

Leprosy Pathophysiology, Clinical Features and Management

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How to cite this article:

Amrutha J.S., Ravi Kumar Chittoria. Leprosy Pathophysiology, Clinical Features and Management. J Microbiol Relat Res. 2023;9(2): 53-70.

Abstract

Leprosy, also known as Hansen's disease, is a chronic infectious disease caused by the bacterium *Mycobacterium leprae*. Clinical features depend on the immune status of the patient. Proper management of leprosy involves a comprehensive approach that includes diagnosis, treatment, rehabilitation, and prevention of disabilities.

Keywords: Leprosy; Pathophysiology; Paucibacillary; Multibacillary; Multidrug therapy; Hansen disease; *Mycobacteria leprae*.

INTRODUCTION

Hansen disease, or leprosy, is a chronic granulomatous bacterial infection that primarily affects the skin and peripheral nerves. Though nonfatal, leprosy is one of the most common causes of non-traumatic peripheral neuropathy worldwide. DNA taken from the shrouded remains of a man discovered in a tomb next to the old city of Jerusalem shows him to be the earliest human proven to have suffered from leprosy. The remains

were dated by radiocarbon methods to 1-50 A.D.¹ The disease probably originated in Egypt and other Middle Eastern countries as early as 2400 BC. The disease is caused by an obligate intracellular bacillus, *Mycobacterium leprae*, which was identified in the 19th century by the Norwegian physician Gerhard Henrik Armauer Hansen.² The clinical presentation and histopathologic changes depend on the patient's immune status at the time of infection and over the natural course of the disease. Diagnosis is currently based on 3 cardinal signs specified by the World Health Organization (WHO): hypopigmented or erythematous macules with sensory loss, thickened peripheral nerves, and a positive acid-alcohol fast smear or skin biopsy.³ Modern multidrug therapy and new antibiotics of proven efficacy have made it possible to meet the WHO's targeted reduction in the incidence of *M leprae* infection to a single case per 10,000 inhabitants in countries where the disease is endemic. A new pathogen, *Mycobacterium lepromatosis*, has recently been found to cause endemic disease in Mexico and the Caribbean.⁴ These developments call for new medical perspectives on how to cope with a problem that is still far from resolved.

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Received on: 17.01.2023

Accepted on: 19.02.2023

Epidemiology

Mycobacterial infection is endemic in more than 15 countries, but 83% of the cases are found in 3 countries: India, Brazil, and Birmania.^{3,5} India registered 64% of all cases. At the beginning of the 1990s, the WHO proposed their "final push strategy" for leprosy with the clear purpose of elimination, defined as a prevalence below a single case per 10,000 inhabitants in endemic regions.⁵ Countries like the Democratic Republic of the Congo and Mozambique reported reaching the goal, but the disease remains highly prevalent in other parts of the world.

Pathophysiology

M leprae is an acid-alcohol-fast, gram-positive obligate intracellular bacillus that shows tropism for cells of the reticuloendothelial system and peripheral nervous system (notably Schwann cells). M leprae organisms are slightly curved, measure from 1 to 8 μm in length and 0.3 μm in diameter. They replicate by binary fission. The leprosy bacillus has a predilection for macrophages, collecting in intracellular groups called globi. Although never cultured in vitro, M leprae has been grown in the foot pads of 9-banded armadillos. Replication takes from 11 to 13 days. Predisposed to infect cold areas of the body such as the skin, nasal mucosa and peripheral nerves (Especially superficial ones Figure:1), M leprae grows best at temperatures

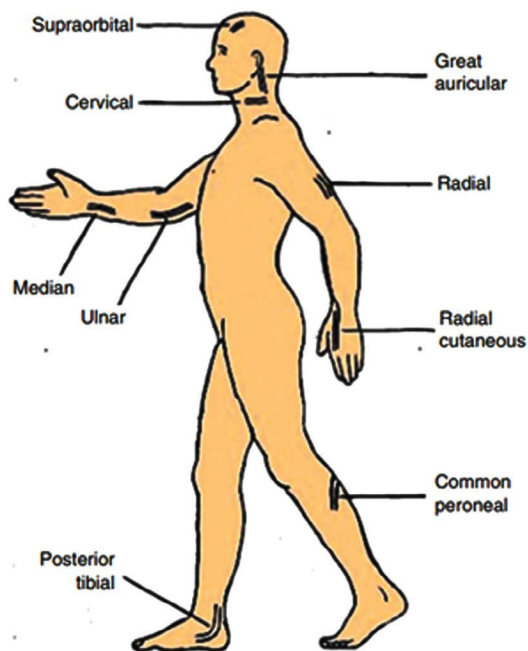


Fig. 1: Sites of predilection of peripheral nerve involvement with enlargement of nerves

between 27 °C and 30 °C. It has a capsule and a cell wall.⁶ The capsule is made up of a large number of lipids, mainly phthiocerol dimycocerosate and phenolic glucolipid-1, which is the target of an intense immunoglobulin M-mediated humoral immune response.^{3,6,7} Another important component of the cell wall is lipoarabinomannan, which is an antigen for the macrophage.

Clinical manifestations depend on the patient's immune status. A role for genetics, associated with a susceptibility locus at chromosome 10p13 near the mannose receptor 1 gene, has now been suggested.⁸ In addition, class II HLA/major histocompatibility complex genes at chromosome 6 have also been implicated in the type of leprosy a patient develops. An intense, organized, specific cellular response is seen in cases at the tuberculoid pole, whereas an absence of a specific immune response is seen at the opposite pole, in lepromatous leprosy. The lepromatous form affects the skin and peripheral nerves, causing well-defined infiltrated plaques that are annular or ovoid. These lesions are usually anesthetic and may affect any area of the body. Biopsy of the skin and region surrounding nerves reveals granulomas with an abundance of epithelioid histiocytes, multinucleated giant cells, and CD4+ T cells that secrete interferon- γ . One of the most important findings is the scarcity or absence of acid-alcohol-fast bacilli, although a few may sometimes be observed. The immunologic and clinical situation is different in lepromatous leprosy as there is no specific immune response. Bacilli proliferate in the tissues and foamy macrophages can be observed, few CD4+ and CD8+ T cells are present, and granulomas do not usually form. Reactions are related to immune system changes, such as those caused by antileprosy medication, stress, or pregnancy.

Transmission

Two exit routes of M. leprae from the human body are often described as the skin and the nasal mucosa. Lepromatous cases show large numbers of organisms deep in the dermis. Although there are reports of acid-fast bacilli being found in the desquamating epithelium of the skin, there are reports that no acid-fast bacilli were found in the epidermis, even after examining a very large number of specimens from patients and contacts.⁹ However, fairly large numbers of M. leprae were found in the superficial keratin layer of the skin of lepromatous leprosy patients, suggesting that the organism could exit along with the sebaceous secretions. Majority of lepromatous patients show

leprosy bacilli in their nasal secretions as collected through blowing the nose.¹⁰ The entry route of *M. leprae* into the human body is also not definitively known. The skin and the upper respiratory tract are most likely. The minimum incubation period reported is a few weeks and the maximum incubation period reported is as long as 30 years with average incubation period is between three and ten years.

