

## Nerve Conduction Studies in Leprosy- A Review.

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**Abstract:** Leprosy involves peripheral nerves sooner or later in the disease course leading to gross deformities. However, by the time it becomes clinically apparent, the nerve damage is already quite advanced. If the preclinical damage is detected early, it can be prevented to a large extent. Nerve conduction studies (NCS) are very important for the study of peripheral neuropathy. These studies can be helpful in the early diagnosis of neural involvement, and in the follow-up of patients under treatment.

**Keywords:** Leprosy, electrophysiology, nerve conduction, neuropathy

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### I. Introduction

Leprosy is a chronic disease caused by *Mycobacterium leprae*<sup>1</sup>, which primarily affects the peripheral nervous system and the skin. Leprosy neuropathy is a complex, with the superimposition of acute and chronic sensory, motor and/or autonomic events. Peripheral nerve involvement in leprosy may vary from involvement of an intradermal nerve in the cutaneous patches to a major lesion in the peripheral nerve trunk. A stage of functional blockade of conduction of nerve impulse almost always precedes the visible pathological changes in the nerve.<sup>2</sup>

Neuropathy is often clinically silent in its evolution making early diagnosis exceptionally challenging so that even highly skilled clinical management may not be able to prevent permanent nerve damage. Clinical neurological examination, especially of sensory function, is essentially subjective in that it is based on a certain level of patient awareness. Accordingly, distinct techniques aiming toward a more objective detection of early nerve function impairment, imperative for successful therapeutic interventions, have been developed and tested. Nerve conduction study provides reliable information regarding large myelinated nerve fibre impairment.<sup>3</sup>

The role of electrophysiological evaluation of nerve function in the diagnosis and assessment of different neuropathies is well established. There have been few studies of motor nerve conduction in leprosy affected nerves and still fewer regarding sensory nerve conduction. These studies have shown that marked slowing of conduction may occur in leprosy affected nerves. A significant decline of motor nerve conduction velocities has also been reported in clinically normal nerves in leprosy.<sup>2</sup> Nerve conduction studies are the gold standard for detecting peripheral neuropathy.<sup>4</sup>

### II. Nerve Involvement In Leprosy

Leprosy is one of the principal causes of nontraumatic neuropathy. Functional derangement of nerves can be shown by nerve conduction studies before the appearance of clinical signs and symptoms of the disease. Clinically absent nerve function impairment probably represent the preclinical stage of damage which becomes manifest when certain defined quantum of nerve fibres becomes non-functional. Thirty percent of the sensory nerve fibres need to be affected by the lepra bacilli before sensory deficit becomes clinically manifest.<sup>5</sup> Sensory loss is the earliest and most frequently affected modality but a predominantly motor loss can also occur.<sup>6</sup> It is generally observed that the nerves of lower extremity are more frequently and severely affected than in the upper extremity in both PB and MB patients of leprosy. However, the nerve action potentials in upper limbs are more easily elicited than in lower limbs.<sup>7</sup> Leprosy most commonly affects the posterior tibial nerve causing anaesthesia on the soles of the feet followed by the ulnar, median, lateral popliteal and facial nerves.<sup>8</sup> Other nerves affected by the disease include the greater auricular, radial and the radial cutaneous nerves. The effect of the disease on nerves leads to disability and deformity.

### **III. Nerve Conduction Studies**

The study of the electrophysiological activity of resting and contracting skeletal muscle with the help of Electromyography (EMG) and the conduction of the nerve impulse along the peripheral nerve, also called Nerve Conduction Study(NCS) have become most useful diagnostic tools in the assessment of nerve function in leprosy.

### **IV. Principle**

Nerve conduction studies involve the application of depolarising square wave electrical pulses to the skin over a peripheral nerve producing: (1) a propagated nerve action potential (NAP) recorded at a distant point over the same nerve: and (2) a compound muscle action potential (CMAP) arising from the activation of muscle fibres in a target muscle supplied by the nerve. In both cases these may be recorded with surface or needle electrodes.

