

Leprosy/Hansen Disease: Management of reactions and prevention of disabilities

Technical guidance



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Contributors

N. Agebigo (Papua New Guinea)
M. Balagon (the Philippines)
T. Bauru (Kiribati)
A. Beshah (Congo)
J. Brandão (Brazil)
T. Budiawan (Indonesia)
J. Chukwu (Nigeria)
E. Cooreman (India)
M. Da Palma Caldas (Angola)
J. Darlong (India)
S. Dogra (India)
F. D. H. Estrada (the Philippines)
O. Faye (Mali)
A. Fomba (Mali)
M. D. Gupte (India)
K. Itoh (Japan)
K. Jetton (Marshall Islands)
A. John (India)
R. C. Johnson (Benin)
J. Joshua (India)
E. Keller (Federated States of Micronesia)
S. Lambert (Ethiopia)
L. Lehman (Brazil)
D. Lockwood (United Kingdom)
A. Maghanoy (the Philippines)
M. Murhekar (India)
V. Narsappa (India)
M. Nobre (Brazil)
S. K. Noordeen (India)
V.V. Pai (India)
T. T. Pakasi (Indonesia)
V. Pannikar (India)
S. Paul (India)
V. R. R. Pemmaraju (India)
S. Pennini (Brazil)
M. Puri (Nepal)
B. Quao (Ghana)
K. Rahevar (the Philippines)
J. Richardus (the Netherlands)
Y. Rie (Japan)
I. Roger (Brazil)
M. Roses (Argentina)
P. Saunderson (Norway)
S. Sermrittirong (Thailand)
V. Shetty (India)
G. Sridevi (india)
A. Srikantam (India)
K. Stanley (India)
T. Tadesse (Ethiopia)
A. Tobiki (Japan)
S. Warusavithana (Egypt)
S. L. S. Watdhani (Indonesia)
C. Wiens (Paraguay)
Zaw Lin (India)

Abbreviations

BI	bacillary index
BL	borderline-lepromatous
DALY	disability-adjusted life year
ENL	<i>erythema nodosum leprosum</i>
ENLIST	ENL International Study Group
ILEP	International Federation of Anti-Leprosy Associations
LL	lepromatous
<i>M. leprae</i>	<i>Mycobacterium leprae</i>
MB	multibacillary
MDT	multidrug therapy
MRC	Medical Research Council
NFI	nerve function impairment
NSAID	non-steroidal anti-inflammatory drug
PB	paucibacillary
ST	sensory testing
TNF α	tumor necrosis factor-alpha
VMT	voluntary muscle testing

Foreword



Treatment with multidrug therapy (MDT) has been the main strategy for leprosy control for almost 40 years. This strategy has dramatically reduced the registered prevalence of leprosy, from over 5 million cases when MDT was first introduced to less than 200 000 today. The treatment has been widely accepted, in large part because it has few, mostly manageable side effects. Antimicrobial resistance to more than one of the drugs has rarely been documented. Early case detection and prompt initiation of treatment with MDT is crucial to controlling leprosy, limiting deformity and disability, and reducing the future disease burden.

Leprosy is often characterized by immunological reactions, triggered by the body's immune response against *Mycobacterium leprae*. These reactions can occur prior, during and after treatment with MDT. If unrecognized or improperly managed, such reactions usually progress to irreversible nerve damage and deformities.

This document provides updated guidance on how to recognize and address reactions early to avoid irreversible nerve damage. By periodically assessing nerve function, nerve damage can be recognized early on, even before it is clinically manifest. Providing treatment early will prevent further damage and protect the patient from manifesting disabilities. Conducting periodic nerve function assessments is integral to good clinical practice for leprosy. Such services should be available in any facility where leprosy patients are managed.

Prevention is better than cure. By preventing nerve damage from developing into permanent disability, clinicians will enhance the quality of life of leprosy-affected persons. They will also reduce the burden on a country's health and welfare systems by reducing the need rehabilitative interventions.

I am certain that this document will help health workers take care of leprosy patients, especially in peripheral settings, and ensure they are equipped with the necessary skills to recognize leprosy reactions and take prompt action to prevent disabilities.

A handwritten signature in black ink, appearing to read 'Poonam Khetrpal Singh'.

Dr Poonam Khetrpal Singh
Regional Director
WHO South-East Asia Region

Executive summary

Leprosy is an uncommon but widespread disease, with over 200 000 new cases per year, globally. Leprosy is unusual in that many of the most problematic complications occur as a result of the host's immune response to the infecting organism, *Mycobacterium leprae*. These intermittent and recurring inflammatory episodes are known as leprosy reactions. They appear in two distinct forms, with differing underlying immuno-pathology, clinical features and treatment requirements. The involvement of certain peripheral nerves (neuritis) often leads to disability and devastating psychosocial consequences.

Reactions occur with varying frequency and severity. In some settings, as many as 50% of patients may be affected. Because leprosy is a disease of poverty, access to expert care in referral centres is often not possible.

Several important tasks remain, however, in the fight to prevent disability from leprosy. The first priority remains early case detection, so that treatment can begin as early as possible after symptoms appear. Secondly, it is important to recognize and manage leprosy reactions and neuritis effectively, so that nerve function is preserved. A third task is the primary prevention of leprosy, which is gradually being developed as a working possibility. All of these tasks must be carried out at the peripheral level if they are to be of worthwhile benefit to the at-risk population.

The objective of this *Technical Guidance* document is to review current management practices for leprosy reactions and neuritis and to describe ways in which they can be improved, so that national programmes can achieve their goals of preventing and minimizing disability due to leprosy.

Reactions are acute exacerbations of the signs and symptoms of leprosy occurring during the natural course of the disease as well as during or after treatment. They result from the body's immune response to *M. leprae*. They can affect the skin, nerves, eyes or limbs. Left untreated or improperly managed, reactions can lead to severe nerve function impairment and subsequently to disabilities. Reactions constitute the main pathway by which leprosy causes nerve damage and disability. Effective management of reactions is thus the key to preventing disability. The diagnosis of reactions requires certain clinical skills; effective treatment requires careful judgement, as the clinical course is rarely straightforward.

Managing reactions typically involves the four following steps:

- (1) Recognizing that a reaction is occurring in a person known to have leprosy, remembering that a reaction may already be present at the time of diagnosis.

- (2) Assessing the situation accurately, in particular testing nerve function.
- (3) Prescribing and starting the correct treatment.
- (4) Follow-up, monitoring and adjusting the treatment, according to the response.

This document presents updated guidance on the diagnosis and management of reactions in different settings. The focus should be on the peripheral nerves and their functioning. The goal for national programmes should be to improve the level of nerve function assessment across all facilities where leprosy is treated, including in remote areas, where standards are likely to be lower.

An introduction to leprosy reactions and neuritis

1

1.1 Background

Although leprosy usually manifests itself as a skin disease and is often managed by dermatologists, it is now being regarded much more as a disease of the peripheral nerves (Lockwood, 2012) – a neuropathy whose long-term consequences relate particularly to loss of function in the nerves supplying the eyes, hands and feet. Studies suggest that nerve involvement in leprosy is more widespread than previously thought and often goes undetected (Smith, 2009). Insidious damage causing few symptoms is a well-recognized phenomenon and is often referred to as “*silent neuritis*”, or “*quiet neuritis*”.

This nerve involvement and loss of function apply in varying degrees to all three modalities of the peripheral nervous system: the sensory, motor and autonomic functions. It leads to well-known sequelae:

- The sensory function is itself composed of different modalities (light touch, pressure, heat and cold, pain, etc.). Loss of these functions, especially loss of protective sensation, allows injury and damage to occur with few symptoms, leading to ulceration, infection and chronic inflammation. It is the high blood flow related to chronic inflammation, which causes resorption of tissue, with shortening and eventual loss of digits.
- When the motor function is compromised, muscles become weak or paralyzed, leading to the recognizable deformities of leprosy: lagophthalmos, various types of claw hand, claw toes, footdrop, etc.
- The autonomic nerves have various control functions, including sweating and blood flow. Damage often leads to dry skin, which more easily cracks and ulcerates. High blood flow contributes to the resorption of tissue, as mentioned above.

The leprosy bacillus has a predilection for the skin and nerves, and also for the cooler parts of the body. The nerves most commonly and most seriously affected are those near the skin surface, usually cooler than the internal organs. The ulnar nerve at the elbow is the prime example. The presence of leprosy bacilli in the nerves, especially in the Schwann cells, is the precursor for subsequent damage.



The mechanisms by which *M. leprae* causes nerve damage are varied and complex. Historically, it was well-known that nerve damage often occurred quite suddenly as part of a leprosy reaction. The host's immune-mediated inflammatory response was regarded as the primary cause of any clinical neuropathy (Hastings, 1985). Over the following decades a number of molecular and biochemical mechanisms have been proposed to describe how *M. leprae* interacts with host cells, especially the Schwann cell (Rambukkana, 2002, Serrano-Coll, 2018), with the suggestion that not all leprosy-related nerve damage is due to an immune response. So far, however, this has not led to any new therapeutic approaches. While steroids remain the only proven treatment for acute neuritis in leprosy, other drugs that act on the immune system are being studied, especially as potential treatment for Type 2 reactions (Cogen, 2020; Hatemi, 2019).

1.2 Definitions of terms

Many of the terms used in this document to describe nerve damage are broad and are often used interchangeably. "**Nerve damage**" covers any damage to the structure or function of a nerve. It is well recognized that in leprosy many nerves are affected or damaged, even if the damage is too mild to be measured. "**Neuropathy**" is another term encompassing damage to nerve function from any cause. "**Neuritis**" strictly means inflammation of the nerve, implying involvement of the host's immune system. This is still regarded as the main mechanism of nerve damage in the acute phase of the disease.

From a clinical point of view, the focus is on what can be measured. Nerve function is measured by various means to be described later, collectively called "**nerve function assessment**". Any loss of function is called an impairment, or more specifically "**nerve function impairment**" (NFI). The terminology concerning impairments and disability is described in the *International Classification of Functioning, Disability and Health* (WHO, 2001). An impairment may lead to difficulty in doing certain activities (activity limitations). These may have certain social implications, including stigma and discrimination (participation restrictions), which commonly affect the lives of persons affected by leprosy.

Leprosy reactions are immune-mediated episodes of inflammation that are often self-limiting but may also be severe and prolonged. Leprosy reactions are regarded as

the underlying cause of most disability in leprosy and, thus, of many of the psychosocial consequences that may follow. Two main types of reaction are recognized: Type 1 and Type 2 reaction. The distinctive features of each of them are described below.

Long after leprosy has been treated, there can be several causes for a recurrence of nerve pain, which must be borne in mind during follow-up:

- A leprosy **relapse** may lead to further reactions and neuritis. It is managed in the same way as a first experience of leprosy.
- Pain is a prominent feature of **neuropathic pain**, which is a significant cause of late morbidity in persons who have experienced leprosy.
- An **entrapment neuropathy** may also occur, in which the nerve (perhaps somewhat enlarged because of leprosy) is trapped in one of the fibro-osseous tunnels in the body, such as the cubital tunnel at the elbow or the carpal tunnel at the wrist. The symptoms include pain and loss of function. Splinting may be helpful, but otherwise surgery is indicated.

A brief word is required about the classification of leprosy. New cases present with a wide range of clinical features. They can be grouped according to the clinical signs and histopathology results along a spectrum of disease, which corresponds well with the host's immune response and the bacillary load (Ridley, 1966; Lockwood, 2012). A patient's position on this spectrum of disease is an important factor in determining the risk of complications, including the risk of developing a reaction. The five-group Ridley-Jopling classification was simplified into two groups by WHO for treatment purposes when multidrug therapy (MDT) was introduced in 1981, as two separate regimens were deployed, for **paucibacillary** (PB) and **multibacillary** (MB) disease, respectively (WHO, 1982). A practical difficulty has arisen subsequently in that the operational definitions for the PB/MB classification have changed several times, making it difficult to compare published results from different eras. In general, more and more patients are now classified and treated as MB cases, when they may previously have been classified as PB.

1.3 Type 1 reactions and neuritis

Important early clinical studies of Type 1 reactions: occurrence and risk factors

Several large clinical studies of Type 1 reactions and neuritis have been carried out, as listed below. The clinical picture of reactions is variable. Large studies with long follow up were needed to identify risk factors and understand the clinical diversity and long-term prognosis of the condition.

Retrospective study:

- India (Risk of facial nerve damage) (Hogeweg M et al., 1991)

Prospective cohort studies:

- Thailand (Routine programme) (Schreuder P, 1998)
- Bangladesh Acute Nerve Damage Study (BANDS), Bangladesh (Croft R et al., 1999 & 2000)
- ALERT MDT Field Evaluation Study (AMFES), Ethiopia (Saunderson P et al., 2000)
- ILEP Nerve Function Impairment and Reactions study (INFIR), India (van Brakel W et al., 2005; Smith W et al., 2009)

Hogeweg et al. showed that 85% of cases with recent onset of lagophthalmos had a leprosy skin lesion on the face, allowing such cases to be watched more carefully to detect nerve damage early. Any signs of a reaction in the skin should warn of the potential involvement of nearby nerves (van Brakel, 2005). Schreuder et al. followed up 640 new cases (66% PB) in Thailand for five to eight years. During follow-up, few PB patients (3.7%) had worsened while the same number had improved. For MB cases the change was greater: 19% improved while 18% worsened. A high proportion of MB cases with new nerve function impairment improved on treatment with prednisolone: 47/62 cases (76%).