Schwann cells (SCs) are a major target for infection by *M. leprae* leading to injury of the nerve, demyelination, and consequent disability. Binding of *M. leprae* to SCs induces demyelination and loss of axonal conductance. Macrophages are one of the most abundant host cells to come in contact with mycobacteria. Phagocytosis of *M. leprae* by monocyte-derived macrophages can be mediated by complement receptors CR1 (CD35), CR3 (CD11b/CD18), and CR4 (CD11c/CD18) and is regulated by protein kinase.^{11,12}

Table 2: Histopathological classification of leprosy

	TT	BT	BB	BL	LL
Grenz Zone	-	+	+	+	+
Epithelioid granuloma	+++ (well formed)	++ (less well developed)	± (variable)	-	-
Foamy macrophages	-	-	-	++ (focal/nodular)	+++ (diffuse)
Location of granuloma	Perineural, perivascular	Perineural, perivascular, periappendageal	Perivascular	Perivascular	Diffuse
Langhans giant cells	+++ (large well developed)	++ (smaller)	±	Rare	-
Lymphocytes	+++ (periphery of granuloma)	+ (within granuloma, when present)	+	++ (seen throughout the macrophage granuloma)	+ (focal aggregates)
Acid-fast bacilli (AFB)	±	±	+	++	+++ Globi

II. Indian Classification

It includes six groups that have maculo-anesthetic (MA) and pure neuritic as separate categories. The main drawback was the classification was not entirely clinical and its usefulness at all levels of leprosy workers was doubtful. But it adds the pure neuritic leprosy cases which were not in the Ridley-Jopling classification.

1. Lepromatous (L)
2. Tuberculoid (T)
3. Maculo-anesthetic (MA)
4. Polyneuritic (P)
5. Borderline (B)
6. Indeterminate (I)

Classification

Types:

- I. Madrid classification
- II. Indian
- III. New IAL
- IV. Ridley-Jopling
- V. WHO classification

I. Ridley-Jopling Classification

Defined five groups based on clinical, bacteriological, histological, and immunological features.¹³ (Table 2)

1. Tuberculoid leprosy (TT)
2. Borderline tuberculoid (BT)
3. Borderline borderline (BB)
4. Borderline lepromatous (BL)
5. Lepromatous leprosy (LL)

III. New IAL Classification

A modification of Indian classification has been adopted by IAL where maculoanesthetic (MA) leprosy was merged with tuberculoid (T) leprosy.

1. Lepromatous (L)
2. Tuberculoid (T)
3. Polyneuritic (P)
4. Borderline (B)
5. Indeterminate (I)

IV. WHO Classification (1988)

It was the most important classification of the disease for any treating leprologist. The patients were categorized depending upon whether slit skin smears demonstrate any bacilli or not.

1. **Paucibacillary leprosy (PB):** Only smear negative cases and include indeterminate (I), tuberculoid (T), and borderline tuberculoid (BT) cases under Ridley-Jopling.
2. **Multibacillary leprosy (MB):** All smear positive cases and mid-borderline (BB), borderline lepromatous (BL), and lepromatous (LL) types under Ridley-Jopling classification.

V. WHO Classification (1998)

In 1998, the WHO categorized PB and MB leprosy depending on the number of skin lesions to overcome the operational problem of slit skin smear.

1. Paucibacillary single lesion leprosy (SLPB)
2. Paucibacillary leprosy (PB) (two to five skin lesions)

Table 1: NLEP classification of paucibacillary and multibacillary leprosy

Characteristics	PB	MB
Skin lesions	One to five lesions (including single nerve lesion if present)	Six and above
Peripheral nerve involvement	No nerve/only one nerve with or without one to five lesions	More than one nerve irrespective of number of skin lesion
Skin smears	Negative at all sites	Positive at any site

ACUTE REACTIONS

Erythema nodosumleprosum (type 2 reaction) is accompanied by systemic symptoms with changes in the patient's general state of health: fatigue, weakness, fever, joint pain, and weight loss. This leprosy reaction develops in around 60% of patients with lepromatous leprosy and may recur several times along the course of disease. Painful nodules appear, mainly on the lower limbs but occasionally on the trunk. The course of these nodules is subacute. A variant of a type 2 leprosy reaction causes necrotic erythema, or Lucio's phenomenon, which consists of red congestive macules that progress to blisters and necrotic slough, followed by atrophic scarring. Immune complex deposition is the mechanism of action. The relationship between Lucio's phenomenon and M lepromatosis is under study.

A reversal reaction (type 1) can develop in interpolar cases and is associated with hormonal changes, such as occur in the puerperium, or with drug treatments, particularly antileprosy regimens. This antigenic reaction is caused by variations in the patient's immune status and is due to a cell mediated

3. Multibacillary leprosy (MB) (six or more skin lesions and all smear-positive cases)

VI. Current WHO Classification

For field workers, the WHO has classified leprosy based on the number of skin lesions for treatment purposes.

VII. Classification under NLEP, India (2009)

This classification is currently used in India for treatment purposes. It considers the number of nerve involvement along with skin lesion count while categorizing PB and MB leprosy. (Table 1). The main advantage includes early diagnosis of pure neuritic leprosy which constitutes around 4-5 percent of all leprosy cases in our country

hypersensitivity mechanism that develops within months of starting treatment or after treatment has stopped. Typical manifestations are erythematous macules with a congestive appearance and blisters, ulceration, and/or necrosis. An important aspect to watch for in these patients is neuritis. Timely start of effective treatment, before irreversible damage has occurred, is essential.

Clinical findings and Examination

Clinical examination includes the following steps:

- A. General examination
- B. Cutaneous examination
- C. Examination of peripheral nerves
- D. Examination of musculoskeletal system
- E. Mucosal examination
- F. Genital examination
- G. Other systemic examination

A. General Examination

A thorough general physical examination should be done to check pallor, icterus, edema, lymphadenopathy, pulse rate, blood pressure,

temperature, and respiratory rate. The general condition of the patient should be assessed. If the patient is acutely ill with fever, arthralgia, and myalgia, type 2 leprosy reaction (T2R) or severe type 1 leprosy reaction (T1R) should be suspected and cutaneous examination should be directed to confirm those. Bilateral pedal edema is often seen in lepromatous leprosy patients, sudden onset of edema of hands and feet suggestive of T1R, generalized edema, widespread tender lymphadenopathy is associated with T2R.

Tachycardia may be noted in patients with reactions. Hypertension in patients with leprosy indicates chronic renal impairment due to repeated T2R or renal amyloidosis.

B. Cutaneous Examination

While doing the skin examination the patient must be stripped as far as possible to examine the entire skin surface, after ensuring privacy. It is preferable to examine the patient under direct sunlight. A thorough inspection should be carried out to rule out diffuse fine and coarse cutaneous infiltration over the face, back, extensor aspects of upper and lower limbs, evident by shiny erythematous or brownish in dark skin, sparse body hair, prominent follicular openings. All the above skin features are indicative of early LL. Later on due to progressive nature of the disease, if remain undiagnosed and untreated, the ill-defined macules become diffuse infiltrative and already existing infiltrative skin becomes more thickened with appearance of papules, plaques and nodules, particularly on face with thick skinfolds and nodularity (leonine facies). Depressed nasal bridge, sparse beard, and moustache, unilateral or bilateral gynecomastia in males are to be meticulously checked. Diffuse brownish pigmentation of skin and conjunctiva indicates treatment with clofazimine, either currently or in the recent past.

While doing the cutaneous examination, the following points should be carefully looked for;

Number of Skin Lesions

Total number of skin lesions may be one or few or innumerable. The calculation of total number of skin lesions is required to classify the disease as paucibacillary or multibacillary.

The Distribution of Skin Lesions

To see whether the lesions are symmetrical or asymmetrical. Asymmetry in distribution indicates borderline spectrum of the disease and bilaterally symmetrical distribution indicates LL spectrum.

Examination of Individual Skin Lesion

Morphology: Macules / Patches / papules / plaques / nodules / vesicles / bulla / ulcer.

Size: Individual lesions may be small or large in the tuberculoid spectrum [TT, BT] or they may be small and innumerable in BL and LL. Widespread innumerable ill-defined macules may coalesce to form diffuse infiltration, papules, nodules are suggestive of LL spectrum of disease

Shape: Regular (round/oval), irregular/bizarre, annular.