Surface electrodes are designed to give information about the whole of a muscle stimulated, giving data for the time taken for the fastest axons to conduct an impulse to the muscle and the size of the response. The recording or active electrode is placed over muscle or nerve segment to be studied. While the reference electrode for motor response is positioned off and distal to the muscle being tested on a nearby bone or tendon, whereas the reference electrode for sensory response is placed distal to and on the nerve segment being studied. The ground electrode is usually a metal plate that provides a large surface area of contact to reduce stimulus artefacts. The ground electrode is usually placed on the body prominence between the stimulating and recording electrodes. Stimulating electrodes are usually two metal electrodes or felt pad electrodes placed 1.5-3.0 cm apart.

In conventional nerve conduction studies, mono-polar needle electrodes can also be used with certain advantages including: nerves that lie anatomically deep can also be stimulated, requires smaller intensity stimulus and nerve stimulation is more selective. These electrodes give very accurate conduction time information but, because they record from only a small area of muscle or nerve, they give poor or, in the case of the latter, more complex information making numerical analysis difficult. However, needle recordings are most appropriate when severe muscle wasting has occurred, or when the depth of a muscle under study makes a surface recording impossible.<sup>9</sup>

The peripheral nerves contain many nerve fibres of different diameters, degrees of myelination, and afferent or efferent connections. In NCS, the fastest 20% of these fibres are studied.<sup>10</sup>

There are a number of physical parameters that require correction. The most important is temperature. The fastest motor nerve conduction velocity is reduced by approximately 1 m/s per °C temperature fall. Conventionally, studies are performed as close to a surface recorded temperature of 34 °C. If that is not achieved by adequate heating of the limb, rarely a temperature correction must be applied. Some measures of conduction require correction for limb length or height. Finally nerve conduction data alter with age. The motor conduction slows by 0.4–1.7 m/s per decade after 20 years and the sensory by 2–4 m/s.<sup>10</sup>

### **V. Contraindications**

The two important relative contraindications are:

- a) The presence of cardiac pacemakers. With most there is no risk but, discussion with the patient's cardiologist is advised if (1) the NCS are likely to involve stimulation close to the chest wall, and (2) if a life threatening event would be risked should the pacemaker either be triggered if subject to an external voltage.
- b) In Patients with neuritis, as the procedure is painful in these patients.

### **VI. Specific Nerve Conduction Study Techniques**

#### **Sensory Nerve Conduction Study**

A compound nerve action potential produced by electrical stimulation of afferent nerve may be recorded over peripheral sensory nerves. Sensory nerve action potentials (SNAP) can be measured in two ways – antidromically and orthodromically. The reference in antidromic (stimulating towards the sensory receptor) studies is placed distal to the recording electrode. For orthodromic (stimulating away from the sensory receptor) recording, the reference electrode is placed proximal to the recording electrode.

The routine sensory conduction techniques for various nerves are as follows<sup>9</sup>:

#### ***Ulnar sensory study***

Recording Site: Little finger (digit 5) - Ring electrodes with G1 placed over the metacarpal-phalangeal joint, G2 placed 3-4 cm distally over the distal interphalangeal joint.

Stimulation Site: Wrist: medial wrist, adjacent to the flexor carpi ulnaris tendon.

#### ***Median sensory study***

Recording Site: Index or middle finger (digit 2 or 3) - Ring electrodes with G1 placed over the metacarpal-phalangeal joint, G2 placed 3-4 cm distally over the distal interphalangeal joint.

Stimulation Site: Wrist: Middle of the wrist between the tendons to the flexor carpi radialis and palmaris longus.

***Radial sensory study***

Recording Site: Superficial radial nerve - G1 placed over the superficial radial nerve as it runs over the extensor tendons to the thumb, G2 placed 3-4 cm distally over the thumb

Stimulation Site: Over the distal-mid radius.

***Superficial peroneal sensory study***

Recording Site: Lateral ankle - G1 placed between the tibialis anterior tendon and lateral malleolus, G2 placed 3-4 cm distally

Stimulation Site: Lateral calf

***Sural sensory study***

Recording Site: Posterior ankle - G1 placed posterior to the lateral malleolus, G2 placed 3-4 cm distally

Stimulation Site: Posterior-lateral calf

***Saphenous sensory study***

Recording Site: Medial ankle: G1 placed between the medial malleolus and tibialis anterior tendon, G2 placed 3-4 cm distally

Stimulation Site: Medial calf: Stimulator placed in the groove between the tibia and the medial gastrocnemius muscle.

