

PERIPHERAL NEUROPATHY AND ITS MANAGEMENT: A REVIEW

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Summary

Peripheral neuropathy is very common and serious manifestation leading into partial or even complete disablement with pain killing, tingling and continuous instinct pain. Diabetes Mellitus, hypertension and any viral infectious diseases are bound to cause peripheral neuralgia. How to overcome this disorder, we have attempted to review peripheral neuralgia, causes and their preventive measures. Medicines like multivitamin with zinc, methyl cobalamin, high rich protein and yoga, acupuncture can help to get some remedies. The negligence of neuralgia will surely cause severe conditions. In this regard our review will help to know more about neuralgia and its managements.

Keywords: Neuropathy, Diabetes Mellitus, Methylcobalamin, Disablements

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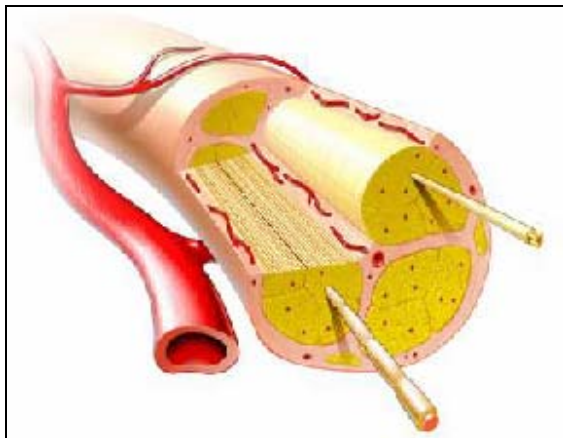
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Introduction

According to the Research and Market report, Peripheral Neuropathy (PN) and Neuropathic Pain (NP) affect 170 to 270 million individuals globally¹. Peripheral Neuropathy (PN) is one of the most common neurological disorder encountered in general medical practice. All clinical, electrographic and morphological evidence state that there is a involvement of an axon and their supportive structure of the neurons(Sensory, motor, autonomic) in the persistent disorder. Therefore, **Peripheral Neuropathy describes**, “Disorder of peripheral nerves, including the dorsal or ventral nerve root ganglia; brachial or lumbosacral plexus; cranial nerves (except I and II); and other sensory, motor, autonomic, or mixed nerves². Clinically, PN often manifest as numbness, loss of sensation, electric shock-like sensation, tingling, burning or pain in toes and feet and sometimes in fingers and hands, and weakness”. The nerves are communication channel which relay signal from central nervous system to the muscle and the other organs of the body and from skin, joints and other organs back to the brain. In short, nerve cell alerts a person to the tissue injury and stimulation in their environment.

Normal Nerve



Damaged Nerve:

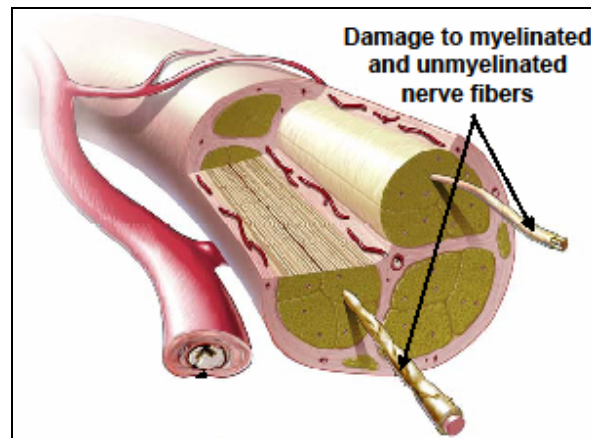


Fig: 1: Normal Nerve

Fig: 2: Damaged Nerve

The failure of such nerves carrying information due to the degeneration of the myelin sheath or axonal damage leads to improper functioning of the nerves which gives rise to the false signaling. Normally, pain is a signal of imminent or actual harm to the body that initiates protective reflexes to prevent or minimize that danger. However, when pain occurs in the absence of dangerous stimuli, does not prompt protective reflexes, nor subsides when the danger is past or when the injury has healed, it is said to be maladaptive or dysfunctional and is called **neuropathic pain** and the pain associated due to the damage of the peripheral nerves is called as

Peripheral neuropathic pain³. A symptom of the neuropathic pain tends to predominate in the peripheral limbs (in the feet more than in the hands) but can also appear in the different locations (e.g: in the cranial nerves as trigeminal neuralgia).