Margin/Edge of Skin Lesions: The margin (in flat lesions) and edge (in raised lesions) are well defined towards tuberculoid end (TT), partially or irregularly defined in BT lesions. Many times the edge is sloppier inwards in TT and BT and abrupt outwards and it is just the opposite in BB called an inverted saucer shaped appearance (outer sloppy and inner abrupt

Satellite Lesions: Presence of pseudopodia and satellite lesions along the margins/edge of large lesions are suggestive of a BT lesion. Commonly these satellites lesions present near the irregular border of the primary lesions

Color of Lesion: Hypopigmented, coppery-red, skin-colored, or erythematous. During Type 1 Reaction (T1R) phase some or all of the old lesions may become reddish, swollen, and edematous. Fresh shiny and reddish new skin lesions may come up during T1R.

Surface: Dry, scaly in TT/BT type, smooth and shiny in BB/BL types, edematous, ulcerated, necrotic in reaction phase of borderline spectrum. Look for presence/ sparseness/absence of hair.

Tenderness: Tenderness over the existing lesions suggests T1R.

Anesthesia: Anesthesia is always present over the skin lesions in tuberculoid spectrum of leprosy, hypoesthesia (certain degree of impairment of sensation) on BT and BB skin lesions whereas no sensory loss observed over the lesions of lepromatous leprosy (Fig. 3, 4). However, due to



Fig. 3: (a) absent corneal reflex, (b) hypopigmented anaesthetic patch



Fig. 4: Hand deformities : claw hand, bananafingers, mitten hands

bilateral peripheral nerve involvement, there will be glove and stocking type of anesthesia lately felt in LL. In the tuberculoid and borderline spectrum, in addition to sensory loss over the skin lesions, there may be loss of sensation over areas other than skin lesions supplied by the involved peripheral and cutaneous nerve. Touch sensation using a wisp of cotton-wool or nylon monofilaments, pain sensation through pinpricks, and temperature sensation using hot/cold water in test tubes should be performed. While testing sensation, the examiner should proceed from uninvolved to the involved skin. The normal range of accuracy on the hand is within 1 cm, the face 2 cm, and up to 7 cm on the back and buttock. Hypoesthesia can be detected when the patient feels less skin lesion than the corresponding area on the other side of the body. The WHO recommends sensory testing sites on palms and soles (10 sites on each side) for disability grading. The signs of autonomic nerve damage are loss of sweating, which is shown by dryness, callosities, and fissuring in the patient. In

case of doubtful lesions, anhidrosis can be detected by the ninhydrin test or pilocarpinetest.

Trophic ulcer: Trophic ulcer if present should be examined for evidence of secondary bacterial infections such as discharge, foul smell, and dirty slough.

C. Examination of Peripheral Nerves

The cutaneous nerves can be palpated near the skin lesions, especially around the plaques of TT/ BT leprosy. However, certain peripheral nerves are commonly affected in leprosy at certain sites and can be palpated at those sites. The common peripheral nerves affected are Ulnar, Median, Radial, Cutaneous branch of the radial, Common peroneal, Posterior tibial, Great auricular nerve, Supraorbital, and Supra trochlear nerve (Figure 1, 2, Table 8). Before palpating the peripheral nerves few points should be kept in mind such as

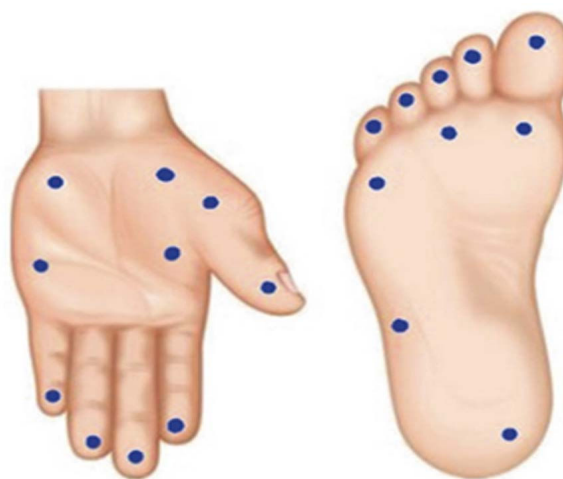


Fig. 2: WHO recommended sensory testing sites in palms and soles

Table 8: Examination of peripheral nerves

Ulnar nerve	The patient should face the examiner and sit or stand with the elbow flexed at 90°. To examine the right ulnar nerve, the examiner should hold the right hand of the patient. With the left hand little finger, he will locate the nerve in the ulnar groove (olecranon groove) on the medial epicondyle of humerus and with other fingers, and he will palpate the nerve upward along the medial aspect of the arm.
Radial nerve	The position of the patient will be the same as that of ulnar nerve palpation. To examine the right radial nerve, the examiner will roll the nerve in the spiral groove on the humerus, posterior to the deltoid insertion with left-hand fingers.
Median nerve	The examiner should hold the wrist of the patient in supination. To examine the right median nerve, the examiner should hold the patient's right hand with his left hand. With right hand fingers, he will roll across the center of the wrist. The enlarged nerve can be palpated proximal to the wrist under the palmaris longus tendon.
Radial cutaneous nerve	Patient is asked to extend the thumb to make the anatomical snuffbox visible the examiner can roll the nerve against the lateral border of radius just proximal to the wrist.
Lateral popliteal nerve	Patient is asked to sit with legs hanging freely. The examiner should stabilize the knee by placing his thumbs on the upper border of patella on both sides and the nerve can be rolled with the pulp of fingers, against the neck of the fibula.

table cont....

Sural nerve	The patient is asked to be in a standing or prone position. The nerve to be palpated in the posterior aspect of leg between the two bellies of gastrocnemius above and tendo-achilles below.
Posterior tibial nerve	The patient should be standing or sitting on bed with knee flexed. The nerve can be palpated by rolling the fingers in the medial aspect of the ankle (deep flexor retinaculum) posterior and inferior to the medial malleolus
Anterior tibial nerve	Patient is asked to sit on bed with legs straight and extend the great toe to make the extensor hallucis longus tendon stand out. The nerve can be palpated by rolling fingers on the dorsum of foot, lateral to the tendon of extensor hallucis longus and dorsalis pedis artery.
Supraorbital nerve	The patient should face the examiner in a standing or sitting position. Run the thumbs across the forehead from the midline laterally. The nerve can be palpated in the supraorbital notch at the junction of medial one-third and lateral two-thirds of supraorbital ridge.
Supratrochlear nerve	It is to be palpated medial to the supraorbital nerve
Infraorbital nerve	The nerve can be palpated in the infraorbital foramen, just below the medial part of inferior orbital margin.
Great auricular nerve	The nerve is easily visible across the sternomastoid muscle when the head is turned to the opposite side. May be palpated with fingers on the lateral side of the neck crossing the sternomastoid muscle.
Clavicular nerves	Clavicular nerves can be palpated along the shafts of both clavicles.

1. Nerves should be palpated gently (pulp of the finger should be used instead of fingertip) without hurting the patient.
2. Tender or not? Neuritis is much more common in T1R.
3. Nerve is palpable or not? Large peripheral nerve trunks are usually not palpable in the indeterminate and TT spectrum of the disease.
4. If the nerve is palpable, then whether it is unilateral or bilateral? Each nerve should be palpated on both sides for comparison. Asymmetry in nerve enlargement is a feature of the borderline spectrum of leprosy.
5. Extent of the nerve thickness in its course.
6. Look for consistency of the nerve.
7. Presence of any abscess or nodularity (fusiform, diffuse swelling).
8. Presence of any tingling sensation along the nerve course.

D. Examination of Musculoskeletal System

Detailed examination of the musculoskeletal system should be done for a definite diagnosis of leprosy. Before going to the motor examination proper a thorough inspection should be carried out to find any deformity like the collapse of the ridge of the nose (destruction of anterior nasal spine), destruction of alar nasi, loss of upper incisor teeth, wrist drop, claw hand, gait abnormality (high stepping gait), foot drop and claw toes.