In Bangladesh, where 83% of cases were PB, Croft et al. showed that the majority of new NFI occurred in the first year after diagnosis. Key risk factors were MB classification and the presence of NFI present at the time of diagnosis (Croft, 2000b). In Ethiopia, a much higher proportion (50%) of cases were MB (in this case, meaning smear-positive), with much higher incidence rates of NFI. If NFI was new, however, results after treatment with prednisolone were good (Saunderson, 2000).

Steroid treatment will be discussed in more detail in Chapter 3. It is important to note that the degree of improvement reported in different studies is very variable and quite dependent on operational factors (Walker, 2008; Croft, 2000b; Saunderson, 2000). Factors which tend to decrease the reported efficacy of treatment (showing a good outcome in less than 50% of cases, for example) include:

- Inclusion of cases with nerve damage of unknown duration (some will have old damage);
- Use of full recovery of function as the required outcome, as opposed to “improvement”;
- Use of a more sensitive test of nerve function, which is more likely to show some residual loss.

Studies showing high efficacy (65–80% improvement) exhibit some or all of the following features:

- Only inclusion of cases in which the timing of new nerve damage is precisely documented;

- Use of “improvement” (however that is defined) as an endpoint, rather than complete recovery;
- Use of a less sensitive test to assess sensory loss (such as the ballpoint pen or a single 10 gm monofilament) which may not detect a low level of residual sensory loss.

The INFIR study in India followed 303 MB cases for two years, with a more intensive search for risk factors for NFI. This was also assessed by a wider range of methods, including nerve conduction studies (van Brakel, 2005). At diagnosis, 38% had a recent or new reaction or nerve damage. The main risk factor for NFI was a leprosy skin lesion overlying a nerve trunk (risk increased three to four times). The presence of signs of inflammation in such a skin patch further doubled the risk for NFI. The study found that sensory nerve conduction studies and warm detection thresholds did detect neuropathy earlier, up to 12 weeks before changes were noted on the monofilament test (van Brakel, 2008). Surprisingly, subsequent studies of prophylactic treatment of all new cases with steroids, or treatment of very early neuropathy, have not led to improved outcomes. This will be described in more depth in Chapter 3 on the medical management of reactions and neuritis.

The INFIR study also measured a range of antibodies and cytokines in the search for useful markers of reactions and NFI. The effects of old NFI tended to mask recent changes (Jadhav, 2011). Further analysis showed that the levels of a number of markers of inflammation increased in the month before the clinical onset of a reaction and then declined with steroid treatment, although there was considerable variation between individuals (Raju, 2014).

Type 1 reactions and neuritis: clinical features and natural history

Type 1 reactions are caused by an inflammatory response to *M. leprae* in the tissues. They occur because of a sudden alteration in cell-mediated immunity, a delayed type hypersensitivity reaction (Britton W, 1998). Type 1 reaction is also known as **reversal reaction**, because the immune response initially appears to be declining and then “reverses” to become more intense. It may be a presenting feature of leprosy or may occur during treatment with MDT or even for three or four years after treatment has been completed (Rose, 1991). Starting treatment with MDT often appears to precipitate a Type 1 reaction, perhaps because the rapid killing of bacilli allows the immune system to recover.

The typical features of inflammation are seen: swelling, redness, heat, pain and loss of function. The central clinical feature of a Type 1 reaction is inflammation around bacilli in the leprosy skin lesions. This is rarely a serious problem, as the reaction is self-limiting. Symptomatic treatment is required until resolution occurs over a period of a few weeks. In severe cases, the inflamed skin lesions may ulcerate.



A more important issue, however, is that a reaction in the skin is very often accompanied by inflammation in one or more nerves, known as neuritis. This can have serious consequences, including permanent nerve damage, impairment and disability. A Type 1 reaction in the skin may therefore be taken as a possible pointer of impending neuritis (van Brakel, 2005; Nery, 2013). Special attention should be paid to reactional lesions located in the face, because they are associated with a higher risk of facial nerve damage, resulting in lagophthalmos and its consequences (Hogeweg, 1991).

Reactions are often present at the time of diagnosis: around 22% of all new cases have some form of reaction, based on data from a study in three countries: Brazil, Nepal and the Philippines (Scollard, 2015). If the reaction is mild and there is no evidence of neuritis, non-steroidal anti-inflammatory drugs (NSAIDs) such as acetylsalicylic acid, ibuprofen or paracetamol are usually sufficient to control symptoms.

Of critical importance in managing all patients with leprosy is regular nerve function assessment. This allows the detection of NFI, either because of an obvious inflammatory event (such as a reaction) or because of so-called silent neuritis. It is, therefore, essential to carry out a nerve function assessment on a regular basis during the treatment of leprosy, in order to detect new NFI and initiate specific anti-reaction treatment with steroids. Tests of sensory and motor function should be done routinely. The methods are described in detail in Chapter 2. There are two important reasons for doing the tests regularly in all leprosy patients on treatment: (i) NFI may occur without any overt sign (e.g. pain) indicating a reaction; (ii) If NFI remains untreated for six months or more, recovery is unlikely.

Apart from these well-known epidemiological and clinical risk factors, several groups have searched for biomarkers which may signal an impending Type 1 reaction, including the INFIR study mentioned above. Some further progress has been made (Tio-Coma, 2019), but the proposed tests are not yet ready for widespread use. A major difficulty with such tests would be the selection of patients and the timing of the tests, when – by definition – there is no other suggestion of an imminent reaction.

Type 1 reaction and neuritis: diagnostic procedures and laboratory tests

The diagnosis of a Type 1 reaction is essentially clinical, with the finding of inflamed skin lesions. The presence of fever or ulceration of skin lesions would indicate a more severe

reversal reaction. There are two specific types of diagnostic procedure that are indicated in patients with a Type 1 reaction: (i) Tests of nerve function to identify any accompanying neuritis; and (ii) Tests to look for any contra-indication to treatment with steroids.

Tests of nerve function are reviewed below. The simple message is that any NFI that has been present for less than six months can potentially be reversed with steroid treatment, thus preventing permanent disability.

Laboratory tests that are indicated prior to prescribing steroids are as follows:

- Routine tests of health status as normally practiced (e.g. haematology, biochemistry, HIV serology);
- Tests to exclude tuberculosis, as indicated (e.g. sputum test, chest X-ray);
- Tests to assess the possibility of diabetes (e.g. urine/blood sugar, test of glucose tolerance);
- Stool examination;
- Any tests indicated to identify suspected infection, including culture of blood/wound swab.

Type 1 reaction and neuritis: management

Drugs used in the treatment of a Type 1 reaction are discussed in Chapter 3. There are important non-pharmaceutical measures that should be taken in parallel. Although this work is usually managed by the physiotherapy department of referral centres, it can be undertaken anywhere where leprosy patients are being seen.

- **Resting** of the affected limb in the acute phase can be aided by splinting, especially at night.
- Once the pain of the acute phase has reduced, **passive stretching** of any weakened muscles preserves joint mobility; **active exercises** then help to strengthen the weakened muscles.
- **Soaking** and **oiling** of dry skin helps to prevent cracking and preserves the integrity of the epidermis.

Surgery is sometimes indicated in the acute phase to relieve pressure on and inside the nerve. This is only available in specialist centres. Very few clinical trials of decompressive surgery have been done (van Veen N et al, 2012). Rehabilitative surgery plays an important role in the later management of those with permanent nerve damage, but is beyond the scope of this document.

1.4 Type 2 reaction

Type 2 reaction: major studies and risk factors

Type 2 reaction, also known as *erythema nodosum leprosum* (ENL), is a multisystem, relapsing and remitting disorder occurring in patients with lepromatous (LL) and borderline-lepromatous (BL) leprosy, and a high bacillary load. The incidence varies in different cohorts. A review of published data indicated that 1.2% of all leprosy cases and 15.4% of LL cases developed a Type 2 reaction (Voorend, 2013). Some case series report up to 50% of LL cases being affected (Kumar, 2004; Pocaterra, 2006). Voorend et al. found that multiple episodes were reported in 39–77% of cases, with an average of 2.6 episodes per patient. In all series, Type 2 reactions are associated with a high bacillary index (BI) at diagnosis, typically above 4.0.

Erythema nodosum itself is a rare immunologically-mediated condition that may be due to a number of underlying causes, such as tuberculosis, sarcoidosis, Crohn's disease and as an adverse effect of various drugs. In leprosy, ENL is thought to be related to circulating immune complexes with widespread effects throughout the body, not just in the skin (Kahawita, 2008).

The ENLIST consortium¹ was formed in 2014 and has contributed significantly to our knowledge of Type 2 reactions. An important reason for forming the consortium was to conduct multi-centre studies in view of the fact that Type 2 reactions are generally uncommon.

Important studies on Type 2 reactions include:

- Systematic review of ENL epidemiology (Voorend C et al., 2013);
- Mortality associated with ENL (Walker S et al., 2014);
- Cross-sectional study of clinical features (Walker S et al., 2015);
- The ENL Severity Scale (Walker S et al., 2017).

Type 2 reaction: clinical features

The first activity of the ENLIST Consortium was to gather comprehensive data on the clinical features of Type 2 reactions (Walker S, 2015). Based on this, a Severity Scale was developed (Walker S, 2017). This allows each case to be assessed objectively and for progress to be measured accurately. This form of reaction comes and goes recurrently. Treatment is often not simple. It is important to be able to detect both a good response to treatment and any worsening of the condition.

¹ ENLIST or ENL International Study Group: a global consortium to improve understanding and treatment of ENL with representatives from Bangladesh, Brazil, Ethiopia, India, Indonesia, Nepal, and the Philippines

The key diagnostic feature of a Type 2 reaction is the presence of inflamed nodules in the skin, the so-called *erythema nodosum*. The nodules may be anywhere on the body and are not related to the skin lesions of leprosy. The nodules are in the subcutaneous tissues and measure usually 1–2 cm across. In severe cases, the nodules may ulcerate. Other typical clinical features form part of the Severity Scale:

- Pain;
- Fever;
- Number and extent of ENL lesions;
- Peripheral oedema;
- Bone pain;
- Inflammation of joints or digits;
- Lymphadenopathy;
- Nerve tenderness.



The natural course of an acute ENL episode is between one and two weeks. Many patients experience multiple occurrences for months (Scollard et al., 2006). Three types of ENL have been described:

- **Acute ENL:** episode of ENL lasting less than six months in which treatment was slowly withdrawn with no recurrence of ENL while on treatment;
- **Recurrent ENL:** at least one further episode of ENL occurring 28 days or more after withdrawal of treatment for ENL;
- **Chronic ENL:** episode of ENL lasting longer than six months during which the patient is on continuous ENL treatment or any treatment-free periods are less than 28 days.

Patients with ENL are likely to have an impaired quality of life and face catastrophic household economic costs (Chandler, 2015). Patients should be warned that ENL may last for over a year or even longer. They should be counselled about controlling symptoms. They should be given a steroid information leaflet and a *Steroid Card*. They should be warned against buying over-the-counter steroids to treat their symptoms. It is important that they are monitored by a clinician experienced in managing patients with ENL. They may develop depression about their condition and the medication they are taking. This should also be given attention during clinic visits.

Type 2 reaction: diagnostic procedures and laboratory tests

Laboratory investigations are not needed to confirm the diagnosis of ENL. They are, however, needed to monitor the complications that may occur as a result of the immunosuppressant drugs that are given. Regular nerve function assessment is also indicated.

1.5 Neuropathic pain

Treated leprosy patients may experience tingling or burning pains in treated skin lesions as well as hands and feet. These may be misdiagnosed as reactions. In the absence of nerve tenderness and new NFI, the diagnosis of neuropathic pain should be considered, especially if the original diagnosis of leprosy was made more than 3–5 years earlier.

Patients should be treated using an analgesic ladder starting with paracetamol as a first step, then using a non-steroidal drug such as ibuprofen, if relief is inadequate. Many patients will need treatment with amitriptyline. Although this is an antidepressant drug, the doses used for neuropathic pain are lower and there seems to be a direct stabilizing effect on the peripheral nerves. Gabapentin can also be used for patients with pain that is not alleviated by other measures. Steroids are not recommended for neuropathic pain in leprosy.

1.6 Disability-adjusted life years in leprosy

Disability-adjusted life year (DALY) is a measure of overall disease burden, expressed as the number of years lost due to ill-health, disability or early death. It was developed in the 1990s as a way of comparing the overall health and life expectancy of different countries as well as the overall burden of different diseases. DALY is a societal measure of the disease or disability burden in populations.

