Furthermore, patients who have longstanding NFI at the time of diagnosis (NFI for longer than 6 months) have been shown to have a 15-fold higher incidence of **further episodes** of acute NFI than those who do not.

Early case detection of leprosy and treatment with MDT rapidly stops multiplication of *M. leprae*. It is the most important activity to prevent NFI. It has been estimated that early detection of new leprosy could prevent disabilities in 30% of all patients whereas prevention of disability activities during and after MDT will prevent disabilities in around 10% of all cases.

2.4.2 Early detection and treatment of NFI

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 (VMT-ST).

2.4.3 Self-care of established impairments

Impairments such as anaesthesia, weakness, and loss of sweating may be too old when discovered to be reversible with Prednisolone, or in 20 to 30% of acute cases, may simply be refractory to this therapy. Self-care routines when supported by access to appropriate medical, surgical and rehabilitation services can prevent the secondary consequences of these impairments (Table 16).

The problems are ulceration (due to loss of protective sensation) and callus formation (due to decrease in sweating) which promotes fissuring and ulceration. Ulceration leads to deep infection and osteomyelitis if not managed early, and loss of digits or limbs can result. Similarly, joint contractures can occur when muscles are paralysed, and active and passive

exercises should be taught to prevent this. Eyes which are vulnerable due to corneal sensory loss (Trigeminal neuropathy) or lagophthalmos (Facial neuropathy) should be inspected in a mirror daily for redness. Redness or visual deterioration should be assessed promptly by health staff. Excellent illustrated resources are available which itemise in more detail these prevention of disability activities for the various impairments. Dr. Grace Warren's excellent manual, 'The care of neuropathic limbs' is highly recommended and is available in the health libraries in Darwin and Alice Springs. Contact the TB/leprosy unit for details.

Table 16. Daily self-care routine for anaesthetic limbs

1. **Look** - for reddened inflamed skin (hot-spots), blisters or ulceration of anaesthetic areas. Inspect footwear for foreign bodies with the potential to damage feet, eg. pebbles in shoe, nail in sole.
2. **Soak** – feet and hands if there is sensory loss, dryness, fissuring, callosity, or ulcer in water for 10-15 minutes daily.
3. **Pare** – after soaking, abrade areas of built up callus, or hardened skin around an ulcer with a scotch-brite pad or pumice stone, until normal tissue is reached. [Health staff can assist this process periodically using a scalpel blade]
4. **Oil** - after soaking and paring to keep the skin supple and retain moisture. Eucerin, Vitamin A, Lanolin or vegetable oil are suitable types of emollient.
5. **Rest** - Where hot-spots or blisters have occurred, avoid pressure to the affected part, eg. rest with leg elevated or avoid another long walk until healed. Health staff may assist healing where ulceration has occurred by providing a sling, crutches, or a Bohler walking iron with plaster of paris cast.

Part 3. After MDT completion

3.1 Follow up of leprosy cases

The rationale for routine follow up after completion of a course of treatment is:

1. the early detection of relapse of disease; and
2. the early detection of new NFI.

The recommended duration of follow up by CDC after leprosy cases have been released from anti-bacterial treatment will depend on the type of treatment received. An MDT regimen which used rifampicin for at least a 6-month (PB) or 24-month (MB) period, whether in daily or monthly administration, in combination with Dapsone (and Clofazimine in MB) is considered a regimen for which there is good WHO data confirming a low risk of relapse. Recent cases who received these regimens should be followed according to Part A of Table 17. The highest incidence of relapse has been reported among MB cases who had a high pre-treatment BI (≥ 4). Cases with less heavy bacterial loads ($BI < 4$) before treatment have a lower rate of relapse after MDT completion and long term routine follow up would not be an efficient use of resources.

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 the presence or absence of NFI at the time of diagnosis of leprosy. A recent study quantified the risk of new NFI for 2510 patients followed for 2 years after MDT commenced:

- PB classification and no NFI at diagnosis – 1%
- PB classification and NFI at diagnosis – 16%
- MB classification and no NFI at diagnosis – 16%
- MB classification and NFI at diagnosis – 65%

Thus PB cases with NFI at diagnosis require VMT-ST monitoring beyond the 6 month period of their treatment whereas PB cases without NFI at diagnosis do not. MB cases will benefit from VMT-ST monitoring throughout the 24 month period of their treatment.