MOTOR EXAMINATION

During motor examination, certain things should

be carefully looked at such as if there are any difficulties in walking or in using hands, deformity, or any other signs of muscle weakness, paralysis, or wasting. The six grades for VMT [Medical Research Council (MRC) scale] in higher centers are as follows:

- **Grade 0:** No movement is observed.
- **Grade 1:** Flicker of movement or fasciculation are observed.
- **Grade 2:** Active movement when the resistance of gravity is eliminated.
- **Grade 3:** Muscle strength is reduced but movement possible without resistance.
- **Grade 4:** Muscle strength is reduced but muscle contraction against slight resistance.
- **Grade 5:** Normal power (muscle contracts normally against full resistance)

E. Mucosal Examination

Examination of mucosa in leprosy clinics is often neglected. Meticulous examination of nasal, ocular and oral mucosa often gives clues to the definite diagnosis of leprosy.

Nasal Mucosa Examination: Look for crusts, bleeding from nose and septal perforation.

Oral Mucosa Examination: Oral cavity involvement is more common in multibacillary leprosy compared with paucibacillary disease. Diffuse enlargement of lips, nodular lesions over the anterior part of the tongue, giving a pavement-stone appearance, swollen uvula, involvement of gums in the form of gingivitis, periodontitis and periodontoclasia may occur in leprosy

Ocular Examination: Look for width of the

palpebral fissure, frequency of blinking, loss of or sparse eyebrow, loss of eyelashes, trichiasis, redness of eyes, and pterygium.

Test for Lagophthalmos: Ask the patient to close the eyes and if there is a space between the upper and lower eyelid margins, is suggestive of lid retraction or lagophthalmos. Ask the patient to look straight. The examiner will approach the patient from one side and touch the cornea, 2 mm inside the limbus at the 6 o'clock position gently with a clean wisp of cotton wool. Normally there should be a brisk blink response. The unilateral absence of corneal reflex may be because of the involvement of ophthalmic nerve (trigeminal) due to a same-sided BT lesion around eye. Bilateral loss of corneal reflex indicates damage to corneal nerves that may be due to advanced LL disease.

F. External Genital Examination

In the case of male patient, examine the testis for size and consistency, tenderness, and testicular sensation.

G. Other Systemic Examination

The lymph-nodes, internal organs like liver, kidney, larynx, and joints are usually involved in lepromatous leprosy and T2R

DIAGNOSIS

Majority of leprosy cases can be diagnosed clinically by eliciting cardinal signs of leprosy.

Cardinal Signs of Leprosy

- Anaesthetic patch
- Skin smear +
- Thickened peripheral nerves

However, some cases of leprosy do not manifest with visible skin patches or nodules but present with changes in the skin like redness, swelling and mild thickening of skin. Such cases with infiltration of the skin are generally multibacillary with positive skin smears. They represent what is called as the 'leprosy of consequence' as they transmit the disease before adequate treatment is initiated. In such cases slit skin smear examination will help in confirmation of diagnosis. On the other hand some of the cases of leprosy manifest with thickening or enlargement of peripheral nerves with sensory or motor impairment along the course of affected nerves. Careful sensory motor testing in the area supplied by the thickened nerve will

help in confirmation of the diagnosis. Sometimes, electrophysiological studies or nerve biopsy may be indicated to rule out other causes.

In cases presenting with planter ulcer, anaesthesia without any other evidence of leprosy must be examined carefully with detailed history and investigations for spinal lesions like meningomyelocele in childhood or spina bifida etc. Similarly, in cases presenting with deformities without nerve thickening or not definite sensory loss, differential diagnosis will need to be carried out with other conditions like trauma, other type of palsy etc. in mind.

Definite confirmation of leprosy may need Nerve Conduction Study, skin or nerve biopsy and PCR technique to detect leprosy infection in certain difficult to diagnose cases. Sometimes hypopigmented lesions on face and no enlarged nerves (indeterminate leprosy) especially in children with no definite loss of sensation are referred for confirmation; such cases may be kept under observation and treated with antifungal ointment or vitamin deficiencies meanwhile. However, if there are suspicious signs such as nodules or swelling on the face or earlobes, redness or infiltration in the patch, it is important to do a skin smear to confirm the diagnosis of leprosy. The positive report will establish the diagnosis while a negative report in the absence of other cardinal signs would rule out leprosy.

Enlargement of cutaneous nerves like great auricular nerve, supraorbital or supratrochlear nerves may also help clinician to diagnose leprosy in patient having facial lesion. When in doubt, histopathological examination of lesion will help in establishing alternative diagnosis

Doubtful leprosy case

1. **Clinical examination:** Elicit cardinal signs of leprosy
2. **Skin smears:** If patch skin biopsy from the patch
3. Nerve conduction velocity
4. **If nerve thickening:** nerve biopsy from the radial cutaneous or sural nerve and ask for nerve staining result, electron microscopy
5. PCR Aspiration cytology of nodules and lymph glands if any

Slit Skin Smear (SSS)

- Tissue fluid from the skin lesion and sites with expected high bacterial load (e.g., earlobe) is

taken on a glass slide and is dried and stained with Ziehl-Neelsen stain or Fite stain

- The number of bacteria is counted under light microscopy at high magnification with oil immersion, and the bacterial index is calculated as per Ridley's logarithmic scale.
- The sensitivity and, hence, diagnostic usefulness depend on the bacterial load and are low in paucibacillary cases.
- Hence, the clinical utility of SSS is limited, as SSS will be positive in multibacillary cases where clinical diagnosis itself is obvious, but it would not help in paucibacillary cases where clinical diagnosis is doubtful and requires diagnostic support.

HISTOPATHOLOGY

For diagnostic purposes, deep biopsy including the complete dermis from the most active part of lesion should be obtained. (Table 1) Tuberculoid leprosy is characterized by well-formed granulomas, often perineural in location and assuming a serpentine shape. On the other hand, in the lepromatous spectrum, there is a diffuse infiltration of histiocytes laden with bacilli throughout the dermis, sparing the upper papillary dermis (grenz zone). However, in several cases, the clinical features do not correlate with the histological findings. Clinically, tuberculoid lesions may show lepromatous features histologically, and vice versa. Further the histological features and bacteriological index may vary from lesion to lesion, even within the same patient. Clinicopathological correlation is essential.

Electrophysiological Studies

Electrophysiologic examination of the peripheral nerves is a sensitive method in early detection of neuropathy when compared with quantitative thermal sensory, vibrometry, dynamometry, monofilament testing, and voluntary muscle testing. These studies have become useful diagnostic tools in the assessment of nerve function in leprosy. They provide vital information to confirm or alter a clinical diagnosis and can prevent major diagnostic errors.

Nerve Conduction Study (NCS)

Direct involvement of the peripheral nerve is the most important outcome of leprosy. The varied manifestations of nerve damage in leprosy

include silent neuropathy, loss of tactile sensations, dryness, muscle weakness, atrophy, or contracture. NCS involves the recording, display, measurement, and interpretation of action potentials arising from the peripheral nerves. It can detect the functional derangement of nerves before the appearance of clinical signs and symptoms.¹⁴

NCS involves application of a depolarizing square wave electrical pulse to the skin over a peripheral nerve, producing

1. a propagated nerve action potential recorded at a distant point over the same nerve and
2. a compound muscle action potential (CMAP) arising from activation of muscle fibers in a target muscle supplied by the nerve

Interpretation

The interpretation of electrophysiological functions of nerve trunks is carried out using distal latency (myelination), amplitude (number of axons), and velocity (myelination).