DALY is the sum of years lived with disability and years of life lost. The DALY results in leprosy show a minimal burden as the mortality due to leprosy is very low, and deaths that do occur may not be notified as being leprosy-related (e.g. death due to dysentery in someone with leprosy being treated with steroids). Significant leprosy-related mortality can occur due to ENL, steroid medication, dapsone hypersensitivity syndrome or suicide. DALYs also do not measure mental health issues well, nor the distressing effects of stigma or the disabling effects of plantar ulceration.

One study in India (Rao P, 2013) showed there is a reduction of 13.4 years from the ideal productive working period of life. The study observed that, on average, 30% of a leprosy-affected person's work life is lost due to disability.

Nerve function assessment in leprosy

2

2.1 Introduction to nerve function assessment

In order to improve the management of reactions and neuritis in leprosy everywhere, this chapter has two key objectives relating to nerve function assessment:

- All programmes and clinics treating leprosy cases should greatly increase routine testing of nerve function, using available tools, whether that means the ballpoint pen or nylon monofilaments.
- All programs and clinics should gradually improve both the precision and the utility of testing being done, through further training, better record-keeping and the use of monofilaments, wherever possible.

This chapter describes sensory testing and voluntary muscle testing, which can be carried out in any setting where people are treated for leprosy (Becx-Bleumink M, 1990). Other tests, such as warm or cold detection, tests of autonomic nerve function and nerve conduction studies are done in some centres, but are beyond the scope of this document.

Nerve function impairment is defined as clinically detectable impairment of nerve functions that necessitates intervention. The severity of clinically detectable NFI depends on the sensitivity of the tool used and the gradations that can be reported. When NFI is not treated within six months of onset, nerve damage can become irreversible and can cause permanent disability. Therefore, periodic assessment is an essential part of proper case management in leprosy.

The purpose of nerve function assessment is four-fold:

- To diagnose leprosy (one of the three cardinal signs) and to classify for treatment with MDT (two or more trunk (not cutaneous) nerves affected is classified as MB);
- To establish the occurrence of NFI in an individual patient during or after MDT and decide on appropriate interventions to prevent permanent nerve damage;
- To monitor the changes (recovery, deterioration) in nerve function following therapy (primary outcome measure); and
- To prevent persons affected from being subjected to social identity of leprosy thereby reducing stigma and discrimination.

For assessing the nerve function, health staff require reliable, affordable and easy-to-use tools along with standard screening methods to detect early neuropathy in field settings. The tools should be sensitive enough (i.e. low number of false-negatives) to correctly diagnose NFI but also specific enough (i.e. low number of false-positives) in order not to over-diagnose NFI. Studies indicate that skills and experience levels of healthcare personnel affect the reliability of testing. Established methods for nerve function assessment are nerve palpation, sensory testing (ST) and voluntary muscle testing (VMT). The ballpoint pen (easily available) or nylon monofilament are commonly used for ST. For VMT, three grades (as suggested by J Watson) or the modified *Medical Research Council (MRC) Scale* with six grades (0–5) is used.

Before NFI is clinically detectable, the majority of nerves already show some subclinical neuropathy that can be detected with more sensitive methods. The warm detection threshold and nerve conduction studies were able to detect subclinical neuropathy up to 12 weeks before neuropathy was clinically noticeable with monofilament testing or VMT (van Brakel, 2008). Significant correlation was observed between clinical parameters – nerve thickening (by palpation), sensory loss and muscle weakness (VMT) – and abnormalities of nerve echotexture, endoneural blood flow and cross-sectional area (by ultrasound examination). Nerve damage was sonographically more extensive and was observed even in nerves that are considered clinically normal (Jain S et al.).

Evidence suggests that the use of Semmes-Weinstein nylon monofilaments is more sensitive than ballpoint pen testing. Substantial levels of under-diagnosis of sensory loss with ballpoint pen testing were observed (Koelewijn L et al., 2003). However, from a practical perspective, detection of mild sensory loss with the more sensitive monofilaments in one group of subjects did not lead to better long-term outcomes, compared to subjects assessed by the ballpoint (van Brakel, 2003).

Nerve function should be assessed at diagnosis (baseline) and repeated every three months during MDT (if possible, it may be done every month for patients at higher risk of neuritis, e.g. MB patients who already have nerve damage) and upon completion of treatment. Nerve function should also be assessed whenever the patient complains about pain, numbness or weakness. When NFI is detected, nerve function should be assessed monthly during steroid therapy and then every three months after steroid therapy. The patient needs to be involved by imparting proper counselling about neuropathy and its consequences explaining the importance of nerve function assessment and detecting symptoms of neuropathy.

A patient is considered at higher risk for developing NFI if:

- There are more than six skin lesions with or without nerve involvement (i.e. only enlarged nerve without existing NFI);
- There is a skin patch on the face or near the eye or in the areas supplied by a palpable or visibly enlarged trunk nerve without existing NFI;

- There is evidence of a reaction (Type 1 or 2) including acute neuritis, either new or treated in the past six months without existing NFI;
- The slit-skin smear is positive;
- The patient is classified as having MB leprosy.

Nerve function assessment should be performed:

- At any health unit treating patients with leprosy;
- During community sensitization and screening campaigns;
- At home (self-examination by persons affected by leprosy).

Nerve function assessment should be performed by any trained health worker or any trained person affected by leprosy.

2.2. Sensory testing

This section describes testing for light touch, using either a ballpoint pen, a single monofilament or a set of graded monofilaments. Routine sensory testing is limited to examining the palms of the hands and the soles of the feet. Testing for loss of sensation on the cornea should not be done routinely. The number of testing sites on each hand or foot is not critical but is usually between 4 and 10.

When testing, make sure the subject understands what is required by demonstrating the procedure. For the actual test, make sure the subject cannot see the part being tested and ask them to point to the place being touched. Identification of the point with an error of less than 2 cm, shows that sensation is present.

Documentation of each result is important so that change over time can be identified (Sample *Patient Card* is provided in Annex 2). It is, therefore, normal that each programme tests a standard set of sites.

When using the ballpoint pen, practice on yourself first to see what a light touch feels like: the aim is to use the lightest touch that you can feel on your own hand. The ballpoint pen has the advantage of being always available. If used carefully, it can greatly improve the management of patients with leprosy. The lack of monofilaments should never be used as an excuse for not testing nerve function, when indicated.



If a single nylon monofilament is used, it will bend and give a standardized force, measured as a weight in grams, which makes it more accurate than the ballpoint. Typically,

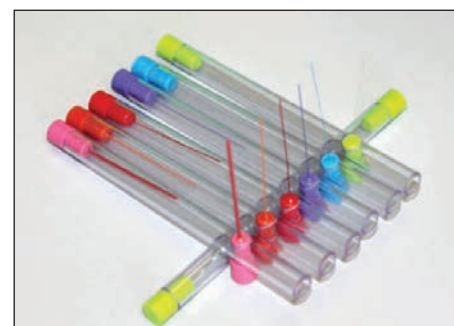
a 2 gm or 10 gm monofilament is used. The 2-gm monofilament is preferred by some, as it may give an earlier indication of NFI. There is concern, however, that it may not be felt by normal skin on the feet where people are used to walking barefoot, and thus give a false positive indication of sensory loss. The 10-gm monofilament is used as the standard in diabetes clinics and may indicate a more established neuropathy. A study in healthy Indian and Nepali subjects, indicated that 4 gm is the normal threshold for sensation in the foot, perhaps increasing to 10 gm in those doing heavy labouring work; the threshold for the ulnar and median nerves in the hand was 200 mg (Wagenaar, 2014).

These findings suggest that, if a single monofilament is used, the 10-gm filament is preferred. If clinics want to use more monofilaments, the next step would be to use 10 gm for the foot and 2 gm for the hand.

Graded monofilaments are manufactured as a standard set (Sorri-Bauru, São Paulo, Brazil), with bending forces ranging from 70 mg to 300 gm (Table 1, Wagenaar, 2014; reproduced with permission). If all six monofilaments are used, it is normal practice to progress from the lightest (70 mg) to the heaviest (300 gm), testing up to a maximum of three times with each filament, at each site; the lightest filament that is felt is recorded. This is quite a time-consuming exercise, and should be done in a quiet room without interruption, which may not be possible everywhere.

Table 1: Characteristics of the standard pocket set of Semmes-Weinstein monofilaments (from light to heavy)

Filament	Filament Index Number*	Bending force (grams)
Green	2.83	0.07
Blue	3.61	0.2
Purple	4.31	2
Red	4.56	4
Orange	5.07	10
Pink	6.65	300



Semmes-Weinstein monofilament test kit

* The filament index number is calculated from the bending force in mg: $\text{Filament Index Number} = \log(\text{force} * 10)$

Interpretation of the results is a key part of the examination. If sensation is definitely reduced since the previous test, new NFI has been identified and should be treated. If ten sites are tested on each hand and foot, it is reasonable to require a significant loss of sensation of at least two sites to diagnose new NFI. If only four sites are tested, loss of sensation at one site confirms the diagnosis.

If only one instrument is used (either the ballpoint or the 10-gm monofilament, for example), new sensory loss is simpler to identify – at any specific site, there is a change from the stimulus being felt, to not being felt. The graded monofilaments may show a changing threshold of sensory perception. The monofilament is standardized and will thus give similar results between different observers; the ballpoint is more variable and dependent on the examiner. If the ballpoint is used, the results will be more reliable if the same examiner tests the patient each time.

2.3. Voluntary muscle testing

Four muscles on each side of the body are routinely tested. The subject is asked to move a specific muscle and the examiner tests the strength of the movement against resistance. Although two scales are used, the examination is the same. The difference is that the simpler scale has only three categories while the more complex *MRC Scale* has six categories (Table 2).

Table 2: Voluntary muscle testing: scales in use

Simple scale	MRC Scale	Interpretation
Strong (“S”)	5	Full strength
	4	Slightly below full strength (compared to the other side, for example)
Weak (“W”)	3	Full range of movement, but no resistance to an opposing force
	2	Some movement, but less than the full range; no resistance
Paralyzed (“P”)	1	A flicker of movement can be felt by the examiner
	0	No movement at all

As with sensory testing, the more precise *MRC Scale* is often used in referral centres while the simple scale is more widely used in the field. The key point is that testing should be done regularly and results recorded, so that any change is easily noted. A change of two levels on the *MRC Scale* or one level on the simple scale confirms loss of muscle strength, indicating the need for treatment.

The four muscles routinely tested are:

- Eye closure (inability to fully close the eye, or lagophthalmos, is caused by weakness of the *orbicularis oculi* muscle):

- Observe and measure (in mm) any gap between the eyelids on gentle closure;
- Gently try to part the eyelids, while the subject shuts the eyes tightly.
- To test muscles in the hand, ask the subject to hold out each hand in turn; the hand should be held out flat, to the front, with the palms up:
 - Ulnar nerve in the hand: Hold the subject's hand steady and ask them to move the little finger out, against resistance; the examiner can provide resistance at the base of the finger;
 - Median nerve in the hand: Hold the subject's hand steady and ask them to point their thumb up towards their own nose (this ensures that the thumb is being abducted [median nerve] rather than extended [radial nerve]); the examiner can provide resistance by pushing down vertically at the base of the thumb.
- Peroneal nerve in the leg/foot:
 - A footdrop may be noted as the subject walks; the front of the foot drags along the ground;
 - With the knee straight, ask the subject to raise the foot at the ankle (dorsiflexion), while the examiner presses down.

Medical management of reactions and neuritis in leprosy

3

3.1. Treatment of Type 1 reaction and neuritis

Steroids: indications and dose

Steroid treatment is indicated in the following circumstances:

- Type 1 reactions that are severe enough to cause skin ulceration or are uncontrolled by paracetamol or NSAIDs (such as ibuprofen);
- Neuritis, as shown by the emergence of new nerve function impairment.
 - Neuritis may accompany a Type 1 reaction, whether mild or severe;
 - It may be associated with pain in one or more nerves;
 - The patient may complain of NFI, e.g. loss of sensation or muscle weakness;
 - It may be silent, i.e. without clear symptoms.

Traditionally, the prescription of steroids would be done by a medical officer in a referral centre. A number of authors have noted, however, that a majority of referred patients never actually attended for further treatment, for one reason or another, leading to the development of protocols to manage patients with steroids in peripheral clinics (Becx-Bleumink M, 1990).

Oral prednisolone is the steroid normally used. When treating with prednisolone, the key parameters are the starting dose and the length of the course. There is a trade-off between giving enough to provide effective treatment while avoiding giving too much and risking the adverse events of the drugs.

In general, the starting dose should be between 0.5 and 1.0 mg per kg of body weight per day. In most settings 0.5 mg/kg daily would be an appropriate starting dose for a first course, meaning 30 or 40 mg daily for most adults. Recent studies suggest that a course lasting 20 weeks gives the best results, starting at either 30 mg or 40 mg, depending on body weight (Table 3).