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

Part B of Table 17 should be used for cases who were treated initially with Dapsone, and later with Rifampicin and/or Clofazimine, but in whom the total duration of combined treatment was less than 6 months (PB) or 24 months (MB). Patients who received Dapsone monotherapy alone have a high risk of relapse and Part C of Table 17 applies.

Table 17. Follow up of leprosy cases after treatment completion

A. Treatment with WHO-MDT[^]				
<i>Classification</i>	PB (after 6 months of MDT)		MB (after 24 months of MDT)	
<i>Risk factors</i>	NFI at diagnosis		Bacterial Index	
	No	Yes	0 to 3	4 to 6
<i>CDC follow up after completion of treatment</i>	None	3 monthly until 2 years after MDT started	None	Annually for 5 years after MDT completed
<i>Type of follow up</i>	---	·Clinical*	---	·Clinical* ·Smear# ·Eyes†
B. Treatment with 3 months of daily rifampicin and long term dapsone				
<i>Bacterial index on skin smear at diagnosis</i>	0 to 3		4 to 6	
<i>CDC follow up after completion of treatment</i>	Discharge after a final examination		Annually for 15 years	
<i>Type of follow up</i>	·Clinical* ·Smear (if MB)#		·Clinical* ·Smear# ·Eyes†	
C. Treatment with long term dapsone alone				
<i>Bacterial index on skin smear at diagnosis</i>	0 to 3		4 to 6	
<i>CDC follow up after completion of treatment</i>	Discharge after a final examination		Annually for 30 years	
<i>Type of follow up</i>	·Clinical* ·Smear (if MB)#		·Clinical* ·Smear# ·Eyes†	

[^] Multiple drug regimen where Rifampicin and Dapsone in combination (and Clofazimine in MB leprosy) was given for at least a 6 month (PB) or 24 month (MB) period, regardless of whether Rifampicin was given monthly or daily.

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

† Eyes means annual slit-lamp examination by an Ophthalmologist to detect silent iritis.

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

3.2 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 age a cure is defined by the completion of an MDT regimen within a fixed time period (page 17). Thus 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.

3.2.1 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. To add to the difficulty, a relapse may present as a Type 1 reaction. Although the clinical features described in Table 18 are of some use in differentiating between the two, 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 very helpful. Granulomas in a biopsy do not prove a relapse since 2 years after the start of MDT, they are still present in 40% of cases. A lymphocytic infiltrate can also be present in the absence of viable bacilli, being maintained by antigens of dead bacilli. One study has shown that around half of 25 BT patients presenting with new activity post-MDT had skin biopsies compatible with active (relapsed) leprosy, and half had histopathology consistent with Type 1 reaction. However, the incidence of viable bacilli (on mouse foot-pad testing) was higher in the lesions with a reactional appearance than the non-reactional lesions! Inoculation of mouse-foot pads with skin biopsy homogenates may confirm relapse if *M. leprae* proliferate. However, this process takes several months, and a clinical decision is required for therapy before the results are available.

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 should be classified as PB or MB in the usual way, and re-treated with MDT.

3.2.2 Treated MB cases presenting with new activity

There are almost as many combinations of criteria for MB relapse as there are studies on the relapse of leprosy after MB treatment. It has been acknowledged that MB relapse is easily overdiagnosed if the following points are not considered:

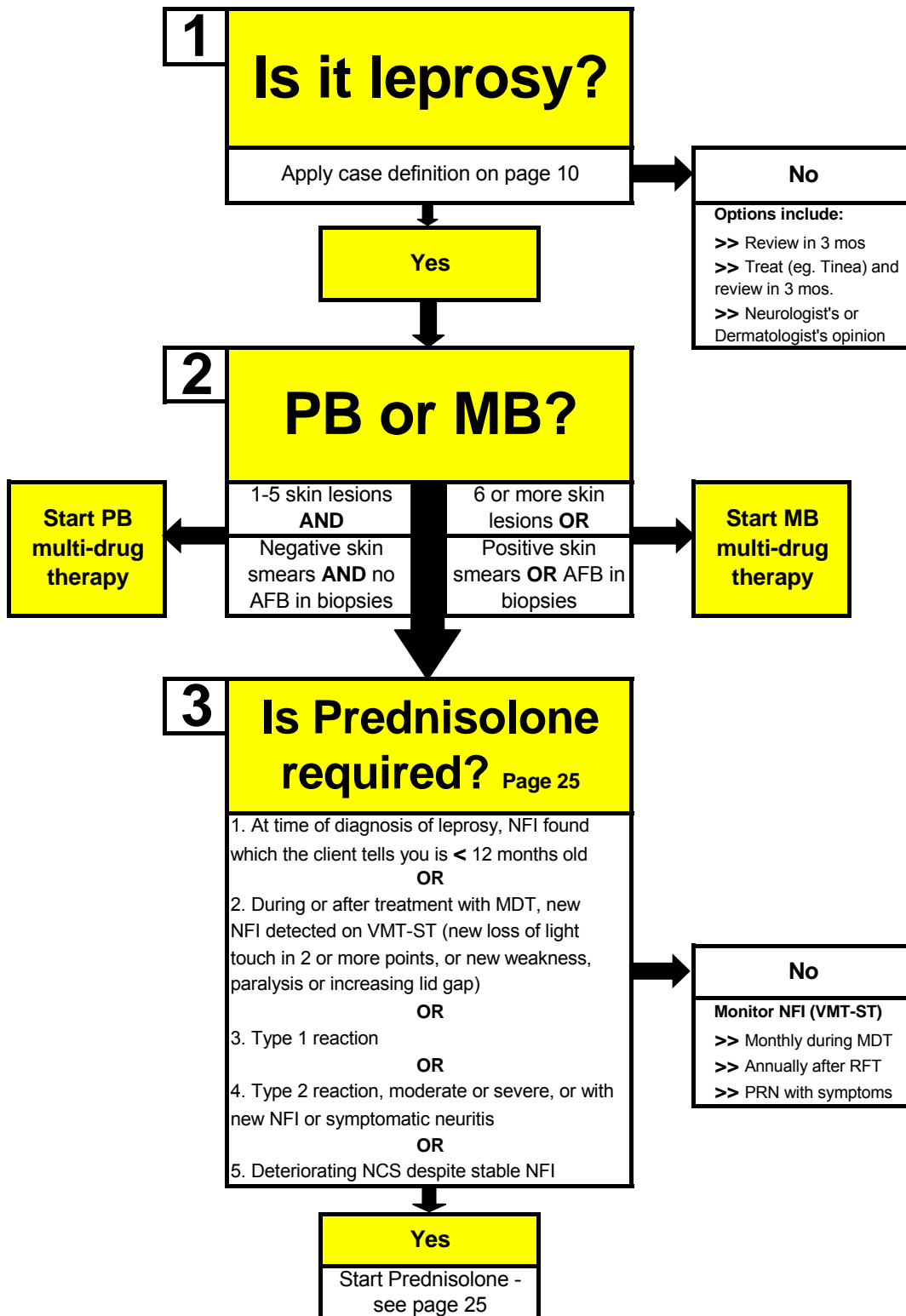
- an increase in BI of 2+ over previously documented BI at that site is required; and
- this increase in BI is confirmed by 2 sets of skin smears 6 months apart.

