

# UNDERSTANDING NEUROPATHY AND THE ROLE OF PHOTOBIOMODULATION

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## INTRODUCTION

Peripheral neuropathy (PN) is a debilitating illness that affects millions of Americans. The Center for Disease Control (CDC) estimates that diabetic peripheral neuropathy (DPN) alone, the most common form of neuropathy, affects nearly 26 million people.<sup>1</sup> The cost to society in terms of medications, treatments, lost work, and sometimes the ultimate damage from peripheral neuropathy amputation is huge. PN can also result in loss of balance, abnormal reflexes and coordination and can be a deadly recipe for disaster: falls. According to the National Council on Aging, falls are the leading cause of fatal injury in the overage 65 population.

Restoring sensation to the peripheral nerves could contribute significantly to fall reduction. This report explores the different types, causes, symptoms, and treatments available for the various peripheral neuropathies.

### A FALL CAN CHANGE EVERYTHING!

- 1 in 4 Americans aged 65+ falls each year.
- An older adult is treated in the emergency room for a fall every 11 seconds.
- An older adult dies from a fall every 19 minutes.
- Falls result in more than 2.8 million injuries treated in emergency departments annually, including over 800,000 hospitalizations and more than 27,000 deaths.
- The financial toll for older adults is expected to increase as the population ages and may reach \$67.7 billion by 2020.

National Council on Aging

## PATHOPHYSIOLOGY AND SYMPTOMS OF NEUROPATHY

Neuropathies are a group of medical disorders that result from disease or dysfunction in nerves of the peripheral nervous system, which are located outside of the brain and spinal cord. Most commonly, there is an interruption in the blood flow to these nerves which slowly deprives the nerve cells of essential nutrients. The lack of sufficient substrates (primarily oxygen and glucose) results in the degeneration of the nerve tissue and function. (See Figure 1)

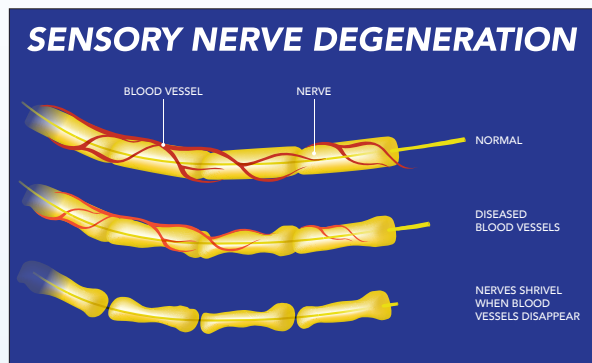


Figure 1

Peripheral neuropathy (PN) can affect either sensory or motor nerves. Sensory nerves carry information regarding touch, pain and temperature to the central nervous system and motor nerves carry electrical impulses as voluntary commands from the central nervous system to various muscle groups. In some cases, unconscious signals pass back and forth between the central and various internal organs via the autonomic nervous system (ANS). The ANS regulates our blood vessels, heart, respiration, digestion and many other unconscious activities.

Clinical symptoms of peripheral neuropathy depend on the location and type of the affected nerves, whether sensory, motor or autonomic. Some types of neuropathy affect all three nerves types simultaneously. And, some neuropathies arise suddenly while others develop gradually over time. Common symptoms include:

- Stabbing, sharp pains which are more pronounced at night. This pain may be described as “electrical” that start with the feet and legs and progress to the hands.
- Burning sensation in the legs and feet which may progress to also involve the arms and hands over time.
- Numbness and tingling of the distant limbs which may progress to the upper extremities.

- Itching or extreme sensitivity to even the slightest touch of a cloth or sheet. These symptoms are generally bilateral and are more pronounced at night with the legs generally being more affected than the hands.
- Coordination and balance problems.
- Muscle weakness or paralysis.
- Increased susceptibility to skin infections with subsequent development of foot ulcers and other problems that affect the feet, including possible amputation.
- In autonomic neuropathies, symptoms such as postural hypotension (dizziness from getting up from sitting or lying position), irregular heartbeat, balance problems difficulty swallowing, constipation, bladder problems, impotence or decreased perspiration may occur.

## TYPES AND RISK FACTORS ASSOCIATED WITH NEUROPATHY

There are many different types of neuropathy with different etiologies.