The following figures show early onset and late Peripheral Neuropathy:

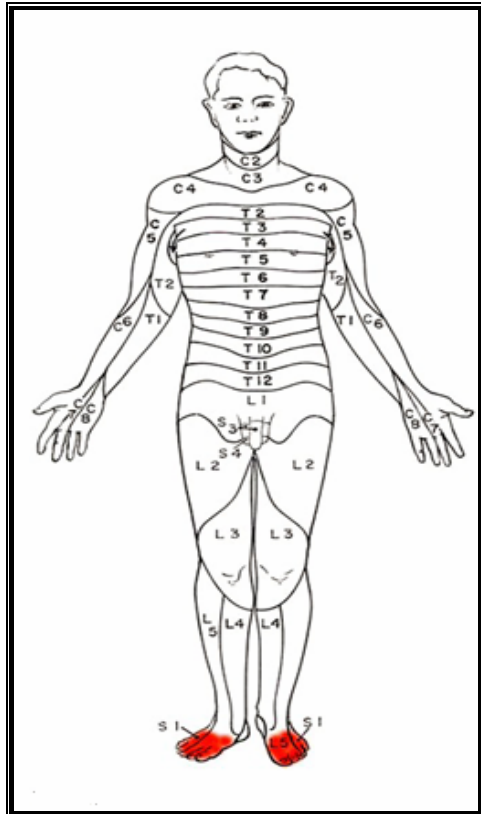


Fig: 3: Early onset PN

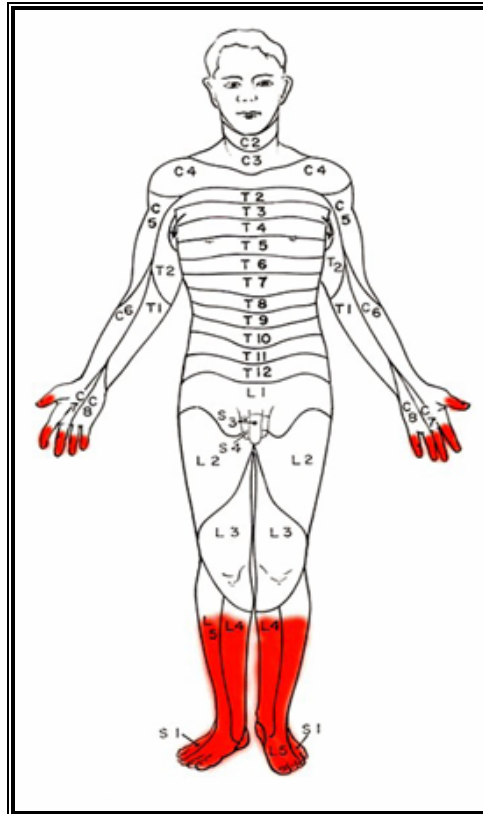


Fig: 4: Late PN

CLINICAL ASSESSMENT

SENSORY SYMPTOMS

- ✓ Numbness or Loss of feeling.



- ✓ Pins and needles.
- ✓ Tingling.
- ✓ Pain: burning, shock-like, stabbing, prickling, shooting, and lancinating.
- ✓ Extreme sensitivity to touch.
- ✓ Loss of balance and co-ordination.
- ✓ Unusual sensitivity or tenderness when feet are touched (Allodynia).

SIGNS

- ✓ Decreased
 - Vibration



- Joint-position sense
- Reflexes
- Pin prick and temperature sensation.



MOTOR SYMPTOMS

- ✓ Cramps in the feet and calves.
- ✓ Weak grip.
- ✓ Foot drop twitching.

SIGNS

- ✓ Reduced strength reflexes.