Table 18. Clinically distinguishing relapse from a late Type 1 reaction

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

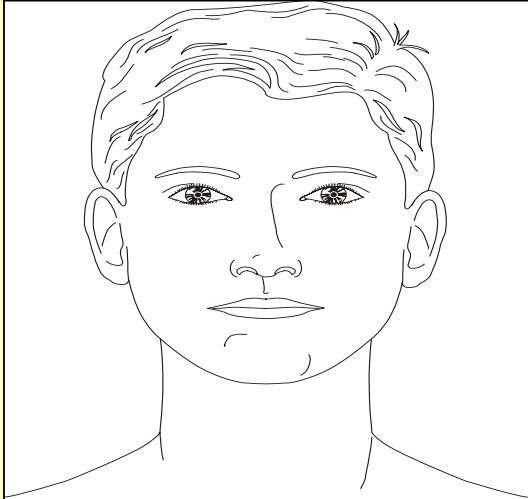
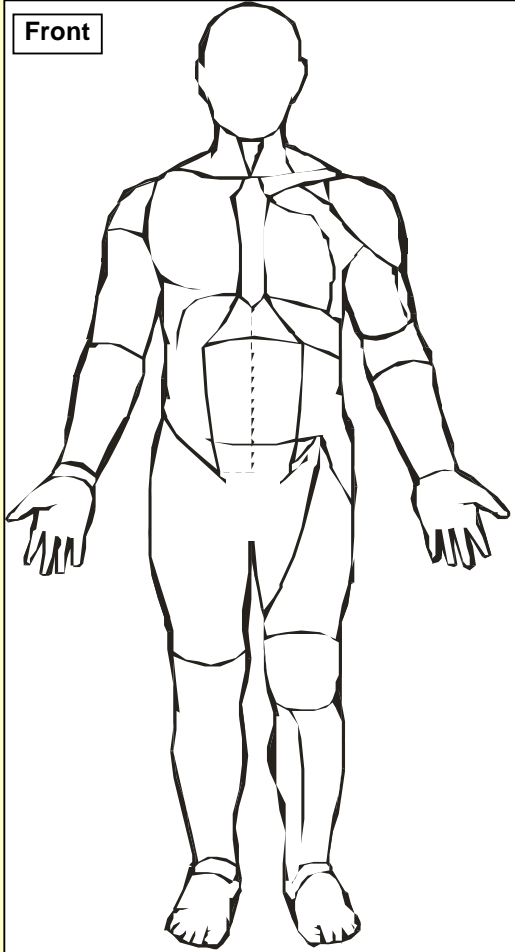
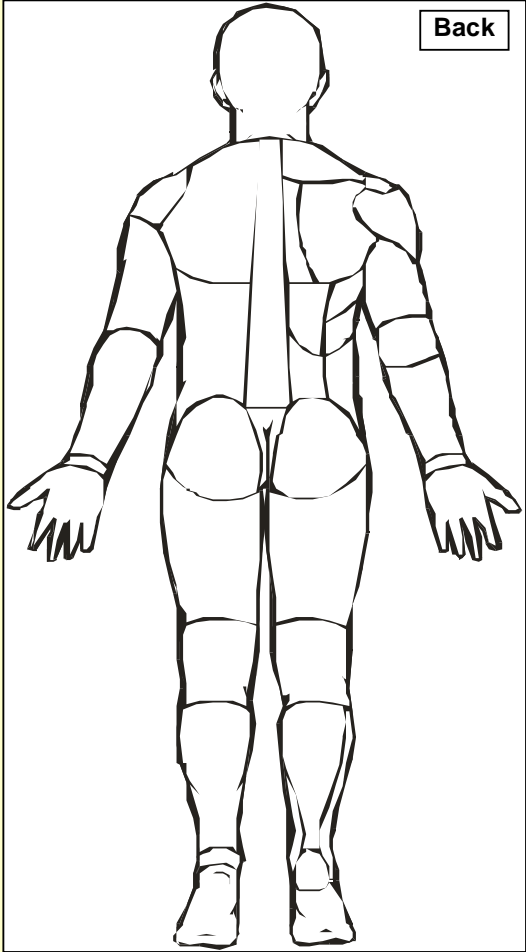
Appendix 1

GENERAL APPROACH TO THE PATIENT WITH SUSPECTED LEPROSY IN THE NT



NFI = Nerve function impairment
 NCS = Nerve conduction studies
 VMT-ST = Voluntary muscle test & sensory test
 MDT = Multi-drug therapy

Appendix 2

LEPROSY EXAMINATION - SKIN		
Surname:	Other name:	
Date:	DOB:	HRN:
Draw and describe all skin lesions suggestive of leprosy below. Include if possible the type of lesion (if macule, nodule, plaque etc), colour, surface (if dry, shiny, sweating, hair, scales), edge (if distinct, raised, pebbled, streaming, satellites), ce		
		