## **VII. Motor Nerve Conduction Study**

Peripheral nerve may be stimulated by passing electrical current through the skin, resulting in a synchronized muscle contraction. When recorded by surface electrodes, this is called the compound muscle action potential (CMAP). Motor responses are recorded over muscle being studied.

***F waves***

F waves (F for foot where they were first described) are a type of late motor response. When a motor nerve axon is electrically stimulated at any point an action potential is propagated in both directions away from the initial stimulation site. The distally propagated impulse gives rise to the CMAP. However, an impulse also conducts proximally to the anterior horn cell, depolarising the axon hillock and causing the axon to backfire. This leads to a small additional muscle depolarisation (F wave) at a longer latency. F waves allow testing of proximal segments of nerves that would otherwise be inaccessible to routine nerve conduction studies.<sup>10</sup> The routine motor conduction techniques for various nerves are as follows<sup>9</sup>:

***Ulnar motor study***

Recording Site: Abductor digiti minimi (ADM) muscle site (medial hypothenar eminence) - G1 placed over the muscle belly, G2 placed over the fifth metacarpal-phalangeal joint.

Stimulation Sites:

1. Wrist: Medial wrist, adjacent to the flexor carpi ulnaris tendon.
2. Below elbow: 3-4 cm distal to the medial epicondyle.
3. Above elbow: Over the medial humerus, between the biceps and triceps muscles, at a distance of 10-12 cm from the below-elbow site.

***Median motor study***

Recording Site: Abductor pollicis brevis (APB) muscle (lateral thenar eminence) - G1 placed over the muscle belly, G2 place over the first metacarpal-phalangeal joint.

Stimulation Sites:

1. Wrist: Middle of the wrist between the tendons to the flexor carpiradialis and palmaris longus.
2. Antecubital fossa: Over the brachial artery pulse.

***Radial motor study***

Recording Site: Extensor indicis proprius (EIP) muscle; with hand pronated, G1 placed two fingerbreaths proximal to the ulnar styloid, G2 placed over the ulnar styloid.

Stimulation Sites:

1. Forearm: Over the ulna, 4-6 cm proximal to the active recording electrode.
2. Elbow: In the groove between the biceps and brachioradialis muscles.
3. Below spiral groove: Lateral midarm, between the biceps and triceps muscles.
4. Above spiral groove: Posterior proximal arm over the humerus.

### **Phrenic motor study**

Recording Site: Diaphragm muscle - G1 placed two fingerbreadths above the xiphoid process, G2 placed over the anterior costal margin 16 cm from G1.

Stimulation Sites: Lateral neck: Posterior to the sternocleidomastoid muscle, approximately 3 cm above the clavicle.

### **Facial motor study**

Recording Site: Nasalis muscle - G1 placed lateral to midnose, G2 placed on the contra lateral side of the nose at the same location.

Stimulation Sites: Anterior tragus: directly in front of lower ear.

### **Tibial motor study**

Recording Site: Abductor hallucis brevis (AHB) muscle- G1 placed 1 cm proximal and 1 cm inferior to the navicular prominence, G2 placed over the metatarsalphalangeal joint of the great toe.

Stimulation Sites: 1. Medial ankle: Above and posterior to the medial malleolus.

2. Popliteal fossa: Mid-posterior knee over the popliteal pulse.

### **Peroneal motor study**

Recording Site: Extensor digitorum brevis (EDB) muscle- Dorsal lateral foot with G1 placed over the muscle belly, G2 placed distally over the metatarsolphalangeal joint of the little toe.

Stimulation Sites:

1. Ankle: Anterior ankle, slightly lateral to tibialis anterior tendon.

2. Below fibular head: Lateral calf, one to two fingerbreadths inferior to fibular head.

3. Popliteal fossa: Lateral popliteal fossa, adjacent to external hamstring tendons, at a distance of 10-12 cm below-fibular head site.

The normal values for various nerves are shown in the Table-1&2.