AUTONOMIC SYMPTOMS

- ✓ Decreased or increased sweating.
- ✓ Dry eyes.
- ✓ Dry mouth.
- ✓ Erectile dysfunction.
- ✓ Bladder incontinence.
- ✓ Gastroparesis/diarrhea.
- ✓ Faintness.
- ✓ Light-headedness.

SIGNS

- ✓ Orthostasis.
- ✓ Unequal pupil size.

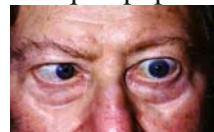


Fig: 5: Clinical Signs and Symptoms of Peripheral neuropathy^{2, 4, 5, 6, 7}.

CAUSES^{2, 8, 9, 10}

The Principle causes of peripheral neuropathy are:

- Metabolic
 - Diabetes mellitus
 - Renal failure
 - Amyloid
 - Porphyria
- Toxic
 - Drugs
 - Alcohol
 - Heavy metals
 - Anticancer drugs
 - HIV drugs
 - Tick bite
- Infectious
 - HIV
 - Lyme disease
 - Cytomegalovirus
 - Syphilis
 - Leprosy
 - Diptheria
- Immune-mediated
 - Guillain-Barre syndrome (GBS)
 - Chronic inflammatory demyelinating neuropathy (CIDP)
 - Multifocal motor neuropathy
 - Anti-myelin-associated glycoprotein (MAG) neuropathy
- Hereditary
 - Charcot-Maries-Tooth disease
- Vasculitic
 - Polyarthritits nodosa
 - Churg-Strauss syndrome
 - Cryoglobulinemia
 - Vasculitis of the peripheral nervous system
- Paraneoplastic
 - Especially lungs
- Nutritional
 - Vitamin B₁₂, B₁, B₆ deficiencies

CLASSIFICATION OF PERIPHERAL NEUROPATHY^{2, 11}

Depending upon the several parameters, Peripheral Neuropathy can be classified as follow:

1. By Predominance of cardinal feature/ or Fiber type:

- a) Sensory
 - o Small- fiber sensory
 - o Large- fiber sensory
 - o Small and large- fiber sensory
- b) Motor
- c) Autonomic
- d) Mixed (sensory+motor+autonomic)

2. By Location / or distribution of involvement:

- a) Polyneuropathy / or distal, symmetrical limbs
- b) Mononeuropathy
- c) Mononeuropathy multiplex
- d) Radiculopathy
- e) Localized neuropathy (i.e. brachial)

3. By time course:

- a) Acute (abrupt onset, fast evolution)
- b) Subacute
- c) Chronic (slow onset and evolution)
- d) Longstanding heritable
- e) Recurrent

Relapsing (acute or chronic with partial or full recovery in the interval)

4. By Histopathology:

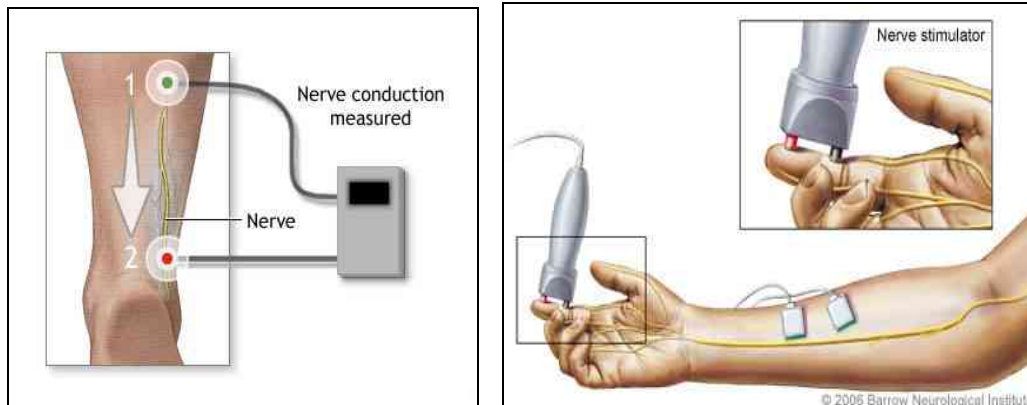
Any pathogenic factor that gives rise to the peripheral neuropathies will damage either axon or myelin sheath or both (i.e. Neuronal), therefore depending on this it is divided into-