Front	Back	
		

Appendix 3

Leprosy Examination—nerves, nerve function impairment (VMT-ST), eyes							
Surname:		Other name		HRN			
Strength & blink		Sensation					
Blink problems? Light closure lid gap Little finger out Thumb across & up Foot up SWP = Strong/Weak/Paralysed	RIGHT		LEFT		Sensation tested by light skin denting with biro tip at dot Key √ = Feels within 3cm X = Does not feel C = Clawed ☹ = Wound or open crack — = Shortening level		
	Yes	No	Yes	No			
	mm		mm				
	S	W	P	S		W	P
	S	W	P	S		W	P
	S	W	P	S		W	P
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							
		R		L			
		/10		/10			
		/4		/4			
		/4		/6			
Neuritis check			Visual acuity				
Sensation or strength change in the last 6 months	Yes	No		Right	Left		
Nerve pain or tenderness?	Yes	No	Uncorrected	6/	6/		
If answering yes, detail below			Corrected	6/	6/		
Assessor			Date				
Comments							
Surname:		Other name		HRN			
Strength & blink		Sensation					
Blink problems? Light closure lid gap Little finger out Thumb across & up Foot up SWP = Strong/Weak/Paralysed	RIGHT		LEFT		Sensation tested by light skin denting with biro tip at dot Key √ = Feels within 3cm X = Does not feel C = Clawed ☹ = Wound or open crack — = Shortening level		
	Yes	No	Yes	No			
	mm		mm				
	S	W	P	S		W	P
	S	W	P	S		W	P
	S	W	P	S		W	P
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							
		R		L			
		/10		/10			
		/6		/4			
		/4		/6			
Neuritis check			Visual acuity				
Sensation or strength change in the last 6 months	Yes	No		Right	Left		
Nerve pain or tenderness?	Yes	No	Uncorrected	6/	6/		
If answering yes, detail below			Corrected	6/	6/		
Assessor			Date				
Comments							

Appendix 4

Drug information

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 Probenicid, Trimethoprim increase levels Rifampicin reduces levels	<ol style="list-style-type: none"> 1. Haemolysis if G6PD deficient and dose >50mg/day 2. Haemolysis/Methaemoglobinaemia in most subjects at dose of >200mg/day 3. GI irritation, nausea, vomiting, anorexia 4. Fixed drug eruption 5. "Dapsone syndrome" – hypersensitivity rash, fever, jaundice, eosinophilia in first 6 weeks of therapy 6. Exfoliative dermatitis 7. Maculopapular rash 8. Headache 9. Nervousness 10. Insomnia 11. Blurred vision 12. Peripheral neuropathy 13. Psychosis 14. Fever 15. Hepatitis 16. Agranulocytosis (rare) 17. Aplastic anaemia

Clofazimine			
Formulation	Dose	Precautions	Adverse reactions
50mg, 100mg capsules	Children 1mg/kg/day Adults 0.8-1.6 mg/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	<ol style="list-style-type: none"> 1. 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 2. Skin discoloration in breast-fed neonates whose mothers take Clofazimine 3. Dry skin, ichthyosis, pruritis 4. Dry eyes 5. 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 6. Crystal deposition in liver and spleen

Rifampicin			
Formulation	Dose	Precautions	Adverse reactions
150mg, 300mg tablet/ capsule	10mg/kg/day	Monitor LFT in elderly and those with hepatic dysfunction	1. Red discoloration of urine/ tears/contact lenses
100mg/5ml liquid	Usual adult dose 450-600mg/day	Increased doses of oral contraceptives, corticosteroids, anticoagulants and oral hypoglycaemic agents may be required	2. GI irritation 3. Liver enzyme induction/ Hepatitis 4. Dermatitis 5. Fever 6. Collapse/shock 7. Influenza-like syndrome 8. Haemolytic anemia 9. Thrombocytopenia 10. Renal failure

Prednisolone			
Formulation	Dose	Precautions	Adverse reactions
1mg, 5mg, 25mg tablets	0.5-1mg/kg/day initially, reducing gradually	Avoid if untreated viral, bacterial, fungal infections	1. Oedema 2. Weight gain 3. Hypertension 4. Glucose intolerance
5mg/ml liquid	See section 2.3.2 on p22	Monitor weight, BP, electrolytes, glucose Avoid live vaccines Pregnancy – avoid if possible Rifampicin increases metabolism	5. Peptic ulceration 6. Osteoporosis 7. Proximal myopathy 8. Aseptic necrosis femoral head 9. Hypercorticalism (moon face, acne, bruising, striae, truncal obesity, muscle wasting, amenorrhoea and hirsutism in females) 10. Growth retardation in children 11. Exacerbation psoriasis (withdrawal) 12. Adrenal insufficiency (sudden withdrawal) 13. Posterior subcapsular cataracts 14. Glaucoma 15. Insomnia 16. Depression, psychosis 17. Raised intracranial pressure in children 18. Hypercoagulability of blood 19. Delayed tissue healing 20. Activation of latent infections (TB, strongyloidiasis) 21. Increased susceptibility to infections (>20mg/day immunosuppressive) 22. Fetal adrenal developmental impairment, cleft palate