## **VIII. Interpretation**

The interpretation of electrophysiological functions of nerve trunks is usually based on the analysis of three basic criteria - velocity, latency and amplitude of the evoked response (Figure-1).

a) **Amplitude:** represents a summation of activity of the axons within a nerve trunk.

b) **Latency:** The time taken for the stimulus to travel to nearest muscle is known as the distal latency and includes not only the time taken for the impulse to travel down the nerve but also the delay at the end-plate and initiation of contraction.

c) **Velocity:** The difference in the time taken for the impulse to traverse a measured length of nerve. From this conduction velocity (meter/sec) is obtained.

Based on the changes in velocity, amplitude, and latency, the nerve function impairment is divided into three types – axonal, demyelinating and mixed type. Mixed type has changes of both axonal and demyelinating types (Table-3).

## **IX. Application**

Electrophysiological studies help in demonstrating and detection the integrity of nerve function in leprosy. They are useful not only in assessing nerve function at the time of diagnosis but also in the follow-up study of leprosy patients and complement clinical tests for nerve function assessment. NCS give data on peripheral nervous system (PNS) function which may be used to provide:

a) Diagnosis.

b) Description of disease state (old/new; dynamic/static pathophysiology).

c) Longitudinal monitoring of disease with multiple studies.

d) Advice on prognosis and management based on tests results and disease detected.

## **X. Contributions Of NCS In Clinical Managementof Leprosy**

### **I. Surgical management:**

Carayon and Rigal<sup>11</sup> outlined several general guidelines concerning the role of EMG and NCV studies in surgical indications in leprosy. These may be summarized as follows:

**a. Recent neuritis** - Negative Nerve conduction velocity (NCV) and EMG results do not contraindicate surgery after medical treatment. Surgery is especially indicated in the early stages of neuritis, to improve or halt the progression of the sensory-motor deficit. There is often improvement in NCV after surgery. When there is a remission induced by thalidomide, there is often a rebound; in these cases, if NCV drops and EMG worsens, it is a sign of failure of medical treatment and there is surgical indication. When the neuritis is subclinical, and NCV/EMG are stable, medical treatment alone should be pursued; if EMG/NCV results deteriorate in spite of medical treatment, surgery should be considered.

**b. Long-standing neuritis** - If there are clinically complete sensory-motor deficits and EMG/NCV results are very abnormal, surgery is contraindicated; if EMG shows some intact motor units and signs of regeneration, surgery can be indicated. Here Carayon and Rigal provide a "rule of thumb": they have found surgery worthwhile only when NCV is more than 25-30 m/s. A special case is when there is progressive hand mutilation with preservation of motor function; in such instances, it is difficult to propose surgical decompression of the median nerve at the wrist. However, if NCV and EMG are abnormal, showing subclinical motor involvement, surgery can be justified.

## **II. Monitoring of medical treatment:**

Granger<sup>12</sup> found in a patient with tuberculoid leprosy tested serially for NCV, that improvement of these velocities correlated well with periods of apparent remission of the disease, although there were no changes in clinically assessed sensory functions or reflex activity.

Rosenberg and Lovelace<sup>13</sup> studied a patient with lepromatous leprosy with NCV before and after dapsone therapy. There was improvement in 4 out of 12 nerves tested after 5 months of therapy. DeFaria and Silva<sup>14</sup> also detected improvement in NCV in some patients after 4 months of dapsone therapy.

Sheskin et al<sup>15</sup> studied 6 patients with lepromatous leprosy who had 17 leprosy reactions treated with thalidomide, 6 reactions treated with prednisone, 3 with analgesics and 2 with placebo. They found that both thalidomide and prednisone had a suppressive effect upon the neurologic manifestations, including the impairment of Motor nerve conduction velocity (MNCV), and concluded that MNCV can be used to monitor drug efficacy in leprosy reactions.