Latency is the time from stimulus artifact to the onset of the response. In motor nerve studies, this latency includes nerve conduction time and neuromuscular transmission time. Proximal latency starts at the proximal stimulation point and ends at the first deflection from baseline. Distal latency is measured from the distal stimulation point to the first deflection from the baseline.

Amplitude is dependent on the number of axons that conduct impulses from the stimulus point to the muscle, number of functioning motor endplates, and muscle volume. The amplitude is measured from the baseline to the negative peak.

Conduction velocity (CV) is calculated by dividing the length of the nerve segment between the two stimulation points by the difference between the proximal and distal latency.

In sensory conduction studies, sensory nerve action potential (SNAP) is obtained by electrically stimulating sensory fibers by using supramaximal stimulus and recording the nerve action potential at a point further along that nerve.

NCS and Leprosy

NCS can detect subclinical leprosy neuropathy, which is helpful for the prevention of clinical neuropathies.¹⁵ Slowing of sensory velocity and motor nerve conduction velocity (NCV) is observed in patients without any clinical abnormality which represents the preclinical stage of damage. There will

be a significant reduction in MNCV, prolongation of distal latency, and reduction of amplitude. Amplitude is the most affected parameter, followed by velocity and latencies. Early involvement of sensory nerves with marked amplitude changes in motor nerves has been reported in leprosy.

Electromyography (EMG)

Electromyography (EMG) studies the electrophysiological activity of resting and contracting skeletal muscle. Detection and recording of the electrical activity from a portion of a muscle by recording motor unit potentials are accomplished by EMG. The usual method employed in the study of leprosy patients is needle EMG. Muscles selected for the EMG studies should be superficial, easily identified, and should be located away from major vessels and nerve trunks. Abductor pollicis brevis is used for testing the function of the median nerve, abductor digiti minimi for testing the ulnar nerve, and extensor digitorum brevis for testing the lateral popliteal nerve. EMG is performed separately for each muscle to be tested. Interpretation of the abnormal EMG findings indicating neuropathy include fibrillation, fasciculation, giant motor unit potentials, and incomplete interference or reduced recruitment pattern.

EMG and Leprosy

Applications of EPS in leprosy

1. Early detection of subclinical neuropathy.
2. Management of neuritis.

Based on EMG and NCV, several guidelines have been listed for indications of surgery in leprosy.¹⁵

- **Recent Neuritis:** Reduction of NCV and worsening of EMG indicate failure of medical treatment and are an indication for surgical intervention. Stable NCV/EMG with a clinical background of subclinical neuritis warrants continuation of pharmacotherapy.
 - **Long-standing neuritis:** Surgery is contraindicated in a patient of leprosy with clinically complete sensory-motor deficits, and EMG/NCV results are abnormal.
3. Monitoring the Medical Treatment
 - NCV of a patient shows improvement with treatment.
 - Drug efficacy in leprosy reactions can be monitored using MNCV.
 4. Detection of Thalidomide-Induced Peripheral Neuropathy: Features of Thalidomide-Induced

Neuropathy Include Reduction in SNAP Amplitude and Relative Conservation of NCV

The limitation of EPS is that it does not always allow assessment of the exact location, cause, and extent of a nerve lesion and coexistent disease of surrounding tissues.

RADIOLOGIC EXAMINATION

Leprosy can involve the bones and soft tissue due to direct invasion or by indirect influence due to neuropathy. It can be detected by ordering suitable radiological interventions. Radiological investigations relevant in leprosy include the conventional radiography of the hands, feet, and face, high-resolution ultrasonography (HRUS), and magnetic resonance imaging (MRI).

Objectives of the radiological assessment of leprosy in principle include the conventional radiography for the bone changes, HRUS for the structural nerve changes, and MRI for the soft tissue and neuro-arthropathic changes. Radiography of the Hands, Feet, and Face Preliminary radiographs are necessary in assessing the extent of bone involvement and the risks of a pathological fracture in a patient of leprosy.

Hands and Feet

The hands and feet are commonly affected by leprosy, especially in lepromatous leprosy and type 1 lepra reaction. Radiological examination (anteroposterior (AP), lateral or oblique skiagrams) of both the hands and feet is necessary to look for the presence of the bone changes, heel infections, and suspected tarsal infections. Nonspecific changes include bone erosions, absent phalanges (resorption of digits), osteomyelitis (atrophy or trauma), tarsal disintegration, and disuse osteoporotic changes. Specific changes due to direct infiltration by *M. leprae* can present with bone cysts or pseudocysts and sequestrate, honeycomb appearance, enlarged nutrient foramina, subarticular erosions, concentric cortical erosions (pencil-like or sucked candy appearance), and osteoporosis with lepromatous arthritis.^{16,17} Patients of lepra reactions may show terminal tuft dissolution (juxta-articular decalcification), destruction/erosion of epiphyseal bone, sclerosis, subperiosteal bone erosion, and osteoperiostitis.

Face

Atrophy of anterior nasal spine and maxillary

alveolar process are the features to look for on radiologic evaluation. Paranasal sinuses are an important reservoir of *M. leprae* in MB leprosy. CT scan of paranasal sinus studies can reveal localized or diffuse thickening of mucosa and opacity of the sinus. Ethmoid sinuses are most frequently affected, followed by maxillary sinus, while frontal and sphenoid sinuses are least affected. Persistent infection is common among lepromatous leprosy patients, despite previous treatment. Hence, paranasal sinus CT examination is a useful method of evaluating patient response to treatment and follow-up.

High-Resolution Ultrasonography (HRUS)

HRUS is a noninvasive, cost-effective imaging technique that enables real-time examination of soft tissues in static and dynamic states. It gives significant information on nerve structure, morphology, and vascularity in the nerve, and this adds a new dimension in diagnosing leprosy particularly pure neuritic type, and assessment of nerve damage which can prevent disabilities. Clinical examination of nerves in leprosy is subjective and can be inaccurate. Hence, HRUS can delineate peripheral nerves in the upper and lower with accurate morphologic information using improvised spatial and contrast resolution. It also helps in the evaluation of both entrapment and peripheral neuropathy. HRUS with a broadband frequency ranging from 10 to 14 MHz, color Doppler (CD) with the broadband frequency of 6–18 MHz, and linear array transducer are utilized for the imaging of peripheral nerves. Settings of color Doppler ultrasound examination are set to detect signals from low flow velocity vessels in the nerves. After B-mode imaging of the nerve, a color box is put over a small part of the nerve in its longitudinal axis. Sequential increase in color gain till color bleed (noise) appears in the color box is performed, and the color gain is kept just lower to this to avoid the noise. The frequency of pulse repetition is set to pick up very low blood flow with avoidance of noise in the image and arterial pulsations. No significant arterial pulsations are detected in normal nerves. The detection of blood flow signals in the perineural plexus or intrafascicular vessels during imaging is taken as a sign of nerve hypervascularity.

PARAMETERS ASSESSED

1. **Cross-sectional area (CSA):** It is determined from the area within the inner margin of

the hyperechoic rim. This helps in assessing peripheral nerve enlargement

2. **Echogenicity:** The echo density of the nerves assessed on imaging can be graded as follows: mild, some hypoechogenicity; moderate, obvious hypoechogenicity; and severe, absence of any fascicular pattern. Nerves were classified as abnormal if they showed hypoechoic or hyperechoic areas or focal thickening with loss of the normal fascicular pattern.
3. **Size of fascicles:** Enlarged fascicles have been reported in patients with leprosy.
4. **Thickness of the epineurium:** HRUS has shown that the epineurium of the ulnar nerve is often strikingly thickened in leprosy patients when involved
5. **Vascularization of a peripheral nerve:** Increased neural vascularity with interfascicular edema reflects immune-mediated inflammation in leprosy reactions.