- **Hereditary Neuropathies:** There are four main types of hereditary neuropathies affecting the peripheral nervous system:
  1. Hereditary sensory and autonomic neuropathy.
  2. Hereditary sensorimotor neuropathy. EX: Charcot-Marie-Tooth, or CMT disease, is the most common inherited sensorimotor neuropathy. Symptoms include numbness and tingling in the extremities, weakness and decreased muscle bulk especially in the lower legs and feet.
  3. Hereditary sensory neuropathy.
  4. Hereditary motor neuropathy.
- **Mononeuropathy:** These are almost always compressive neuropathies which occur when a single nerve is affected. EX: carpal tunnel syndrome, sciatica and peroneal nerve palsy (crossed leg palsy).
- **Multiple Mononeuropathy:** Occurs less commonly; one example is post-herpetic neuralgia as it typically involves more than one nerve.
- **Polyneuropathy:** This is the medical term used when many nerves are involved. Examples include diabetic neuropathy and Guillain Barre Syndrome.
- **Autonomic Neuropathy:** Damage to autonomic nervous system nerves impacts the cardiovascular system, gastrointestinal tract, and genitourinary system involuntary functions leading to abnormal heart rates, postural hypotension, bowel and bladder dysfunction, sexual dysfunction and lack of perspiration. Thinning of the skin has also been reported.
- **Peripheral Neuropathies (PN):** PN occurs when axons of the nerves of the peripheral nervous system are damaged. Common symptoms include numbness, pain, burning and tingling of the arms, hands, legs and feet, often in a stocking-glove distribution.
- **Diabetic Peripheral Neuropathy (DPN):** Diabetes is one of the most common causes of peripheral neuropathy affecting millions of people across the globe. DPN is medically considered to be an irreversible, progressive disease. Diabetics often live with other co-morbidities including coronary artery disease, stroke, kidney disease and retinopathy. DPN results in the microvascular injury to the blood vessels supplying these organs.
- **Peripheral Vascular Disease (PVD):** Atherosclerosis, or hardening of the arteries that supply the peripheral nerves, can result in symptoms of peripheral neuropathy. Control of the known risk factors of weight, diet, blood pressure, smoking, cholesterol, and blood sugar are all very important in overcoming this type of neuropathy. When lifestyle strategies are unsuccessful, these neuropathies often result in re-vascularization procedures, non-healing wounds, and amputation.
- **Thyroid Diseases:** Both low and high thyroid hormone levels are capable of affecting peripheral nerves bilaterally.
- **Chemotherapy:** There are numerous chemotherapy protocols involving agents that are toxic to peripheral nerves. Symptoms are usually symmetrical and bilateral and may or may not resolve when the medical treatments end.
- **Various Infections:** Guillain Barre, Herpes Zoster (shingles) and Lyme disease are several of the more common infectious etiologies for peripheral neuropathy.
- **Autoimmune Disorders:** Systemic Lupus Erythematosus (SLE) or "lupus" can also attack peripheral nerves.
- **Smoking:** cigarette smoking increases blood levels of carbon monoxide thereby lowering the oxygen carrying capacity of hemoglobin. Smoking is directly toxic to peripheral nerves and almost every organ or tissue in the body.
- **Alcohol Abuse:** Alcohol is not only toxic to nerves, but it also affects nerves secondarily by depleting the body of essential Vitamin B complexes (B1, B6 and B12 in particular) which are essential to peripheral nerve health.
- **Kidney Disease:** Renal disease with increasing levels of blood creatinine and urea levels can be directly toxic to peripheral nerves.



- **Liver Disease:** Increasing ammonia levels of liver failure is directly toxic to nerves. Asterixis, or liver flap, is a very unique form of neuropathy seen with liver failure.
- **Post-Surgical Neuropathies:** External pressure neuropathies from prolonged mal-positioning of a patient intra-operatively or from direct accidental severance or crushing of a peripheral nerve or nerves is an unfortunate, but not infrequently encountered, a cause of peripheral neuropathy.
- **Idiopathic:** Idiopathic is a medical term for “we don’t know,” as in, there is no known cause for the neuropathy symptoms. Next to diabetic neuropathy, the idiopathic category is the second most common type.



## TREATMENT

The underlying pathophysiology of peripheral neuropathies, whether functional, toxic or metabolic etiology, remains under continued scientific exploration, as does the search for therapeutic strategies to relieve the symptoms of PN. For example, compressed or entrapped peripheral nerves are typically managed first with conservative physical therapy or chiropractic adjustment modalities. If unsuccessful, careful surgery might be appropriate to release the entrapped nerve. For neuropathies caused by physical disorders, blood tests can be performed (ex: thyroid, liver or kidney disorders, vitamin deficiencies) to direct treatment of underlying condition(s). Infectious causes (shingles, Lyme disease) are treated with antibiotics. Idiopathic neuropathies have no apparent causative factor consequently symptomatic relief measures in the form of oral medications to creams and special diets are all that can be offered.

The treatment of diabetic peripheral neuropathy (DPN) is challenging. In spite of tight management of blood glucose levels, 50% of diabetic patients will develop peripheral neuropathy. To date, most FDA-approved pharmacological approaches to address the symptoms of diabetic or any other neuropathy include the anticonvulsant medications gabapentin, Neurontin, and Lyrica which diminish the pain signals being sent by affected nerves. Unfortunately, increasing doses of these medications are common as the disease progresses. Antidepressants have been demonstrated to relieve neuropathic pain in people without depression. Narcotic and opioid medications have been consistently effective in reducing neuropathic pain, but their use is less favored because of the

risk of dependency. Adjunctive treatment with topical anesthetics such as lidocaine has been helpful as has the use of topical capsaicin cream. In most cases, these interventions have no impact on the progressive nature of the disease processes.