## **XI. Role Of NCS In Detection Of Thalidomide Induced Peripheral Neuropathy**

Leprosy patients on thalidomide may develop peripheral neuropathy disease per se or due to thalidomide and NCS can be used to differentiate between the two. Peripheral neuropathy occurs in 20% of individuals during first year of treatment.<sup>16</sup> It is characterised by painful paraesthesia and numbness in a glove and stocking distribution. It affects the lower limbs initially followed by the upper limb. It may be associated with weakness. Neuropathy correlates with the daily dose administered, but continues to progress for some time even after cessation of therapy, then gradually shows improvement. However, it remains permanent in 50% of the cases.

Nerve conduction studies reveal a sensory, predominantly axonal, length- dependent neuropathy. Nerves show loss of large myelinated fibres and mild inflammation when examined histologically.<sup>17</sup> The electrophysiological features of thalidomide induced neuropathy include, reduction of sensory nerve action potential amplitude and relative conservation of nerve conduction velocities.<sup>18</sup>

## **XII. Conclusion**

There is extensive involvement of peripheral nerves in leprosy, but statistically some specific nerves and sites predominate. The view that more superficial and therefore cooler nerve paths are preferentially involved in leprosy is challenged by a recent report of involvement of the phrenic nerve.<sup>19</sup> Nerve conduction studies support the notion that segmental demyelination with axonal preservation is the initial form of nerve involvement in leprosy. However, small unmyelinated and myelinated fibres are involved early in the disease. Early identification of nerve function impairment and prompt treatment are crucial to prevent disabilities. Neurophysiological examination should be done along with the clinical examination at the time of diagnosis as these studies are more sensitive than the clinical examination. NCS is rapid, safe and non-invasive technique making it a useful investigation where available.

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**TABLE- 1:** Nerve conduction studies normal values.<sup>9</sup>

Nerve	Record	Amplitude (µV)	Conduction Velocity(m/s)	Latency (ms)
Median Sensory	Digit 2	≥17	≥44	≤3.5
Ulnar Sensory	Digit 5	≥17	≥44	≤3.1
Radial Sensory	Snuffbox	≥15	≥50	≤2.9
Sural	Posterior ankle	≥6	≥40	≤4.4
Superficial peroneal	Lateral ankle	≥6	≥40	≤4.4
Saphenous	Medial ankle	≥4	≥40	≤4.4
Median Motor	Abductor pollicis brevis	≥4.0	≥48	≤4.2
Ulnar Motor	Abductor digiti minimi	≥3.7	≥49	≤3.4
Radial Motor	Extensor indicis proprius	≥2.0	≥49	≤2.9
Phrenic	Diaphragm	≥320	-	≤8
Facial	Nasalis	≥1.0	-	≤4.2
Peroneal motor	Extensor digitorum brevis	≥2.0	≥44	≤6.5
Tibial motor	Abductor hallucis brevis	≥4.0	≥41	.8

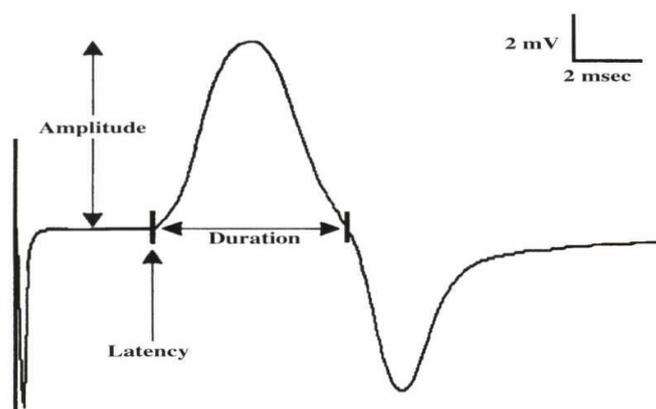
**TABLE-2:** F Responses.<sup>9</sup>

NERVE	MINIMAL F LATENCY (ms)
Median	≤31
Ulnar	≤32
Peroneal	≤56
Tibial	≤56

**TABLE-3:** Type of nerve function impairment.

TYPE	VELOCITY	LATENCY	AMPLITUDE
AXONAL	N/Slight ↓	N/Slight ↓	↓↓↓
DEMYELINATING	↓↓↓	↑↑↑	N/Slight ↓
MIXED	↓↓↓	↑↑↑	↓↓↓

**FIGURE-1:** Compound muscle action potential (CMAP).



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