Interpretation

- a. Objective measurement of nerve damage by demonstrating the nerve thickening, altered echotexture, and abnormal vascularity.
- b. Detection of more extensive changes than those diagnosed clinically in nerves with clinical features of impairment of function.
- c. Calculation of the cross-sectional areas of peripheral nerves. HRUS measurement of increased nerve size is a sensitive indicator of the presence of neuropathy in leprosy.
- d. Study of the structural changes in nerves that cannot be biopsied especially the mixed nerves due to risk of muscle palsy.
- e. HRUS can examine the nerve for a longer length when compared with MRI which can evaluate only a defined segment.

MAGNETIC RESONANCE IMAGING

MRI is an operator-independent imaging modality. MRI can distinctly delineate a nerve from surrounding soft tissues, precisely visualize nerve fascicles, and clearly localize the site of the pathology. In leprosy, peripheral nerve involvement ranges from nerve thickening with preserved fascicular architecture to disruption of fascicular architecture and formation of micro-abscesses. Large abscesses are formed by the

coalescence of micro-abscesses which extend into the surrounding soft tissue. Interpretation MRI findings in leprosy are nonspecific and may show diffuse edema and swelling of the involved nerve. Findings of nodules or nerve sheath granulomas are suggestive of leprosy. Nerve abscesses appear hypointense on T1-weighted images and hyperintense on T2-weighted images and show peripheral enhancement in postcontrast study. MRI is a sensitive modality in ascertaining early neuroarthropathic changes such as degradation and interruption of the subcutaneous fat and effusion and synovitis of the metatarsophalangeal joints in leprosy patients. MRI is more accurate in detecting soft tissue changes, such as subcutaneous fat

infiltration, cellulitis, and abscess.¹⁸

Serological Investigations

Different mycobacterial antigens have been studied for serological assays, and the basic principle is to study the antibodies directed against the antigen by using techniques like ELISA, agglutination, and lateral flow tests. Immunochromatographic lateral flow assay, detecting IgM antibodies against PGL-I and IgG antibodies to LID-1, is being developed as a point-of-care test for diagnosis of leprosy. We will be discussing some of the antigens which have been studied and have been shown promise to be used for the diagnosis of leprosy (Table 3).

Table 3: Serological testing antigens and methods

Antigens	Presence in <i>M. leprae</i>	Efficacy	Drawbacks
Phenolic glycolipid-1	Cell wall protein of <i>M. leprae</i>	80-100% sensitivity in MB patients	<ol style="list-style-type: none"> 1. Low titer in paucibacillary (PB) cases with sensitivity of 30-60% 2. No cut-off point for anti PGL-1 titre to differentiate between disease and subclinical infection in leprosy patients and healthy individuals.
35kD protein	Major membrane components of leprosy bacillus	98.5% sensitivity in MB patients	<ol style="list-style-type: none"> 1. Only 46.7% sensitivity for PB patients 2. Poor performance with antibody levels near the cut-off value
Lid 1 and NDO-LID	Protein	83.3% and 87%, respectively, sensitivity in MB patients	15.4% and 21.2%, respectively, in PB cases
IFN- γ	Pro-inflammatory marker against <i>M. leprae</i>	<i>M. leprae</i> protein in combination with interferon gamma release assay (IGRA) provides better diagnosis	It can be detected in population who have developed sufficient immunity against <i>M. leprae</i>

IgA Antibody-Based Test

Salivary samples are used for the diagnosis of *M. leprae* using *M. leprae*-specific IgA antibodies in order to overcome the problem of invasive sampling. Different studies have used assays to measure salivary IgA/IgM antibodies against PGL-1 in patients and contacts and have found good correlation with serum IgM levels and recommend its use as a diagnostic tool for the contacts of leprosy patients. Major problem with the serological assays in the diagnosis of leprosy is their poor performance for the detection of paucibacillary and pure neuritic leprosy.

Cytokines/Chemokines as Biomarker in Leprosy

During *M. leprae* infection, T cells get activated and secrete IFN- γ (interferon gamma) which is a pro-inflammatory marker against *M. leprae* and *M. tuberculosis*.¹⁹ IFN- γ can be used as a marker for

the diagnosis of *M. leprae*; however, we cannot differentiate between patients who have the disease and those who only have the infection or people who have been treated. *M. leprae* protein such as ML-2478 in combination with interferon gamma release assay (IGRA) can be used as a novel method for anticipating the extent of *M. leprae* transmission in a given population and identifying people who are prone to contracting *M. leprae* infection and acquiring leprosy.

Gene-Based Assays

Molecular approaches like polymerase chain reaction (PCR) or real-time (RT)-PCR are routinely used for the identification of specific *M. leprae* DNA sequence in clinical samples. These are highly sensitive assays which can be used for diagnosis of infection in doubtful/difficult cases, for assessing bacterial load, for detection of drug resistance, and for monitoring the response of treatment.

M. Leprae-Specific PCR

M. leprae-specific PCR could be carried out on routine basis in laboratory using DNA isolated from a wide range of biological specimens such as blood, skin smear, saliva, skin biopsy, oral or nasal swab, nerve section, and urine.

Multiplex PCR (M-PCR)

M-PCR is a better alternative and sensitive type of PCR technique in which two or more set of primers are used simultaneously for amplification of different target genes present in the same reaction. In M. leprae clinical diagnosis, M-PCR employs more than one specific gene to its DNA. This technique is used for the detection of paucibacillary forms or indeterminate leprosy by targeting pseudo genes of M. leprae such as ML1545, ML2180, and ML2179. Different types of clinical samples can be used like blood, nasal swab, saliva, and SSS for the detection of PB and MB cases with the help of M-PCR using RLEP, 16S rRNA, and sodA targets.

In Silico Molecular Techniques

In silico molecular techniques for drug resistance are used for patients who are not responding to MDT. Resistance to anti-leprosy medicines like dapsone, rifampicin, and fluoroquinolones has been detected using molecular-based techniques to find mutation in drug resistance-determining regions (DRDR).

Loop-Mediated Isothermal Amplification (LAMP) Assay

It is a DNA amplification method that has been used to develop assays for various diseases like tuberculosis, nontuberculous mycobacteria, and COVID-19. This is an isothermal amplification method to amplify a limited amount of DNA copies into a million copies within an hour.²⁰ It utilises a set of four (or six) different primers which bind to six (or eight) different regions on the target gene making it highly specific. The result or a positive test can be assessed easily by observing a change in turbidity or color of the reaction with the naked eye or by using a turbidimeter or colorimeter or even a smartphone-based application for reading the colour or turbidity.

According to a recent meta-analysis of all leprosy diagnostic tests, agglutination tests had the highest sensitivity of the three serological tests studied (ELISA, agglutination test, and lateral flow), and

all had comparable specificity. Among molecular analysis, qPCR had better sensitivity but lower specificity than traditional PCR. The PCR method was significantly more reliable than ELISA.