Table 3: Treatment schedule for managing Type 1 reaction with steroids

Dose	Week					
	1–2	3–4	5–8	9–12	13–16	17–20
40 mg						
30 mg						
25 mg						
20 mg						
10 mg						
5 mg						

Steroids: Adverse events

The list of adverse events associated with steroids is long. They are all made worse by prolonged treatment at high doses (ILEP, 2002). Appropriate tests and strategies to manage these events are suggested. Note that the first two problems listed are the ones most often encountered.

- **Immunosuppression:** Problems may occur with unrecognized tuberculosis, septicaemia and osteomyelitis. Relevant radiology and microbiology tests may be indicated. Various intestinal infections and infestations may be exacerbated, including with *Strongyloides* and various causes of dysentery. Stool microscopy and culture may be helpful. It is normal to give albendazole (adult dose: 400 mg twice a day for three days) to anyone being started on steroids for neuritis.
- **Diabetes:** The possibility that a course of steroids will precipitate or worsen diabetes should be borne in mind. Urine sugar and a random blood sugar are the most basic tests; a single blood sugar level done two hours after a glucose drink is also a useful screening test and is simpler to arrange than a full glucose tolerance test. If diabetes occurs, it can be treated in the normal way, but it may resolve when steroids are stopped.
- **Osteoporosis**, avascular necrosis of the femoral head: This is mainly a problem in an elderly, sedentary population.
- **Mental** disturbance, euphoria: Some feelings of euphoria are common, and may be a reason why some patients do not want to stop the medication.
- **Dyspepsia**, peptic ulceration: This is not usually a major problem and can be managed easily with antacids, an H₂-receptor blocker (e.g. famotidine) or a proton pump inhibitor (e.g. omeprazole).
- **Cushing's syndrome:** This is a collection of signs and symptoms caused by a high intake of steroids and includes: swelling of the face (so-called *moon face*), acne, hirsutism and weight gain. It resolves when the steroids are stopped.

- **Growth suppression:** Prolonged steroid use in children can limit growth due to suppression of the adrenal cortex and the pituitary axis.
- **Intra-uterine growth retardation:** For similar reasons, growth of the foetus may be retarded when steroids are used in pregnancy.
- Adrenal atrophy (**Addison's disease**): Steroids mimic the action of glucocorticoids produced by the adrenal gland, so the activity of the gland may become suppressed when steroid medication is given. This is why the steroid dose is reduced gradually after any course of more than three weeks, to give time for adrenal function to recover. Addison's disease can lead to collapse and hypotension if steroid medication is stopped suddenly.
- Hypertension, glaucoma, cataracts: Steroid use is not a major causal factor in these conditions, but it can make them worse. Blood pressure and eyesight should be regularly monitored.

Studies on treatment of neuritis

Prospective, randomized controlled trials:

- TRIPOD 1 – prevention of neuritis, Nepal and Bangladesh (Smith W et al., 2004)
- TRIPOD 2 – treatment of mild NFI, Nepal and Bangladesh (van Brakel W et al., 2003)
- TRIPOD 3 – treatment of old NFI, Nepal and Bangladesh (Richardus J et al., 2003)
- India – comparison of three steroid regimens (Rao P et al., 2006)
- Nepal – methylprednisolone (Walker S et al., 2011)
- Ethiopia – cyclosporine (Lambert S et al., 2016)
- AZALEP – azathioprine, India (Lockwood D et al., 2017)
- TENLEP – 20 vs 32 weeks of prednisolone, multicenter (Wagenaar I et al., 2017)

Cochrane reviews:

- Decompressive surgery for treating nerve damage in leprosy (van Veen N et al., 2012)
- Corticosteroids in the treatment of nerve damage in leprosy (van Veen N et al., 2016)

By the beginning of the 21st century, treatment of neuritis with prednisolone had become reasonably standardized although no randomized controlled trials had been conducted. Subsequent studies looked at the possibility of preventing neuritis and also sought to more clearly define the indications for treatment with prednisolone. Alternative

or steroid-sparing drugs were also studied in order to reduce the adverse events associated with long-term steroid treatment.

A Cochrane review (van Veen, 2012) on the use of corticosteroids for treating nerve damage in leprosy examined five studies published before 2012. Three of these gave negative findings:

- Treating mild NFI did not provide lasting benefit over placebo (van Brakel W, 2003); in this study, “mild sensory loss” was defined as sensory loss detected by the careful use of graded monofilaments but where sensation was found normal when the ballpoint was used;
- Treating NFI that occurred more than six months previously was not beneficial (Richardus J, 2003);
- An initial burst of high dose IV methylprednisolone did not improve outcomes (Walker S, 2011).

The other two studies – unfortunately both with several methodological flaws – showed a beneficial effect of steroids. They suggested that a longer course of prednisolone was more important than a high initial dose (Rao P, 2006; Garbino J, 2008).

An important reason why nerve function may not recover when treated with steroids, is that the problem may have been present for more than six months, by which time steroids are ineffective (Richardus J, 2003). This is especially likely in new cases who present with NFI when it may be difficult to get accurate information about duration. Ideally, all patients on MDT are assessed regularly (at least every three months, often every month) so that, when new NFI occurs, it can be identified easily by comparison with past records and treated in a timely manner.

The best steroid regimen to treat reactions and neuritis continues to be debated, both in terms of dose and duration. The TENLEP trial showed that prolonging the course to 32 weeks provided little additional benefit (Wagenaar, 2017). The currently recommended course of steroids, therefore, lasts for 20 weeks (Rao, 2006).

In the TENLEP study, the 20-week regimen started with a higher dose (1 mg/kg, up to 60 mg) for one week. In other respects it was very similar with an 8-week period in the middle at 20 mg daily (Wagenaar, 2017). It is important to note that around 15% of patients in both groups of this trial (i.e. 20- and 32-week treatments) required extra prednisolone because of a lack of improvement or worsening of nerve function once the standard course ended. The reactions were eventually well controlled with this additional treatment.

The TRIPOD 1 study looked at the possible effect of a prophylactic dose of prednisolone (20 mg per day) given for the first three months (plus a tapering dose in month 4) of treatment with MDT: there was a prophylactic effect in the short term, but this was not sustained. Both the intervention and control groups had similar levels of reaction and neuritis at one year (Smith WC, 2004).

Second-line drugs used in the treatment of neuritis included azathioprine and cyclosporine (Lockwood D et al., 2017; Lambert S et al., 2016). Cyclosporine could be a safe alternative for patients with neuritis who are not improving with prednisolone or are experiencing adverse events related to prednisolone and where azathioprine is not recommended.

Evidence from randomized controlled trials does not show a significant added benefit of surgery over steroid treatment alone (van Veen N, 2009b).

3.2. Treatment of Type 2 reaction

Recommended treatment

Relevant studies include:

- Cochrane review – Interventions for ENL (van Veen N et al., 2009);
- Thalidomide versus prednisolone (Kaur I et al., 2009);
- Additional clofazimine to prevent ENL (Balagon M et al., 2011; Maghanoy A et al., 2017).

Mild ENL is managed with analgesics (aspirin, indomethacin, ibuprofen, diclofenac, acetaminophen, tramadol). If there is worsening and increase in the *ENLIST Severity Score* to 8 or more, ENL should be reclassified as ‘severe’ and managed accordingly. Monitoring should be done every two weeks, using the Severity Scale and tests of nerve function.

Severe ENL is best treated initially with moderate doses of 30–40 mg prednisolone (for an adult) per day. This has a rapid and defined therapeutic action (Mahajan et al., 2003; van Veen et al., 2009).

Recurrent and **chronic ENL** require increased or prolonged doses of steroids to control the inflammation and symptoms. Patients with chronic ENL may become dependent on steroids. Serious side effects of long steroid treatment course have been reported. Walker et al., 2014 found a 9% mortality in Ethiopian patients taking steroid treatment for ENL; this was caused by steroid-related complications such as sepsis and occurred mostly in young people.

The Cochrane Review (van Veen, 2009) looked at 13 studies involving 445 participants. The overall quality of the studies was poor and the samples sizes often small. Prednisolone, thalidomide and clofazimine generally gave better results than other treatments (such as NSAIDs and pentoxifylline).

The indications for using thalidomide or clofazimine as additional or second-line drugs are:

- Steroid non-responders: those requiring higher doses of steroids with each episode of ENL;

- Steroid dependence: those for whom tapering the steroid dose results in flares;
- Patients with a serious comorbidity.

Thalidomide is an effective alternative, giving rapid symptom control. Kaur et al. showed that thalidomide gave better symptom control than prednisolone. Nabarro et al., 2016 showed that using thalidomide reduced dependence on prednisolone. Thalidomide is not useful in managing neuritis, which is less frequent in Type 2 as compared with Type 1 reactions. It is useful in managing the general malaise, fever and pain of severe ENL. The adult dose varies between 100 mg and 400 mg daily, in divided doses. A typical regimen used in India started with 300 mg per day in divided doses, tapering down to 100 mg daily over two to three weeks, depending on the response (Kaur, 2009). A maintenance dose may be required in chronic cases, the dose being determined by the response.

There are recognized adverse events with thalidomide including sedation, peripheral neuropathy and venous thrombosis. Low-dose aspirin could be used to reduce the risk of thrombo-embolism (van Veen, 2009; Mahmoud, 2019). Thalidomide may initiate teratogenic effects when taken early in pregnancy. Women can be given thalidomide but only when being supervised in a prevention of pregnancy programme. This includes patients being seen every 28 days, having negative pregnancy tests and using two different methods of contraception, before receiving a prescription for thalidomide.

Clofazimine is widely used in the management of ENL. However, supporting data are generally of poor quality and more studies are needed to show how it can be most effectively used. It takes four to six weeks to become effective. The dose required to control ENL is higher than the dose (50 mg daily) used in MDT (van Veen et al., 2009). A widely used regimen is as follows:

- 300 mg, daily, for 1 month;
- 200 mg, daily, for 3–6 months;
- 100 mg, daily, for as long as ENL symptoms remain.

It has no effect on acute episodes but might be effective in mitigating chronic and recurrent ENL. The associated skin pigmentation may be stigmatizing (van Veen et al., 2009). A small study in the Philippines, in which patients were randomized to receive clofazimine 100 mg per day or placebo, showed no benefit from clofazimine in reducing ENL frequency or severity (Maghanoy, 2017).

Other drugs have been used as second-line treatments for ENL. They have all been used in small-scale studies. They are: pentoxifylline, methotrexate, cyclosporine and azathioprine. The effectiveness of methotrexate in this regard is currently being tested in a large randomized controlled trial.

Tumor necrosis factor-alpha (TNF α) inhibitors (e.g. infliximab in one case (Faber, 2006) and etanercept in three cases (Ramien, 2011; Santos, 2017; Thangaraju, 2016)) have been used to treat patients with recurrent ENL (Cogen, 2020). This is an area that

will see expansion over the next few years as biological agents become cheaper and more widely used. The dangers are severe immunosuppression and opportunistic infections.

Another promising class of drugs is the phosphodiesterase-4 inhibitors which prevent degradation of cyclic adenosine monophosphate, thereby decreasing the production of pro-inflammatory cytokines. One example, apremilast, is used in the treatment of psoriasis and Behcet's syndrome (Hatemi, 2019). An analogue of apremilast is currently being studied in ENL patients, with promising initial results.

Availability of thalidomide for treatment of Type 2 reactions

Thalidomide was first produced in 1957 and was withdrawn in 1961 because of its teratogenic effects when given in early pregnancy. It is, however, useful for the treatment of severe ENL.

The Seventh WHO Expert Committee on Leprosy (WHO 1997) stated: "Thalidomide is also effective for the treatment of severe ENL. It must be pointed out, though, that because of its teratogenic effects, thalidomide should never be given to women of childbearing age. Thalidomide should be used only in male or postmenopausal female patients who have become dependent on corticosteroids; it must be given only under close medical supervision at the nearest referral centre."

In 1998, the United States Food and Drug Administration approved the use of thalidomide for ENL, under a comprehensive programme to control prescribing, dispensing and the use of the drug (Zeldis, 1999).

In 2003, a document was produced by WHO, entitled "No role for thalidomide in leprosy". It argued that severe ENL is now a rare occurrence, and that because thalidomide did not treat neuritis, it was of little benefit; it warned of a new generation of deformed babies, if thalidomide were promoted for the management of ENL.

The Eighth WHO Expert Committee on Leprosy (WHO 2012) stated: "Although several studies have demonstrated the usefulness of thalidomide in the treatment of acute ENL reactions, its use is restricted because of its teratogenic effects and of ethical and legal considerations. In addition, thalidomide availability is limited by restrictions on its import and supply in many endemic countries. WHO, therefore, recommends its use only under strict medical supervision in specialized referral facilities".