Alternative therapies for peripheral neuropathy include: dietary supplements, cannabinoids, Botox, chiropractic massages, meditation, yoga, cognitive therapy, and acupuncture. Neuromodulators such as TNS units and deep brain stimulators have also been used. All have been found to be helpful on occasion. What remains to be demonstrated is whether these interventions affect the reversal of the disease process.

## PHOTOBIMODULATION & NEUROPATHY

Photomedicine is arguably one of the fastest growing fields in biomedicine. As industry experts continue to refine the nomenclature in the field the National Institute of Health recently adopted the term “photobiomodulation” (PBM) and “photobiomodulation therapy” (PBMT) as the most accurate term for the clinical application of light. The proposed definition of photobiomodulation is: “A form of light therapy that utilizes non-ionizing forms of light sources, including lasers, LEDs, and broadband light, in the visible and infrared spectrum. It is a nonthermal process involving endogenous chromophores eliciting photophysical (i.e., linear and nonlinear) and photochemical events at various biological scales. This process results in beneficial therapeutic outcomes including but not limited to the alleviation of pain or inflammation, immunomodulation, and promotion of wound healing and tissue regeneration.”<sup>2</sup>



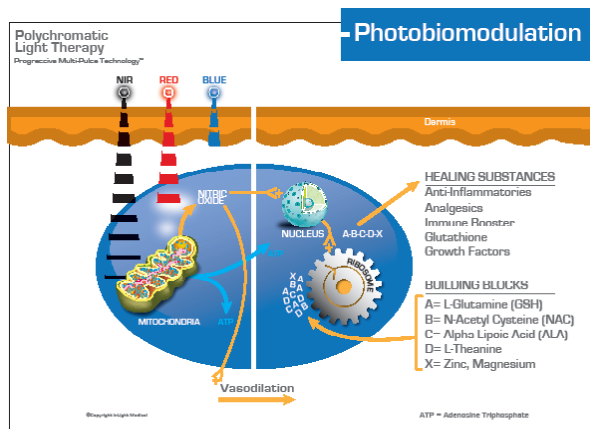


Figure 2

oxide (NO). NO exerts many beneficial effects on the body. Most notably, it acts as a local vasodilator to bring more blood flow to the treatment area and, additionally, it acts as an intracellular signaling molecule to the nucleus of the cell triggering the manufacture of various healing substances. (See Figure 2)

In the case of blood vessels injured by diabetes or atherosclerosis, one of these healing substances causes the proliferation of more blood vessels in a process called angiogenesis to further increase the blood flow to the affected nerve.<sup>5</sup> (See Figure 3) Angiogenesis and neurogenesis (birth of new nerve tissue) contribute to the restoration of damaged tissue in wound healing and recovery from neuropathic tissue damage. Vasodilation, angiogenesis, and neurogenesis are among the many healing processes triggered by the photobiomodulation release of nitric oxide.

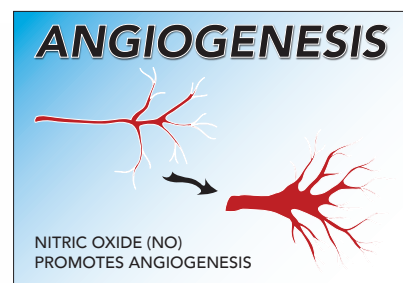


Figure 3



Figure 4

SOURCE: Arnall et al, 2006

Measuring changes in PPS with Semmes-Weinstein monofilament, this study demonstrated photobiomodulation therapy improved PPS of all subjects.

DiDuro (2016) demonstrated that using an FDA-cleared red/NIR device for 20 minutes, three times a week for six weeks in 152 patients with diabetic neuropathy resulted in a 30-40% overall improvement in their symptoms of diabetic neuropathy.<sup>12</sup> Mounting evidence suggests the improved nerve function was achieved by PBMT improving blood flow via angiogenesis and vasodilation.<sup>6,13,14</sup>

Peripheral neuropathies often lead to the loss of peripheral protective sensation (PPS) leading to the development of infections and wounds. In a study with 22 diabetic patients, Arnall et al<sup>10</sup> used red/NIR light emitting diode delivery of 650 nm and 880 nm photon energy in 30-minutes sessions pulsed at variable rates increasing from 73 Hz to 4672 Hz, three times per week for eight weeks.

## CONCLUSION

Peripheral neuropathy is a complex medical problem that is the source of significant morbidity and mortality in the United States. Understanding the primary underlying causes for any one of the dozens of different types of peripheral neuropathy may lead to appropriate treatments. By activating the process of photobiomodulation, newer technologies using polychromatic LED light are proving to be a safe, effective intervention for peripheral neuropathic pain and other symptoms associated with the condition. This is particularly true when decreased circulation is one of the underlying causes as in both diabetic peripheral neuropathy (DPN) and peripheral vascular disease (PVD). Additionally, studies are demonstrating PBMT improves peripheral sensation which suggests this non-pharmacologic, non-invasive technology might become instrumental in reducing falls among seniors. InLight Medical light therapy systems are cleared by the FDA to decrease pain and increase circulation and represent a safe, cost-effective, easy-to-use, evidence-based intervention for many of the peripheral neuropathies.

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