DIFFERENTIAL DIAGNOSIS

1. Vitiligo
2. Tinea Versicolor
3. Pityriasis Alba
4. Nutritional dyschromia
5. Herpes Zoster
6. Lupus Vulgaris
7. Granuloma annulare
8. Psoriasis
9. Post-Kalaazar Dermal Leishmaniasis
10. Neurofibromatosis

Treatment

1. The WHO FD-MDT Regimen PB: (1-5 skin lesions) – Rifampicin 600 mg monthly plus dapsone 100 mg daily; 6 cycles in 9 months. MB: (≥ 6 skin lesions) – Rifampicin 600 mg plus clofazimine 300 mg monthly and dapsone 100 mg plus clofazimine 50 mg daily; 12 cycles in 18 months.
2. National Leprosy Eradication Programme (NLEP) is implemented with major objectives of reducing the disease burden, preventing disabilities and to improve awareness about leprosy in the country through general health care system. According to NLEP, the standard adult treatment regimen for MB leprosy is:

Rifampicin - 600 mg once a month

Clofazimine - 300 mg once a month

50 mg daily Dapsone - 100 mg daily

Duration: 12 months (12 blister packs)

The standard adult treatment regimen for PB leprosy is:

Rifampicin.....600 mg once a month

Dapsone.....100 mg daily Duration: 6 months (6 blister packs)

The standard child (ages 10 - 14) treatment regimen for MB leprosy is:

Rifampicin.....450 mg once a month

Clofazimine.....150 mg once a month, and 50

mg every other day

Dapsone.....50 mg daily Duration: 12 months (12 blister packs)

The standard child (ages 10 - 14) treatment regimen for PB leprosy is:

Rifampicin.....450 mg once a month

Dapsone.....50 mg daily Duration: six months (six blister packs)

The appropriate dose for children under 10 years of age can be decided on the basis of body weight. Rifampicin: 10 mg per kilogram body weight, clofazimine: 1 mg per kilogram per body weight daily and 6 mg per kilogram monthly, dapsone: 2 mg per kilogram body weight daily. The standard child blister pack may be broken up so that the appropriate dose is given to children under 10 years of age. Clofazimine can be spaced out as required.

Adverse reactions to MDT

MDT is remarkably safe and serious adverse effects are very rare. Generally the problems are seen with MDT are shown in table 4.

Table 4: Adverse effects of MDT

Minor problems	Drug	Management
Red urine	Rifampicin	Reassurance
Brown discoloration of the skin	Clofazimine	Counseling
Gastro-intestinal upset	All three	Give drugs with food
Anaemia	Dapsone	Give iron and folic acid
More serious problems	Drug	Management
Itchy skin, rash, Steven Jhonson Syndrome	Dapsone	
Allergy, urticaria	Dapsoner or Rifampicin	Stop the drugs and consider alternative regimen
Jaundice	Rifampicin	
Shock, purpura, renal failure	Rifampicin	

TREATMENT OF LEPRO REACTIONS

It includes Prednisolone, bed rest, and rest to the affected nerves by splint and analgesics. For neuritis, treatment with Prednisolone should be prolonged to four weeks from 20 mg onwards. Added Clofazimine for Type 2 reactions may be extremely useful for reducing or withdrawing corticosteroids in patients who have become dependent on them; though it is less potent than

steroids and often takes 4-6 weeks to develop its full effect. Total duration of Clofazimine therapy should not exceed 12 months. Cases of lepra reaction, where Prednisolone is contraindicated or ineffective may be put on alternative drugs such as Thalidomide. It is an effective drug in the treatment of severe ENL in leprosy. It has serious teratogenic risks. Thalidomide is started at 200 mg twice daily or 100 mg four times daily and ENL is usually controlled within 72 hours and the dose can then gradually be tapered off. Maintenance dose of 50-100 mg daily may be required for prolonged period in some cases. Thalidomide must be administered under the strictest possible supervision. If a patient develops lepra reaction during the treatment, do not stop MDT (rather complete the course of MDT). Lepra reactions, which occur after completion of treatment, should also be managed as mentioned earlier. MDT should not be restarted for such cases.

Follow-Up

A complete physical examination and smear test should be scheduled every 6 months while multibacillary cases are being treated. Histopathology should be performed at the end of each treatment cycle. In paucibacillary cases, histopathology is performed only at the end of treatment.

Relapse

Relapse is defined as the re-occurrence of the disease at any time after the completion of a full course of treatment. MDT is a very effective treatment for leprosy. If a full course of treatment has been taken properly, relapse is generally rare. Relapse is indicated by the appearance of new skin lesions and, in the case of an MB relapse, by evidence on a skin smear of an increase in BI of 2 or more units. Fortunately, the use of a combination of drugs has prevented the development of drug resistance in leprosy, so relapse cases can be treated effectively with the same drug regimen - MDT.

Resistance to MDT

Resistance to multidrug therapy (MDT) is one of the major obstacles in the treatment of Hansen's disease. It can manifest in two forms:

1. **Primary Resistance:** Presence of already resistant strains.
2. **Secondary Resistance:** Development of resistance due to inadequate therapy or monotherapy.

In cases where resistance to a standard anti-leprosy drug is identified and documented, treatment regimens may be altered for the patient.

Rifampicin-resistant MB Cases: A fully supervised regimen in two phases is recommended.

- **The intensive phase:** Moxifloxacin 400 mg—clofazimine 50 mg—clarithromycin 500 mg—minocycline 100 mg all taken daily for 6 months.
- **The continuation phase:** Moxifloxacin 400 mg—clarithromycin 1000 mg—minocycline 200 mg all taken once monthly for 18 months.
- If available, ofloxacin may be replaced by moxifloxacin 400 mg, which has stronger bactericidal activity against *M. leprae*.

DEFAULTER

A defaulter is a person who has not completed the scheduled 6 months of PB-MDT in 9 months and 12 months of MB-MDT in 18 months. It results in subtherapeutic dosing leading to drug resistance, disease progression, and continuation of transmission. A defaulter showing signs of new skin lesions or nerve involvement and any indication of lepra reaction should be immediately put on a new course of MDT according to the classification.

Primary and Secondary Impairments in Leprosy

Due to Nerve Damage

The primary impairments occur because of nerve damage in leprosy, whereas the impairments resulting out of primary impairments are called secondary (Table 5).

Table 5: Types of impairment in leprosy

Primary impairments	Secondary impairments
Face	Stiff joints
Facial nerve: Lagophthalmos	Joint contractures
Trigeminal nerve: Corneal anesthesia	Shortening
	Ulcers
	Disintegration of bones
	Exposure keratitis, corneal ulcer, and corneal opacity
Hand	
Ulnar nerve: Ulnar clawing	
Median nerve: Ape thumb deformity	
Ulnar and median nerve: Total clawing	
Radial nerve: Wrist drop/finger drop	

Feet

Lateral popliteal nerve: Foot drop

Posterior tibial nerve: Claw toes

Posterior tibial nerve: Plantar anesthesia

WHO Grading of Impairments: The WHO grading system has separate components for the hands, feet, and eyes (Table 6).

Table 6: WHO disability grades for the hands, feet and eyes

0	Absence of anesthesia and absence of any visible impairments in the hands and feet
1	Presence of anesthesia and absence of visible impairments in the hands and feet
2	Severe impairment to vision (vision is worse than 6/60; cannot count fingers at 6 m)

Eye-Hand-Feet (EHF) Scoring: This scoring system takes into account the sum of the scores for the individual impairment grade for the hands, feet, and eyes to calculate the impairment sum score. The maximum sum score is 12 (2 for each of the hands, feet, and eyes).