Two developments have intensified discussion on the use of thalidomide. A large retrospective study in Ethiopia indicated the chronic nature of the condition, which persisted for more than 24 months in 50% of patients diagnosed with ENL, and for more than four years in 14%; in addition, those patients with chronic ENL had a significantly increased mortality rate, which in most cases could be attributed to the prolonged use of steroids (Walker, 2014). This clearly demonstrated the need for steroid-sparing treatment in the management of severe and prolonged ENL, with thalidomide being the most effective drug in this regard.

The second development involves greater familiarity of health staff globally with the use of potentially dangerous drugs; and the use of more robust protocols for the management of drug prescriptions and oversight, so that a dangerous drug (such as thalidomide) can be used safely, when indicated. National protocols can be derived from those developed in the United States in 1998 (Zeldis, 1999). Key elements include:

- Registration of prescribers, pharmacists and patients, to control access; adequate means to keep thalidomide in a secure place, as with other dangerous drugs;
- Education of prescribers, pharmacists and patients, concerning contraceptive measures and pregnancy testing (e.g. the use of two different methods of contraception and the need for a monthly pregnancy test, as well as the availability of emergency contraception). It is also advised that contraception is used when the male partner is using thalidomide. Adequate provision of relevant supplies;
- Compliance monitoring and reporting.

3.3 Treatment of reactions: summary

Steroids remain the drug of choice for both Type 1 and Type 2 reactions. They provide significant benefit, both in the relief of symptoms and in the restoration of nerve function. There are significant adverse events, however, especially when the course of steroids is prolonged, including a mortality risk. Every effort should be made to reduce steroid dependence through the use of so-called steroid-sparing drugs.

At present, thalidomide is the most widely used steroid-sparing drug in leprosy, although it is only applicable to Type 2 reaction. Further efforts should be made to increase the availability of thalidomide to people with ENL, taking the necessary precautions to avoid the adverse events of that drug also.

Managing reactions and neuritis: Step-by-step approach

4

4.1 Principals of managing reactions and neuritis

Reactions and neuritis often occur together. Disability in leprosy is largely caused by damage to the peripheral nerves. To prevent this, it is essential that health workers have a basic understanding of nerve function and how to measure it: loss of nerve function is a sign of nerve damage and is the most important indication for steroid treatment.

Prednisolone is the most widely used steroid medication and is the mainstay of the treatment of reactions and neuritis. The inflammation that occurs during reactions is driven by the immune system, responding to the presence of *M. leprae* in the skin and nerves. There are many features of inflammation. One of the most important in this context is oedema or swelling of the tissues. The peripheral nerves are covered in a fibrous sheath that does not expand much; when oedema occurs, the pressure inside the nerve rises, leading quickly to loss of function of the nerve fibres themselves. Steroids have a broad anti-inflammatory effect, which includes a rapid reduction in oedema. When used in leprosy reactions with neuritis, the effect is often quite a dramatic improvement. Non-steroidal anti-inflammatory drugs, such as ibuprofen, do not have this effect on oedema. While they may reduce some of the pain associated with reactions, they do not help to restore nerve function.

Steroids unfortunately produce quite complex adverse events, especially if taken for long periods. These are summarized here and further discussed in more depth in the previous chapter. It should be noted at this stage that there is always a balance to be struck between using steroids for their beneficial effect in preventing disabling nerve damage and overuse leading to serious complications.

The recognition and management of reactions and nerve damage varies considerably across the world. A large number of leprosy cases, perhaps even a majority in global terms, are treated with MDT medicines in clinics that are currently not able to assess or manage reactions on the spot: patients with symptoms suggesting a reaction need to be referred to a higher level. Another group of patients are managed by health workers who are able to use basic tools to assess nerve function, and who are then able to give treatment with steroids. In some clinics, staff are trained in the use of more complex tools, including nylon monofilaments, which are more precise and allow nerve damage to be identified at an earlier stage.

While it would be ideal for all patients to be assessed and treated with the best tools, this does not happen at present for various reasons: in particular, a lack of training in the required skills and a lack of the tools or medicines needed. In this technical guide, these levels of care are explained in more detail (Table 4). This guide aims to help health staff improve their understanding and performance at their current level; and then, if conditions allow, to step up to the next level of care. Crucial limiting factors in the management of reactions in the field are the availability of corticosteroids, such as prednisolone, and nylon monofilaments to accurately test for sensory loss.

The levels depend firstly on the availability of prednisolone to treat neuritis. Albendazole should normally be given when a course of prednisolone is started, so this medicine should also be available. Similarly, nylon monofilaments are a more precise method for detecting early nerve damage. If national leprosy programmes are able to make these items available wherever MDT is provided to leprosy patients, better management of reactions is possible. A second requirement is additional training and supervision for staff who manage leprosy cases, so that they understand nerve function and are better able to test for nerve function impairment.

At every level, it is now much easier to consult a senior colleague by phone or text, and this opportunity should be used to the full, to manage each case effectively. Similarly, practicing how to use the tools available, perhaps on oneself or on a friend, can give additional confidence in the method.

Table 4: Levels of care depend on the equipment and medication that is available at the clinic

Clinical setting	Level 1 Identify possible reactions and refer	Level 2 Use simple tools to assess the patient and begin treatment	Level 3 Use more complex and more precise tools for early detection of neuritis
Staff have the time, training and nylon monofilaments for more accurate assessment			Use available tools to check for early nerve damage and treat with prednisolone
Prednisolone is available; nylon monofilaments are not available		Use a ballpoint pen to test for sensory loss; treat new episodes of neuritis with prednisolone	
Prednisolone and albendazole are not routinely available	Understand the symptoms and signs of reactions and neuritis; consult and refer		

4.2. The four steps in managing leprosy reactions

Recognition: Knowing when a reaction is present

Is the patient at high risk of a reaction?

At the time of making a diagnosis of leprosy, it is often possible to determine whether that person has a high risk of developing a leprosy reaction:



Patients at high risk of reaction should be monitored carefully while on MDT.

Does the patient have symptoms of a reaction?

Following are possible symptoms of reaction:

- Pain in the skin lesions or in the nerves;
- Numbness in the hands or feet;
- Weakness of muscles in the hands or feet;
- Inability to close the eyes properly

Are there any signs of inflammation in the skin?

Skin lesions may look red and inflamed.

There may be a slight fever.

Two types of reaction: Type 1 and Type 2

- **Type 1 reaction:**
 - The leprosy skin lesions are inflamed;
 - There may be a slight fever, but the patient doesn't feel too ill.
- **Type 2 reaction:**
 - There are several red and inflamed 1–2 cm nodules in the skin;
 - The leprosy lesions themselves are less inflamed;
 - The fever is often high; the patient feels ill; and has pain.

Questions for patients about their nerves

The following questions can be asked to the patient in whom a leprosy reaction is presumed:

- “Do you have recent pain in any of your limbs?”
- “Do you have any numbness or loss of feeling in the hands or feet?”
- “Is there any weakness in the hands or feet?”
- “Do you have difficulty closing your eyes?”

The problem of silent neuritis

Sometimes the nerves can become damaged without obvious symptoms, which is called “silent neuritis”. In order to detect this, it is advisable to check nerve function regularly during MDT. This should be done at least every three months.

Testing nerve function

Testing nerve function involves:

- (a) Testing sensation in the hands and feet (full explanation of ballpoint and monofilaments);
- (b) Testing muscle strength in the eyes, hands and feet;
- (c) Recording the results;
- (d) Interpretation of results: what do the results mean?
- (e) Periodicity of testing: how often should assessment be done?

Treatment to prevent disability

- (a) Treating a mild reaction limited to the skin;
- (b) Treating early nerve damage: steroids and the need for albendazole;
- (c) Treating a Type 2 reaction;
- (d) Recording treatment.

Follow-up: Making sure that good progress is made

- (a) Monitoring treatment and checking for side-effects of steroids;
- (b) Monitoring nerve function and other signs of the reaction;
- (c) When are additional steroids needed?
- (d) Follow-up for Type 2 reactions, using the *ENL Severity Scale*;

- (e) Management of long-term nerve damage;
- (f) Reporting on reactions: an ideal point at which to notify reaction cases is at completion of treatment. The disability grade at treatment completion should be recorded, with an indication (Yes/No) as to whether a reaction occurred at any time.

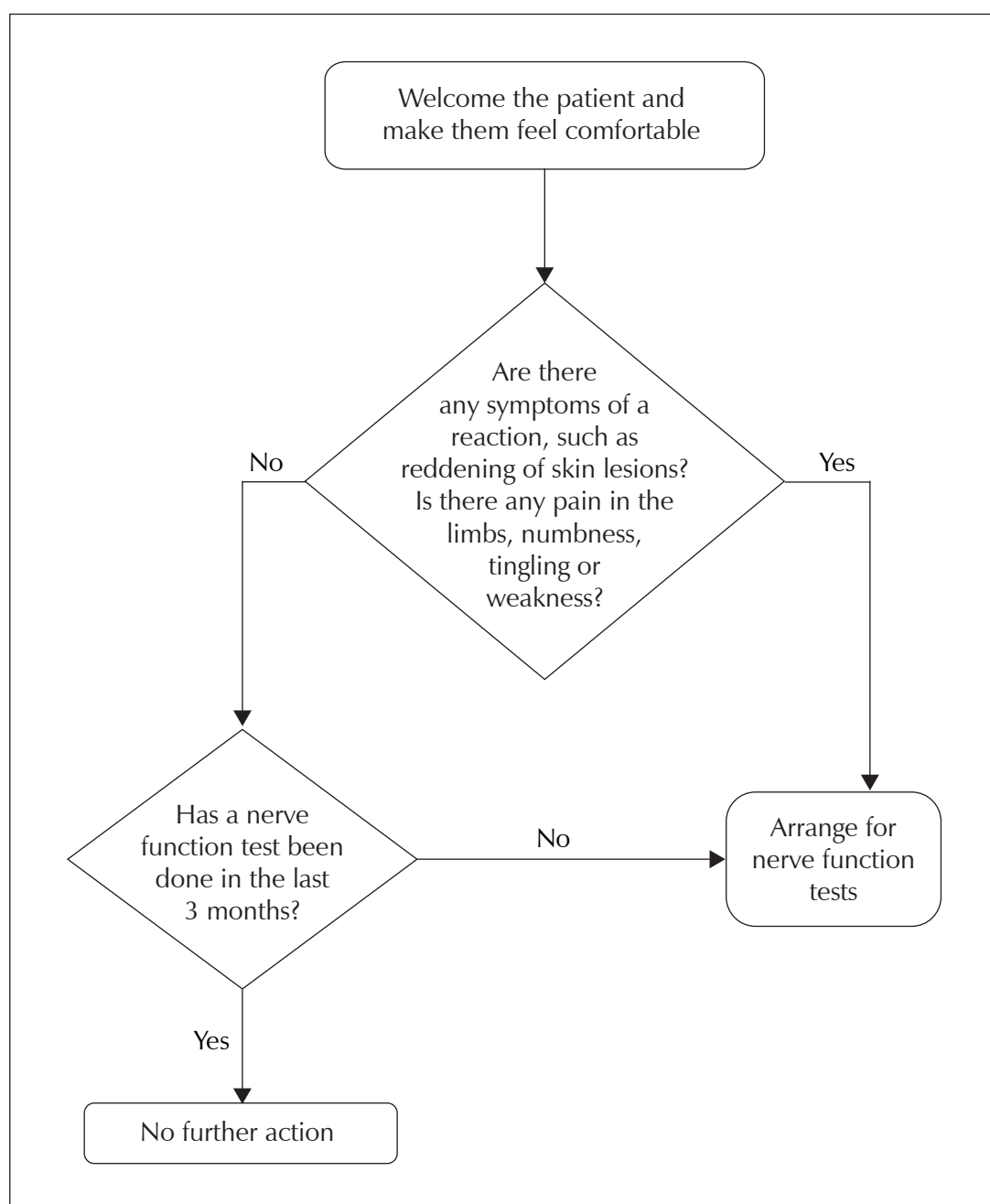
4.3 Counseling and health promotion

Informing patients about their disease and what to expect during treatment is becoming more and more important, as health awareness increases and patients are bombarded with health messages from all sides. While health promotion provides information and seeks to guide healthy behaviour, counseling seeks to understand the specific pressures that individual patients are facing, and to help them develop effective coping strategies of their own.