- a) Axonopathy
- b) Myelinopathy

DIAGNOSIS OF PERIPHERAL NEUROPATHY (PN)^{11, 12, 13, 14.}

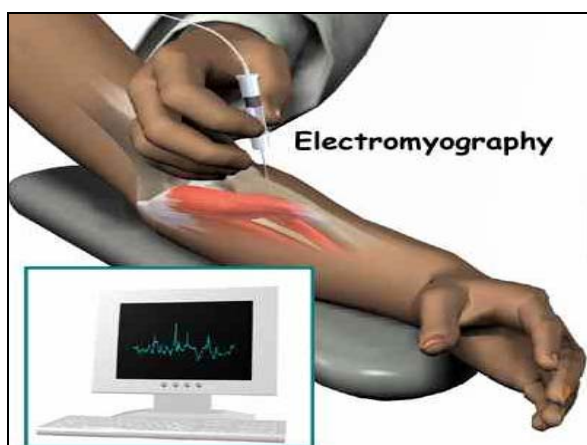
1) Nerve Conduction Study (NCS):

It is carried out to evaluate the ability of electrical conduction, of the motor and sensory nerves of the human body. It Involves stimulation of the nerves by electricity and stimulation is often performed on affected and “normal” parts of the body for comparison.

**Fig: 6: Nerve Conduction Study (NCS):**

2) Electromyography (EMG):

It is a technique carried out by inserting a thin needle into skeletal muscles for evaluating and recording the electrical activity produced. The signals can be analyzed to detect medical abnormalities, activation level, and recruitment order or to analyze the biomechanics of human or animal movement.

**Fig: 7: Electromyography (EMG):**

3) Blood test:

- Oral Glucose Tolerance Test (OGTT)
- Hemoglobin A_{1C} (HbA_{1C})
- Serum protein electrophoresis pattern and immunofixation (SPEP/IFIX)
- Fasting plasma glucose
- Antinuclear antibody (ANA)
- Evaluation of serum level of Vitamin B₁₂
- Westergren erythrocytic sedimentation rate (WESR)
- Thyrotropin (TSH)
- Folate
- Urine level for heavy metals

4) Genetic testing:

- Charcot-Marie-Tooth disease
- DNA testing for familial amyloid polyneuropathy (TTR mutations)
- DNA testing for mitochondrial disease
- DNA testing for the SCA syndromes, nearly all of which have an associated sensory neuropathy of varying severity
- If clinically suspicious, testing for defect of lipid metabolism

5) Examination of the Cerebrospinal Fluid (CSF) :

CSF examination is helpful in inflammatory demyelinating neuropathies. Because cranial and spinal roots bathe in CSF, demyelinating neuropathies that involve roots cause elevation of CSF protein. Also, inflammation in nerve roots causes CSF pleocytosis

6) Nerve biopsy:

The sural nerve is usually chosen for biopsy because it is superficial and easy to find and it is predominantly sensory and studied by light microscopy, electron microscopy, morphometry, and teased fiber preparations.

7) Skin biopsy:

A 3-4 mm plug of skin is removed with a punch and sectioned with a microtome. The sections are treated with antibodies to Protein Gene Product 9.5 which reveal small nerve

fibers that penetrate the epidermis. The density of these fibers is reduced in small fiber neuropathies.

- 8) Quantitative sudomotor axon reflex testing (QSART), Quantitative sensory test (QST), Lumbar puncture (LP), Chest X-ray, infrared tele-thermography, Cancer screening are also some tests carried out for the diagnosis of peripheral neuropathies.

TREATMENT MODALITIES^{15, 16,17,18,19}:

No such a treatment is available for peripheral neuropathy, however therapies for the underlying condition, is treated first which is followed by the symptomatic treatment such as:-

- 1) Glycemic control for diabetic neuropathy
- 2) Supplement of Vitamin B12 in case of B12 deficiency.
- 3) Use of antioxidant in cases of inflammation.
- 4) Control on alcohol intake and smoking.
- 5) Surgery for entrapment neuropathy
- 6) Enzyme replacement for Fabry disease.
- 7) Liver or bone marrow transplant for amyloid neuropathy

Neuropathic pain is found difficult to control, but various classes of drug have proved helpful to control the pain such as shown in Table no.1.