Prevention of the Progression of Impairment

Components of physical rehabilitation are:

Identifying nerve function impairment (NFI)- Assessment of Nerve damage, Primary impairment, Secondary impairment

Monitoring impairments- Grading Impairment, Occupational therapy, Community based Rehabilitation (CBR)

Prevention of further deterioration- Splint and Exercise, Surgeries, Self care

Some of the impairments in leprosy are irreversible due to several reasons, and in such scenarios, the goal of the rehabilitation team is to ensure the prevention of any new impairment along with the worsening of a primary impairment to a secondary impairment. The prevention part includes:

- Exercises
- Use of splints
- Surgical rehabilitation
- Self-care

Splints and their Indications

Ulnar neuritis slab: Extends from the back of the elbow to the palmar crease and maintains the

elbow in flexion of about 60°, providing adequate rest to the nerve

- Acute ulnar neuritis or ulnar nerve tenderness

Posterior slab/functional foot slab: Extends from the mid-calf region to the tip of the toes

Posterior slab/functional foot slab: Extends from the mid-calf region to the tip of the toes

- Posterior tibial neuritis or lateral popliteal neuritis
- Swollen foot or leg caused by a reaction
- Infected or neuropathic foot.
- Supportive device for patients with foot drop or tibialis anterior weakness
- Post-reconstructive surgery of foot drop to protect the transferred tendon, the tibialis posterior

Palmar slab/anterior slab/median neuritis slab: Extends from the upper second/third of the forearm to the palmar crease

- Median neuritis, whether or not muscle weakness exists
- Supports the weak muscles and helps to prevent thumb web contracture

Cock up slab: Extends from the upper second/third of the forearm to the palmar crease. Maintains the wrist in extension. Paralyzed fingers are included in the splint

- Radial nerve damage associated with paralysis or weakness of the wrist extensors

Cylindrical splint: Extends from the tip to the base of the finger

- Interphalangeal joint stiffness or contracture
- Finger wounds and cracks

Thumb web spica/tuck-in splint: Maintain the thumb in abducted position

- Prevent and treat thumb web contracture
- Protection of the transferred tendon post-reconstructive surgery of ape thumb deformity

Functional slab for hand: It is applied with the metacarpophalangeal joint at 45°, the proximal interphalangeal joints at 25°, and the distal interphalangeal joint at 15°

- Hand swelling due to lepra reaction or wound infection Gives rest to the hand in a functional position, as well as relieves pain and assists in healing

Lumbrical slab: Finger loops maintain the position of the metacarpophalangeal joint in flexion

- Maintain the hand in the lumbrical position post-tendon transfer surgery

Non-weight-bearing cast: Extends from the neck of the fibula to the tip of the toes, with the ankle joint maintained at 90° of dorsiflexion

- After tibialis posterior transfer surgery
- Healing of simple ulcers

Below-knee cast with Bohler Iron: Extends from the neck of the fibula to the tip of the toes. Bohler iron helps transmit weight and pressure to the calf area thereby preventing weight bearing on the foot

- Simple heel ulcer in a foot

Molded double rocker shoe/boot: Cast is applied below the malleoli and covers the entire foot, just like a boot

- Plantar ulcers on the forefoot

Management of deformities with surgery

Surgical Rehabilitation

1. Nerve surgery.
2. Reconstructive surgery

Nerve Surgery

Various nerve surgeries are done according to the condition (Table 7). Common indications for nerve surgery in leprosy patients are as follows:

Table 7: Nerve surgery in leprosy

Type of nerve surgery	Descriptions
Extra-neural neurolysis	Decompression surgery to release the constricting fibrous bands and ligaments and to open fibro-osseous channels: <ol style="list-style-type: none"> 1. Ulnar neuritis: Cubital tunnel at the elbow, medial intermuscular septum, aponeurosis of flexor carpi ulnaris muscle. 2. Median nerve: Carpal tunnel at the wrist 3. Radial nerve: Spiral groove of the humerus 4. Common peroneal nerve: Retor-fibular tunnel at the neck of the fibula
Intraneural neurolysis or longitudinal epineurotomy	Giving longitudinal incision in the epineurium without damaging the vasa nervorum

Table cont...

Interfascicular neurolysis	Dissecting and separating individual nerve bundles
Nerve abscess drainage	Longitudinal incision is given over the abscess to drain the contents
Nerve trans-positioning	Done for the ulnar nerve at the elbow to avoid stretching of the nerve with movement of the elbow joint, to increase blood supply and protect the nerve from injury

- Non-responsiveness or progression of nerve damage despite on corticosteroids.
- Contraindication or intolerance to corticosteroids.
- Nerve abscess.
- Intractable pain despite on adequate immunosuppressive therapy.
- Sudden paralysis.

RECONSTRUCTIVE SURGERY

Reconstructive surgeries are required to correct the irreversible deformities of the face and extremities along with reconstruction of soft tissue in case of contractures and large areas of tissue loss. The deformities of the hand and feet are usually dealt with by tendon transfer procedure in which acting muscle is transferred to do the function of the paralyzed muscles. If the deformity is neglected and chronic resulting in fixed deformities such as a "fixed equines," "fail foot," or "rocker bottom foot," the surgical stabilization is done by using different arthrodesis procedures and then supported by specialized footwear.

The static procedures used for correction of lagophthalmos include fascial slings to suspend the lower eyelid, loading of the upper eyelid, ear cartilage graft, median and lateral tarsorrhaphy, and tarsal strip (shortening the tarsus in the eyelids to approximate the eyelid margins to cover most part of cornea). Temporalis muscle transfer procedure or its modifications are dynamic techniques for correction of lagophthalmos.

Posterior nasal epithelial inlay skin graft and nasolabial skin flap are used for correction of nose collapse.

Madarosis can be managed by free scalp graft, island pedicle scalp graft, or hair follicle implant.

Reconstructive surgeries used for ulnar clawing include transfer of palmaris longus, extensor carpi radialis longus, and flexor digitorum superficialis of the middle or ring finger. If there is associated median nerve palsy resulting in total clawing with loss of opposition and abduction movement of

thumb, in addition to correction of ulnar clawing, transfer of flexor digitorum superficialis of the ring finger or extensor indicis proprius or extensor carpi ulnaris or palmaris longus has to be done.

Triple paralysis, due to damage to all three of ulnar, median, and radial nerves, requires multiple tendon transfers such as the following:

- Pronator teres (active muscle) is transferred to the extensor carpi radialis brevis to provide wrist extension.
- Flexor carpi radialis is transferred to provide four-finger extension.
- Palmaris longus is rerouted to provide thumb extension.
- Flexor digitorum superficialis of the middle finger is transferred to provide metacarpophalangeal flexion of the four fingers.
- Flexor digitorum superficialis of the ring finger is transferred for opponensplasty.

Common peroneal nerve paralysis resulting in foot drop due to loss of dorsiflexion and eversion of foot needs tibialis posterior to be rerouted to the dorsum of the foot and to be attached to the paralyzed dorsiflexor of the ankle.

For clawing of toes due to tibial nerve damaged behind the medial malleolus, the reconstructive surgery used is flexor to extensor transfer, in which for each toe, detachment of the flexor digitorum longus from its insertion and transferring it to the dorsum, and inserting the tendon into the extensor digitorum, is done.

Recurrent wounds of hands and feet

Common causes of wounds include injury due to sharp objects that cut or pierce through the skin like thorns or broken glass, repetitive pressure, friction or shearing forces (e.g. foot ulcers from walking or hand ulcers from using unprotected hand tools), burns etc. The abscess develops following infection and need to be drained surgically. The deep infection may lead to osteomyelitis. Sometimes in severe cases of recurrent wounds, amputation is the only solution, however this should only be considered as a last resort.

Vaccines

Several vaccines have proven effective to one degree or another in countries where leprosy is endemic. The prophylactic effect of a leprosy vaccine is achieved by resetting the immune system against shared mycobacterial antigens. Some of the vaccines currently in use are *Mycobacterium w* proposed by Talwar in 1978; the Convit vaccine introduced in 1992, which is the *Bacillus Calmette-Guérin* (BCG) combined with *M leprae*; and *Mycobacterium* ICRC (based on *Mycobacterium avium-intracellulare*). Others are one based on *Mycobacterium tufo* (proposed by Iushin and Kalianina in 1995) and one using *Mycobacterium habana* (see Singh and coworkers, 1997). The BCG vaccine itself has been reported to confer up to 50% protection against leprosy. In some regions the BCG vaccine is administered to children under the age of 12 years who are in contact with relatives who have leprosy.

CONCLUSION

Hansen disease remains a concern today. Various diagnostic methods and rehabilitative methods are there. The knowledge of immunopathologic mechanisms reveals the complexity of the disease and provides the basis for understanding and treating them. The elimination of leprosy, is a goal that calls combined medical, social, political, and scientific effort.

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