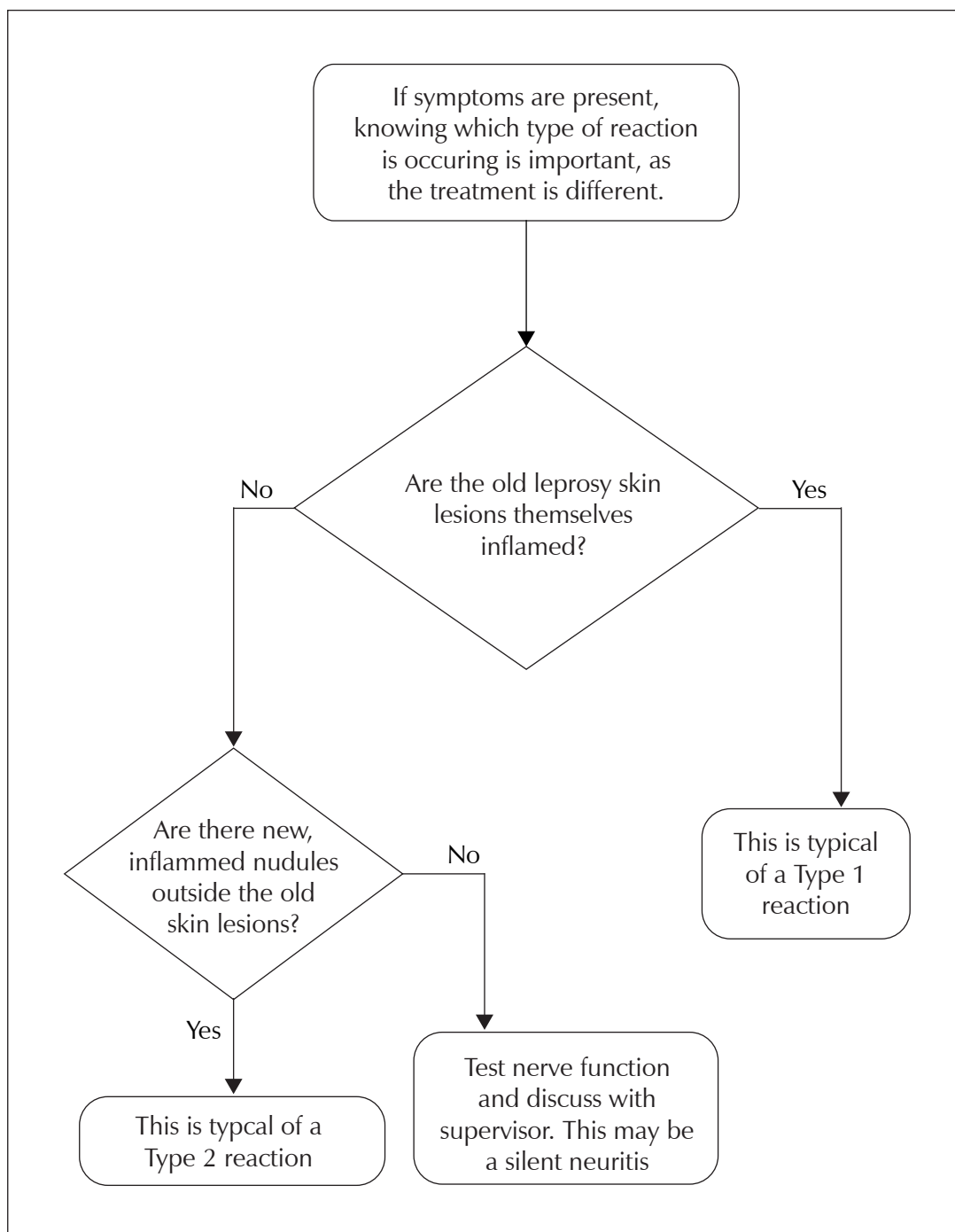
Peer counseling is proving to be an effective tool for patient care: cured patients who have themselves experienced the disease can show greater empathy and understanding. Counseling at the time of diagnosis can reassure the new patient that treatment is effective and that any worsening of symptoms can also be handled with additional treatment. Further reassurance if and when a reaction occurs can help the patient persevere with treatment.