Table no: 1: Treatment Modalities for Peripheral Neuropathy

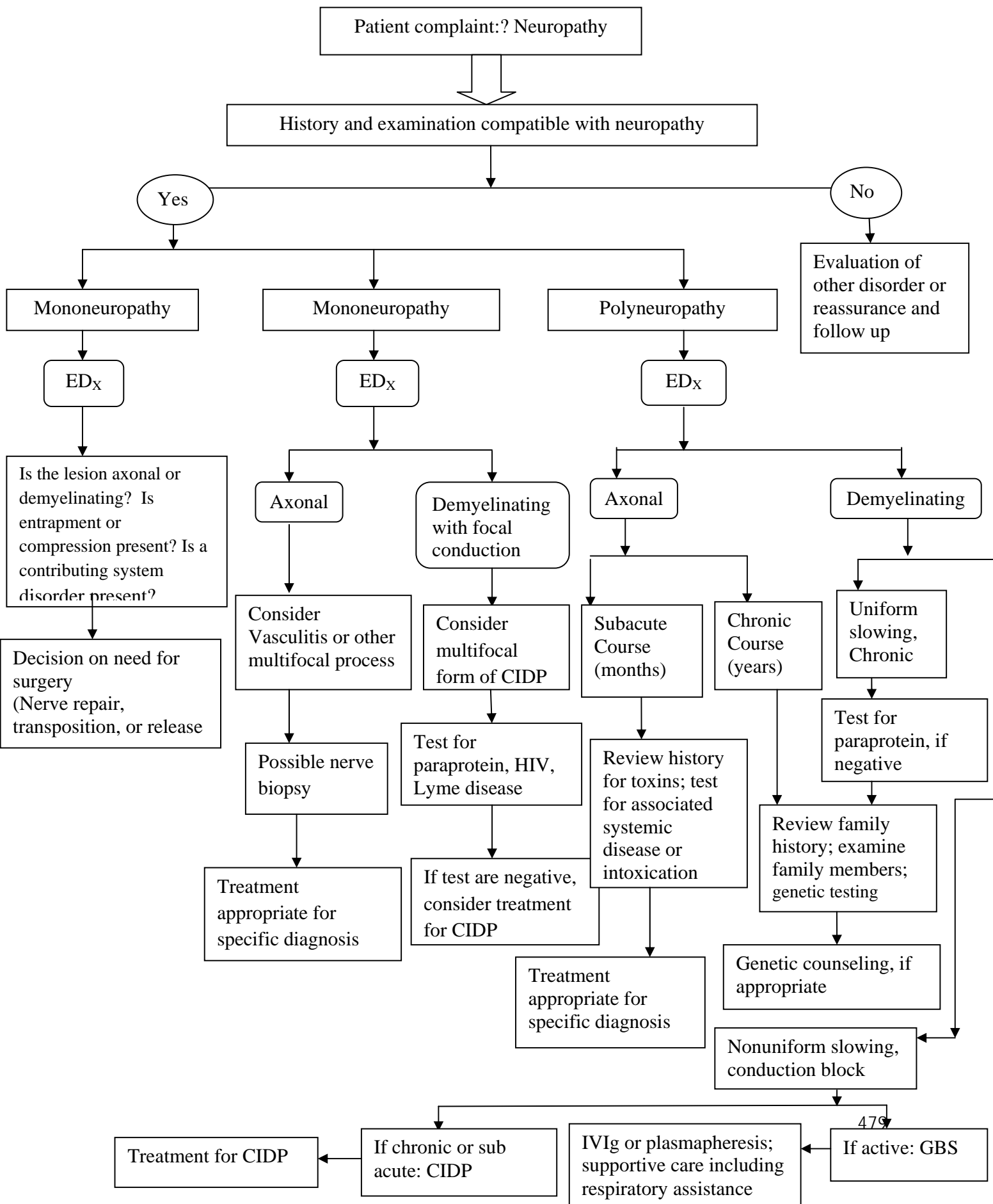
First- Line Therapy	Second -Line Therapy
Tricyclic antidepressant: <ul style="list-style-type: none"> ▪ Amitriptyline ▪ Nortriptyline ▪ Imipramine ▪ Duloxetine 	Opioids: <ul style="list-style-type: none"> ▪ Oxycodone ▪ Tramadol ▪ Morphine ▪ Fentanyl patch
Antiepileptics/ Anticonvulsant: <ul style="list-style-type: none"> ▪ Gabapentin ▪ Pregabalin ▪ Valproic acid ▪ Carbamazepine ▪ Topiramate ▪ Phenytoin 	Topical: <ul style="list-style-type: none"> ▪ Capsaicin ▪ Lidocaine patch ▪ Nitrates
Serotonin-noradrenaline reuptake inhibitor (SNRI) <ul style="list-style-type: none"> ▪ Duloxetine ▪ Venlafaxine 	Antiarrhythmics <ul style="list-style-type: none"> ▪ Mexilitine
	Others: <ul style="list-style-type: none"> ▪ Spinal cord stimulator ▪ Nerve blocks ▪ Transcutaneous electrical nerve stimulation(TENS) ▪ Intrathecal pump ▪ Radiofrequency (RF) and pulsed RF technique ▪ Alpha Lipoic acid