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	<ol style="list-style-type: none"> 1. Photosensitivity 2. Oesophagitis 3. Abnormal osteogenesis 4. Tooth staining 5. Hypoplasia dental enamel 6. Dizziness, vertigo 7. GI irritation 8. Enteritis – coagulase-positive Staphylococci, Clostridium difficile 9. Morbilliform rash 10. Urticaria 11. Fixed drug eruption 12. Cheilosis 13. 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	<ol style="list-style-type: none"> 1. Nausea, diarrhoea, dyspepsia 2. Headache 3. Restlessness 4. Rash, pruritis 5. Dizziness 6. Arthropathy in young animals 7. Crystalluria 8. Seizures (in epilepsy, or in combination with NSAIDs)

Name:		Month		Month		Month		Month		Month		Month		Month		Month		Month			
1	Rx	1	Rx	1	Rx	1	Rx	1	Rx	1	Rx	1	Rx	1	Rx	1	Rx	1	Rx		
2		2		2		2		2		2		2		2		2		2		2	
3		3		3		3		3		3		3		3		3		3		3	
4		4		4		4		4		4		4		4		4		4		4	
5		5		5		5		5		5		5		5		5		5		5	
6		6		6		6		6		6		6		6		6		6		6	
7		7		7		7		7		7		7		7		7		7		7	
8		8		8		8		8		8		8		8		8		8		8	
9		9		9		9		9		9		9		9		9		9		9	
10		10		10		10		10		10		10		10		10		10		10	
11		11		11		11		11		11		11		11		11		11		11	
12		12		12		12		12		12		12		12		12		12		12	
13		13		13		13		13		13		13		13		13		13		13	
14		14		14		14		14		14		14		14		14		14		14	
15		15		15		15		15		15		15		15		15		15		15	
16		16		16		16		16		16		16		16		16		16		16	
17		17		17		17		17		17		17		17		17		17		17	
18		18		18		18		18		18		18		18		18		18		18	
19		19		19		19		19		19		19		19		19		19		19	
20		20		20		20		20		20		20		20		20		20		20	
21		21		21		21		21		21		21		21		21		21		21	
22		22		22		22		22		22		22		22		22		22		22	
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24		24		24		24		24		24		24		24		24		24		24	
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26		26		26		26		26		26		26		26		26		26		26	
27		27		27		27		27		27		27		27		27		27		27	
28		28		28		28		28		28		28		28		28		28		28	
29		29		29		29		29		29		29		29		29		29		29	
30		30		30		30		30		30		30		30		30		30		30	
31		31		31		31		31		31		31		31		31		31		31	
End of month	wt _____ kg	End of month	wt _____ kg	End of month	wt _____ kg	End of month	wt _____ kg	End of month	wt _____ kg	End of month	wt _____ kg	End of month	wt _____ kg	End of month	wt _____ kg	End of month	wt _____ kg	End of month	wt _____ kg	End of month	wt _____ kg
Reaction,	ulcers, burns	Reaction,	ulcers, burns	Reaction,	ulcers, burns	Reaction,	ulcers, burns	Reaction,	ulcers, burns	Reaction,	ulcers, burns	Reaction,	ulcers, burns	Reaction,	ulcers, burns	Reaction,	ulcers, burns	Reaction,	ulcers, burns	Reaction,	ulcers, burns

Method of performing a VMT-ST

NEURITIS CHECK:		
Sensation or strength change within past 6 months?	Yes	No
Nerve pain or tenderness?	Yes	No
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 & 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 & BLINK:						
	RIGHT			LEFT		
Blink problems?	Yes	No		Yes	No	
Light closure lid gap	mm			mm		
Little finger out	S	W	P	S	W	P
Thumb across & up	S	W	P	S	W	P
Foot up	S	W	P	S	W	P
Key: S=Strong; W=Weak; P=Paralysed						

Circle the appropriate letter for Strong (S), Weak (W) and Paralysed (P) for items 2-4.

SENSATION:					
Sensation tested by light skin denting with biro tip at dot					
Key √ = Feels within 3cm		X = Does not feel			
C = Clawed		☞ = Wound or open crack			
— = Shortening level					
Posterior Tibial		Median	Ulnar	Median	
/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.

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