5 Algorithms for managing persons with leprosy in a clinical setting

5.1. Algorithm 1: Recognizing when a reaction is present

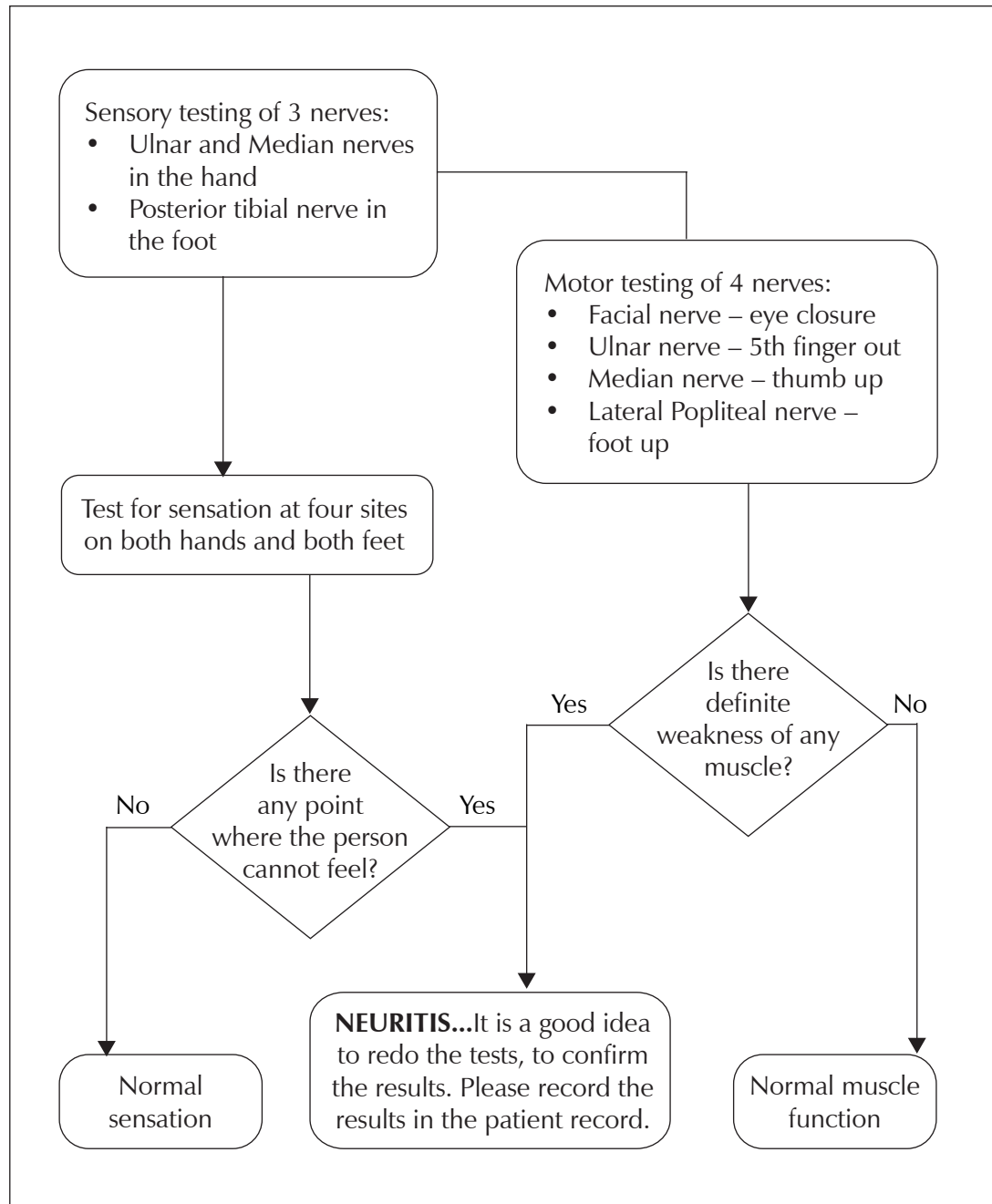


5.2. Algorithm 2: Knowing whether a reaction is Type 1 or Type 2

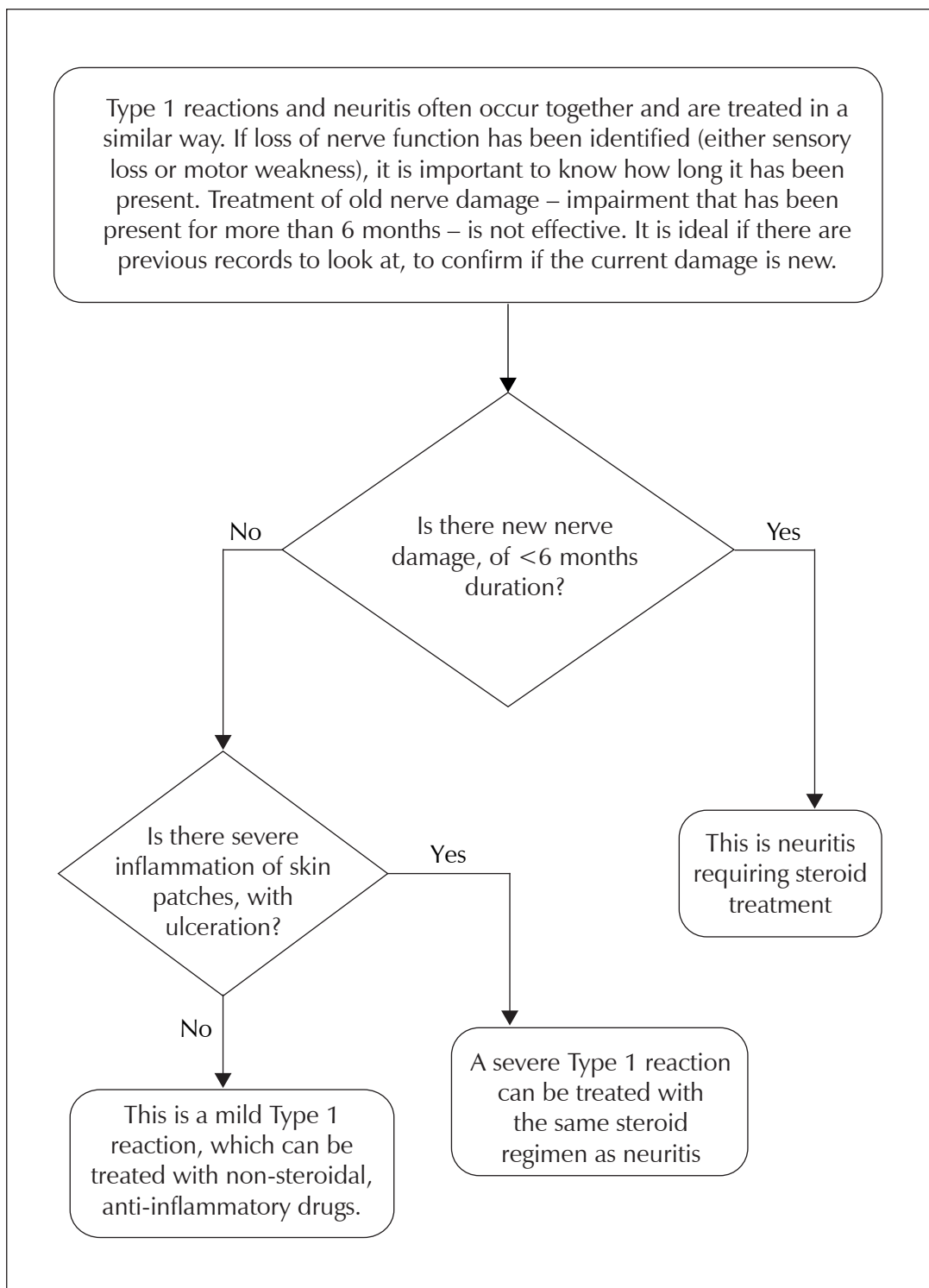


5.3. Algorithm 3: Testing nerve function

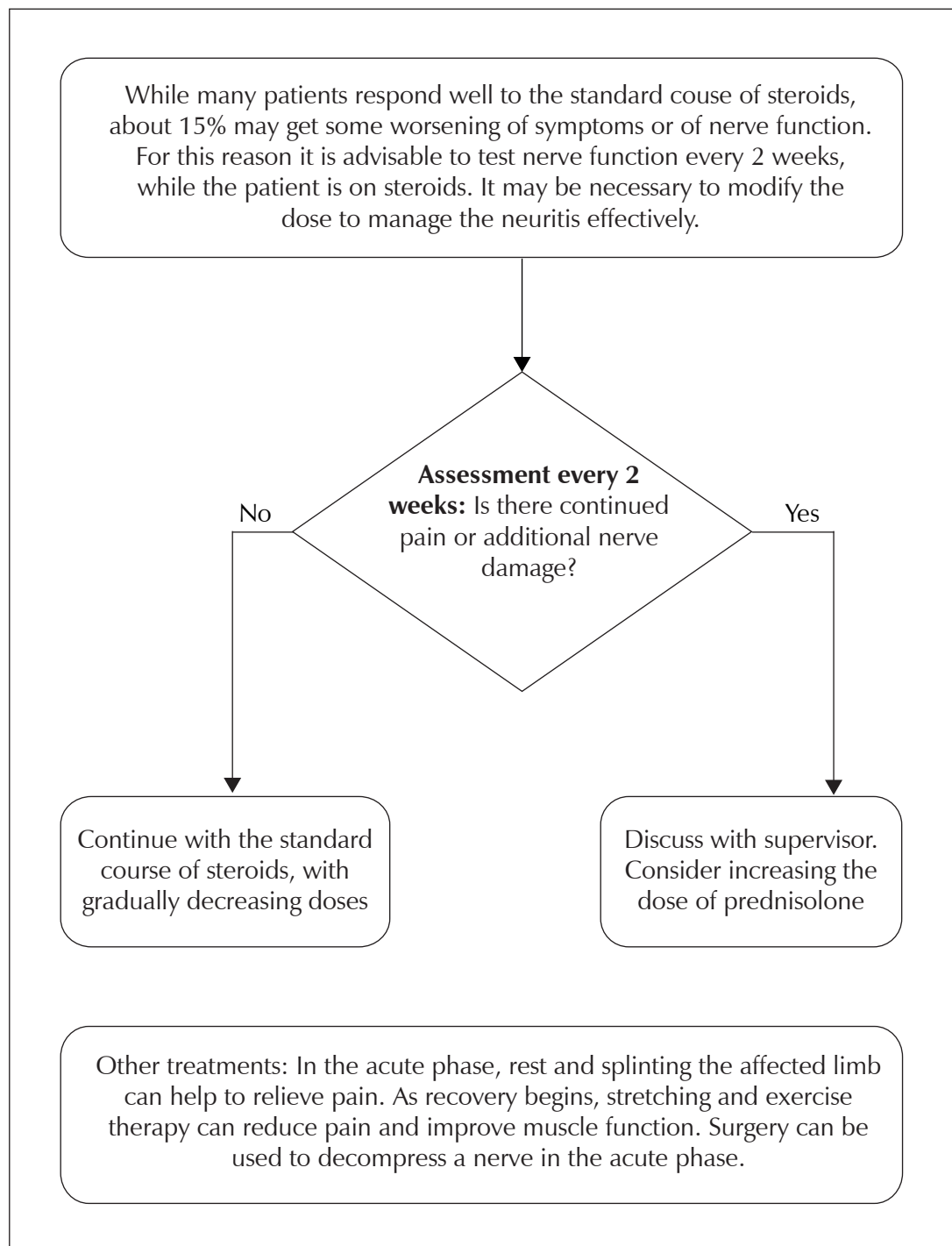
Testing nerve function involves examining first the sensory function and then the motor function of nerves likely to be damaged in leprosy.



5.4. Algorithm 4: Treating Type 1 reaction and neuritis



5.5. Algorithm 5: Follow up of patients with Type 1 reaction and neuritis



Follow-up of patients with Type 1 reactions or neuritis

In most patients, damaged nerve function recovers quickly, but further reaction episodes may occur.

If a patient experiences worsening nerve function while still on lowering doses of steroids, it is advisable to increase the dose to 30 mg daily again, and then reduce over another period of 20 weeks, according to the standard plan. If a patient has already completed one course of steroids but suffers a further episode of nerve function impairment, the same course can be started again from the beginning.

Long-term pain in the nerves or limbs: neuropathic pain

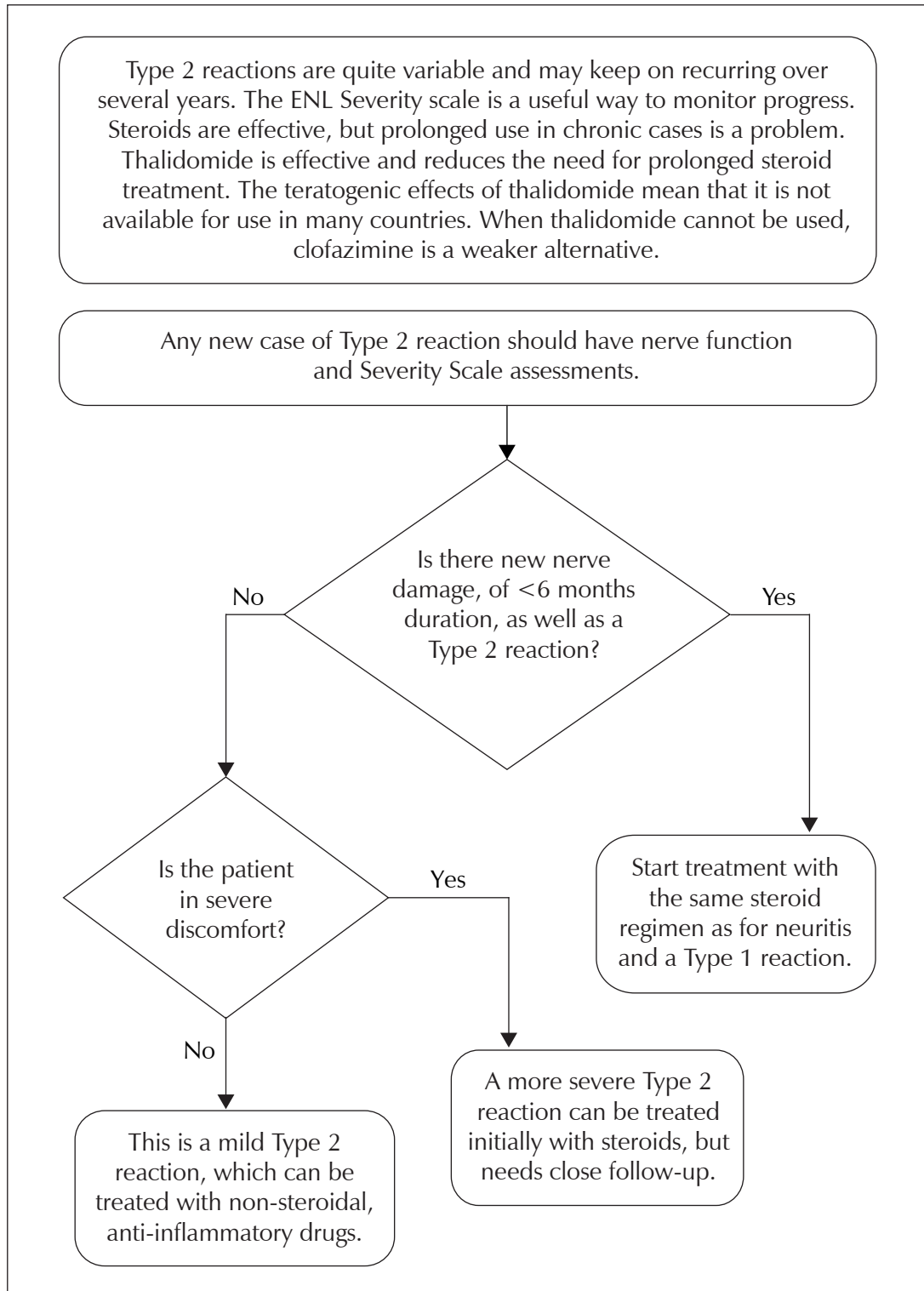
While neuritis often presents with pain, these inflammatory episodes become much less common after three years or so, once the underlying leprosy has been cured. Pain occurring later may be due to one of two reasons:

- (1) Leprosy relapse. The same inflammatory reactions can occur all over again; if the relapse can be confirmed, reactions and neuritis can be treated in the same way as before.
- (2) Neuropathic pain. In this condition, a nerve which has been previously affected by disease or trauma, acts as a locus of pain. Symptoms include tingling or burning sensations. There is minimal inflammation, so treatment with steroids is ineffective, although some other drugs may be helpful. Patients with neuropathic pain should start treatment with paracetamol, then use a non-steroidal such as ibuprofen, if necessary; other possible drugs include amitriptyline and gabapentin.

It is important to avoid continuous use of steroids in leprosy, because of the adverse events. Reactions and neuritis can be treated with the standard 20-week course, which may need to be prolonged for some weeks, in some cases.

5.6. Algorithm 6: Starting treatment for Type 2 reaction

In Type 2 reaction, longer courses of steroids are sometimes needed, but a reduced dose should always be sought by using additional drugs such as clofazimine or thalidomide. Nerve pain in patients treated years ago is most likely due to neuropathic pain, requiring different medication.



Nerve damage

It is important to monitor nerve function in Type 2 reactions. Nerve damage is less common than in a Type 1 reaction. If nerve damage does occur, it should be treated exactly as shown in Algorithm 4.

First episode of a Type 2 reaction

The first episode should be treated with analgesics or steroids, according to the severity. Frequently, there are no more episodes and no further treatment is needed.

If the response to treatment is poor, or the Type 2 reaction recurs, additional drugs are needed.

The ENL Severity Scale

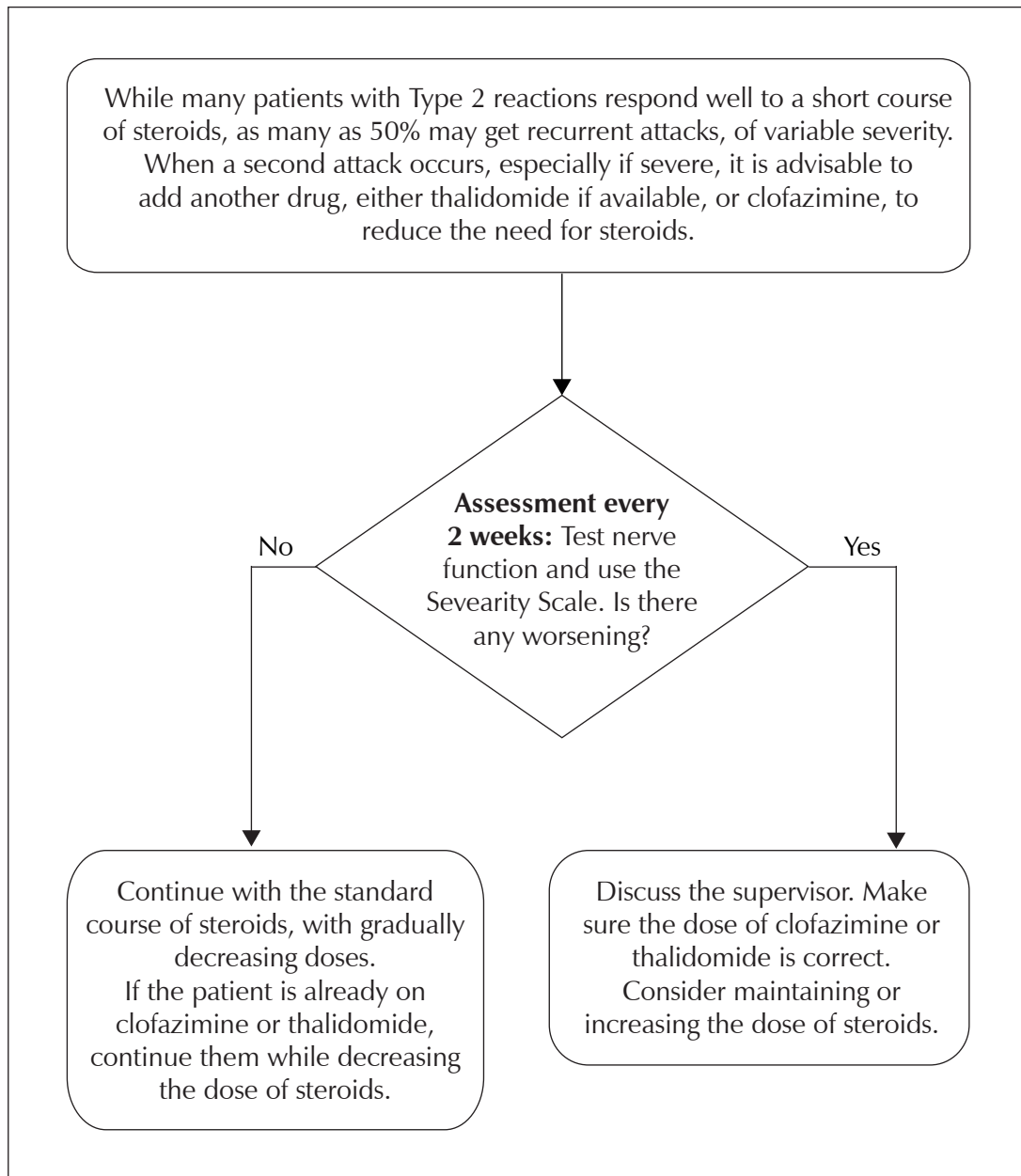
The ENL Severity Scale is provided in Annex 1 and includes a User Guide.

Ten items are given a score of 0–3 points, so the maximum possible score is 30.

The ten items are: pain; fever; number of lesions; level of inflammation; extent of skin lesions over the body; oedema; bone pain; inflammation of joints/digits; lymphadenopathy; and nerve tenderness.

Anyone having a score of 8 or more needs treatment.