ALTERNATIVE REMEDIES FOR THE PREVENTION OF PERIPHERAL NEUROPATHY^{20, 21, 22}:

- ❖ **Regular exercise** can help to reduce some of the symptoms, increase overall muscle strength, increase blood circulation, and prevent muscle wasting or atrophy.

- ❖ Taking **healthy diet** is essential for the persons with neuropathic symptoms.
- ❖ **Avoid Cigarette smoking:** It can affect circulation, which constrict the blood vessel that provide oxygen and nutrient to the peripheral nerves
- ❖ **Avoid Alcohol intake:** Drinking alcohol is a leading cause of peripheral neuropathy.
- ❖ **Avoid overexertion and prolonged pressure:** Excess pressure may cause damage to the new nerve therefore it is necessary to carry out physical practices which may help relieve pressure on hypersensitive feet or hands. This includes limiting walking distances, avoiding standing for lengthy periods, wearing loose-fitting shoes and socks, avoiding repetitive pressure on the hands
- ❖ Regular **massage** of the feet and the hands can improve the blood circulation and provide stimulation to the nerves.
- ❖ **Foot care:** It is essential to take care of the feet, especially in case of diabetic patient because mostly neuropathic pain begins with the lower extremities. Look for red spots, cuts, swellings, blisters and calluses. Always wear comfortable shoes and shocks.
- ❖ **Yoga therapy:** Regular yoga has proved beneficial to reduce pain.
- ❖ **Acupuncture or acupressure:** Acupuncture has been reported to be very effective for the relief of neuropathic pain, with improvement often occurring with the first treatment. Repeated treatments may, however, be necessary for long-term relief. Where acupuncture is not available, acupressure—in which energy points are pressed or massaged—may be another possibility for treating neuropathy.
- ❖ **Sympathetic electrical current therapy:** Recent research has shown that the application of an electrical current designed to affect the nervous system systemically may significantly reduce pain and improve sleep in people diagnosed with chronic peripheral neuropathy.
- ❖ **Physiotherapy:** The exercise and therapy provided by the physiotherapist should be followed which help to reduce pain.

APPROACH TO THE EVALUATION OF PERIPHERAL NEUROPATHIES^{11, 23}:



{ ED_x – Electrodiagnostic studies.

CIDP- Chronic inflammatory demyelinating polyradiculoneuropathy.