5.7. Algorithm 7: Follow up of patients with Type 2 reaction



Key facts to remember

6

- Leprosy reactions are important clinical events (occurring before, during and even after completion of treatment). They can influence treatment and affect the quality of life of persons affected by leprosy.
- A reaction may occur as a single episode that is self-limiting, but in many cases recurrent episodes occur, especially in Type 2 reactions.
- All patients with reactions and neuritis should be assessed regularly, with documentation of nerve function, and Severity Scale measurements for Type 2 reactions.
- Adverse events due to MDT or drugs used for the treatment of reactions should also be documented and reported.
- Mortality associated with reactions (often related to steroid treatment) needs to be documented and reported.
- Steroids (oral prednisolone) remain the main choice for treatment of Type 1 and Type 2 reactions, and neuritis. Frontline health workers need to be trained in recognizing these conditions and either initiate treatment themselves or refer patients to other centers.
- Type 2 reaction needs to be recognized in patients and its severity measured. Patients need to be warned that this may be a chronic complication. They need treatment with steroids, but second-line drugs should be available so that the morbidity and mortality associated with steroid treatment can be reduced. National leprosy programmes should develop recommendations for second-line treatment of ENL. Use of thalidomide in treating ENL should be considered as per the WHO Technical Report Series 968, WHO Expert Committee on Leprosy Eighth Report 2012.
- Silent neuritis (also referred to as *Quiet Nerve Paralysis*) is an important cause of disabilities and is managed in exactly the same way as more overt neuritis.
- Regular nerve function assessment is required for the prevention of disabilities. It should be introduced at all health facilities treating leprosy. It should be done at start and end of MDT, every three months during MDT and at any time when there are complaints suggesting reactions and neuritis.
- Patients at high risk of developing impairments should be assessed at least every three months during MDT and until one year after release from MDT (at least 9 times over 24 months).

- Patients with NFI of less than six months duration should be treated with steroids and assessed after two weeks and then monthly until the end of the steroid course.
- A simple format for carrying out nerve function assessment is presented for use by frontline health workers to ensure regular screening of patients to detect impairments as early as possible.
- Calculation of DALYs in leprosy needs further understanding for finalizing a score considering disabilities, mortality due to reactions and discrimination against persons affected by leprosy.

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Annex 1

ENLIST ENL Severity Scale

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

SI No.	Scale item	Score				Obtained score
		0	1	2	3	
1	Visual Analogue Scale – Pain (mm)	0	1–39	40–69	70–100	
2	Fever (°C)	None (≤ 37.5 °C)	No fever now History of fever in last 7 days	37.6–38.5 °C	≥ 38.5 °C	
3	Number of ENL skin lesions	0	1–10	11–20	≥ 21	
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, 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 in one group	Pain or tenderness in ≥ 2 groups	
10	Nerve tenderness due to ENL	None	Absent if attention distracted	Present even if attention distracted	Patient withdraws limb on examination	
Total score						

User guide

The score for each item should be added to obtain the ENLIST ENL Severity Scale score (“total score”).

Mild ENL is categorized as an ENLIST ENL Severity Scale score of ≤ 8 .

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

SI No.	Scale item	Notes
1	Visual Analogue Scale –Pain	<p>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’.</p> <p>Take the measurement (in mm) using a ruler from the LEFT end of the line to the centre of the cross.</p> <p>Ensure that the line when reproduced from this document is 100 mm long.</p>
2	Fever	<p>Take temperature (in °C) using a thermometer.</p> <p>If the temperature is > 37.5 °C, then the patient has fever. If the temperature is ≤ 37.5 °C, then the patient scores 0 for this item UNLESS they have a history of fever in the last 7 days in which case they score 1. The cause of the fever does not need to be established.</p>
3	Number of ENL skin lesions	<p>Only skin lesions due to ENL are to be considered.</p>
4	Inflammation of ENL skin lesions	<p>Only skin lesions due to ENL are to be considered.</p> <p>“Complex” refers to the following type of skin lesions: vesicular, bullous, pustular, erythema multiforme-like, panniculitis, necrotic, ulcerated.</p> <p>If the participant fulfils criteria for more than one score, then the highest scoring criteria should be applied (e.g. 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).</p>
5	Extent of ENL skin lesions	<p>Only skin lesions due to ENL are to be considered.</p> <p>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.</p>
6	Peripheral oedema due to ENL	<p>The three sites to be considered are the face, hands and feet. Both feet count as one site. Both hands count as one site.</p> <p>Oedema thought to be due to treatment such as corticosteroids or thalidomide should not be counted.</p>

SI No.	Scale item	Notes
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	Only joint inflammation due to ENL is to be considered. 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, then 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. Lymph node groups on the different sides of the body are separate for example: left axillary and right axillary. Therefore, there are six 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 patient 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.

Complex skin lesions

- **Bulla:** a visible accumulation of fluid within or beneath the epidermis more than 0.5 cm;
- **Erythema multiforme-like lesions:** atypical ENL lesions resembling those of erythema multiforme; they include macular, papular or urticarial lesions, as well as the classical iris or 'target lesions'.
- **Panniculitis:** inflammation of the subcutaneous adipose tissue;
- **Pustule:** accumulation of free pus;
- **Target lesions:** 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:** a visible accumulation of fluid within or beneath the epidermis, 0.5 cm or less in diameter

Annex 2

Model Leprosy Patient Card

[Country] National Leprosy Programme

1. Registration data

Country	
State/Province	
District/County	
Health facility (name and address)	
Patient registration number	
Date of registration	

2. Personal data

Patient name	
Father's/husband's name	
Sex	<input type="checkbox"/> Male <input type="checkbox"/> Female
Year of birth (or age)	
Place of birth	
Present address	
Number of years of residence at present address	
Permanent address	
Nationality	
Telephone/mobile number	
Occupation	
Marital status	<input type="checkbox"/> Single <input type="checkbox"/> Married <input type="checkbox"/> Divorced <input type="checkbox"/> Widow(er)
Contact person (name, address, phone/mobile)	

Mode of detection	<input type="checkbox"/> Voluntary <input type="checkbox"/> Referred <input type="checkbox"/> Other <input type="checkbox"/> Contact survey <input type="checkbox"/> Other survey
Previous treatment details	(specify drug regimen, duration, year of treatment)
Type of patient	<input type="checkbox"/> New <input type="checkbox"/> Transferred-in <input type="checkbox"/> Relapse after PB-MDT <input type="checkbox"/> Relapse after MB-MDT <input type="checkbox"/> Re-admission after dapsone monotherapy <input type="checkbox"/> Treatment after default
Any known leprosy case in family?	<input type="checkbox"/> Yes <input type="checkbox"/> No

Details of household contacts

Sl No.	Name	Sex	Year of birth (or age)	Relationship with patient
1				
2				
3				
4				
5				
6				

3. Disease status (Initial)

Presenting symptom(s)	<input type="checkbox"/> Patch(es) <input type="checkbox"/> Visible impairment <input type="checkbox"/> Reaction
	<input type="checkbox"/> Other (specify):
Duration of presenting symptom(s)	_____ months/years

Number of skin patches	<input type="checkbox"/> 1 <input type="checkbox"/> 2–5 <input type="checkbox"/> > 5	
Reaction	<input type="checkbox"/> No	
	<input type="checkbox"/> Yes	<input type="checkbox"/> Type 1 reaction (reversal reaction)
		<input type="checkbox"/> Type 2 reaction (ENL)

Nerve status

Status	Ulnar		Median		Radial		Lateral popliteal		Posterior tibial	
	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left
Thickening	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Pain	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Tenderness	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

WHO disability grading

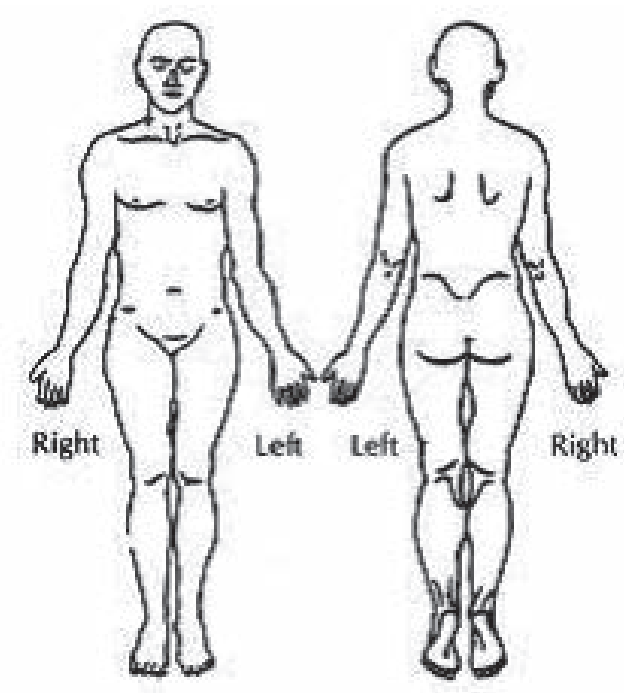
	Eye	Hand	Foot
Right			
Left			

EHF Score

Disease type

<input type="checkbox"/> PB
<input type="checkbox"/> MB

Body charting (Date: ___ / ___ / 20___)



4. Details of other conditions

Medical history	<input type="checkbox"/> Diabetes <input type="checkbox"/> Hepatitis <input type="checkbox"/> Tuberculosis <input type="checkbox"/> HIV/AIDS <input type="checkbox"/> Any other disease (specify):
-----------------	---

Other conditions	<input type="checkbox"/> Pregnancy <input type="checkbox"/> Drug allergy
------------------	---

General physical examination

Body weight	_____ kg
-------------	----------

5. Treatment details

Drug regimen prescribed	<input type="checkbox"/> PB-MDT <input type="checkbox"/> 3-drug MDT <input type="checkbox"/> 2-drug MDT
	<input type="checkbox"/> MB-MDT (3-drug MDT)
	<input type="checkbox"/> Any other regimen (specify):

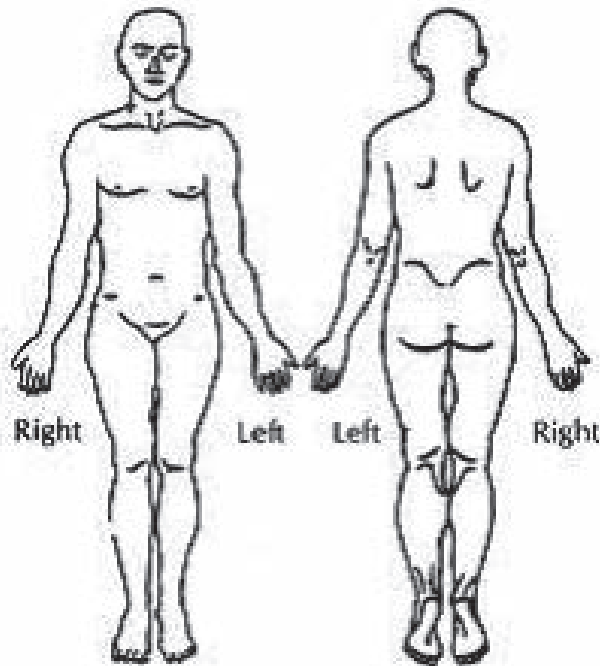
Treatment monthly attendance

Dose (pulse)	1	2	3	4	5	6
Date						
Dose (pulse)	7	8	9	10	11	12
Date						

Treatment outcome

Type of outcome	<input type="checkbox"/> Treatment completed <input type="checkbox"/> Defaulted <input type="checkbox"/> Died <input type="checkbox"/> Transfer out <input type="checkbox"/> Change of classification
Date	_____ / _____ / 20 ____

Body charting (at completion of treatment). Date: ____ / ____ / 20 ____



6. Bacteriological examination (slit-skin smear)

Date				
Number of sites taken				
Slit-skin smear result				

7. Assessment of disability and nerve function

Voluntary Muscle Test

























Right							Left					
						← Date →						
						Vision (0 / 1 / 2)						
						Light closure lid gap (in mm)						
						Blink reflex (present / absent)						
						Little finger out						
						Thumb up						
						Wrist extension						
						Foot up						
						Disability grade hands						
						Disability grade feet						
						Disability grade eyes						

Muscle power: S = strong; W = weak; P = paralysis


Score of vision (counting fingers at 6 metres): 0 = normal; 1 = blurring vision; 2 = unable to count fingers




Date						
Max disability grade						
EHF Score						
Signature of assessor						

Sensory testing

Date / Assessor	Palm		Sole		Comments
	Right	Left	Right	Left	
					
					
					
					
					
					

Key : (Put these marks/icons on the site where lesion is seen)

Sensation Present within 3 cm ✓ Contracture S Scar/Callus 

Anaesthesia X Wound  Shortening level  Crack 

Leprosy (Hansen Disease) is an infectious disease caused by *Mycobacterium Leprae*. More than 200 000 new cases occur every year. Multidrug therapy constitutes the main treatment strategy. During the course of the disease, nearly 50% of the patients experience immunological reactions, characterized by nerve damage. Left untreated or improperly managed, these may lead to visible deformities and disabilities. Prevention of disabilities is an important component of the management of leprosy and a means to improve the quality of life of the person affected.

Early identification and treatment of reactions remain challenges for frontline health workers. This technical guidance aims to address these challenges. The simple algorithms included in this document highlight how to recognize and manage reactions in leprosy.