GBS- Guillain-Barre syndrome}

Systems Affected with Peripheral Neuropathy

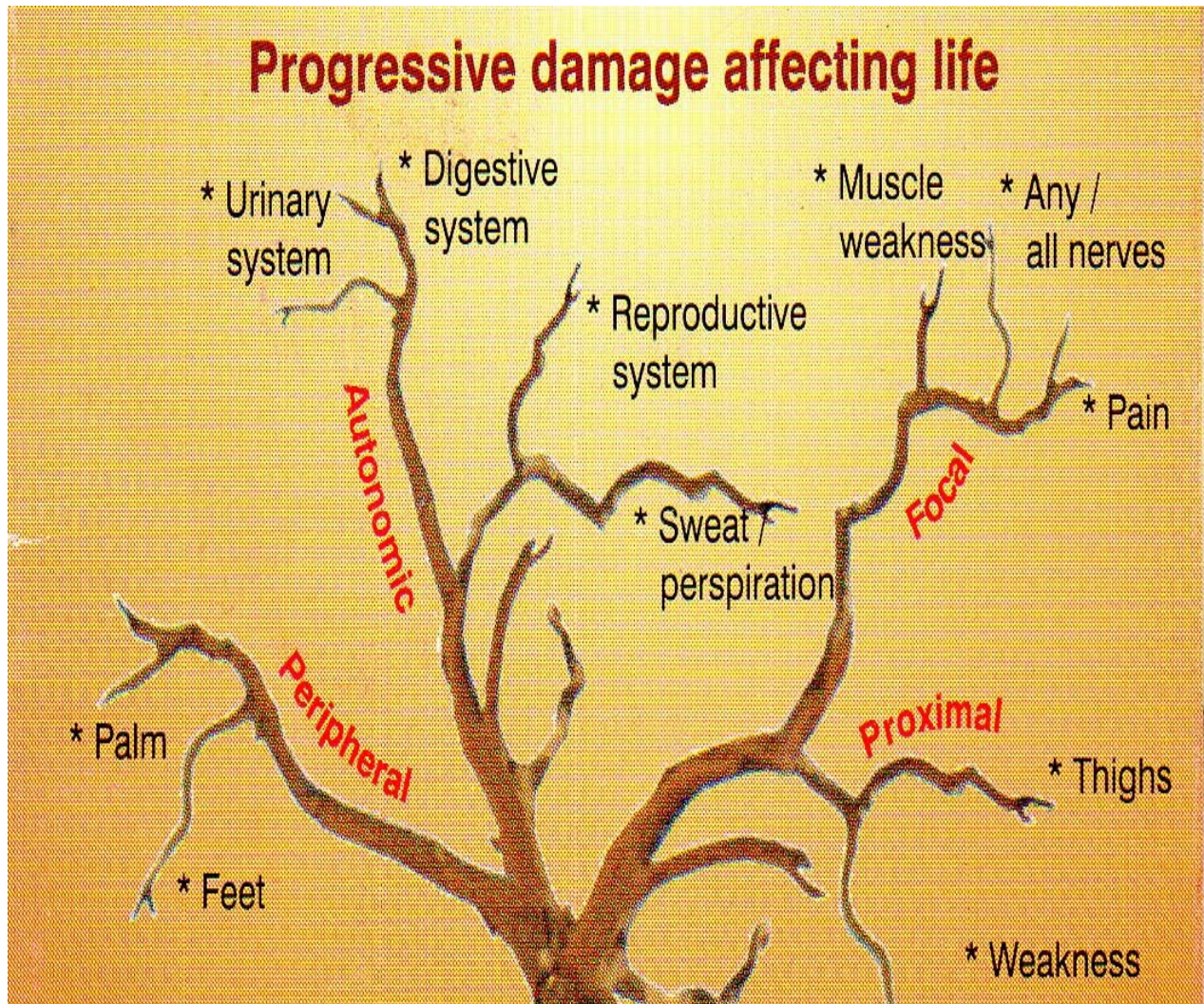


Fig: 7: Systems Affected with Peripheral Neuropathy

Conclusion

Peripheral Neuropathy is very humiliating, painkilling factor. More than 100 types of peripheral neuropathy have been identified. Severe sensitivity, numbness, tickling effect is very common. Myelin sheath which is responsible as insulating the neurons is being badly damaged, which is irreversible loss. However with the known desired medication and with methyl cobalamine, Rich protein diet, controlled exercise, pranayama, and yoga’s can help to prevent further damage of such complication issues protein supplements will help to overcome neuropathy.

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