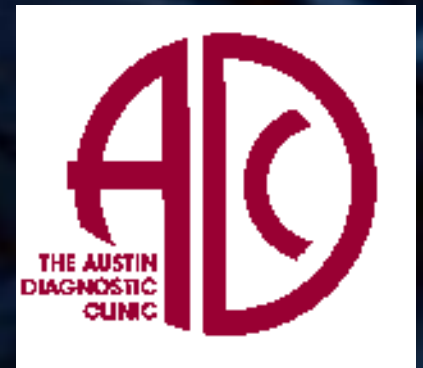


# Peripheral Neuropathy

**Patrick C. Nolan M.D., Ph.D.**  
**Austin Diagnostic Clinic**



# Objectives

- **Define peripheral polyneuropathy.**
- **Review common causes of peripheral neuropathy.**
- **Suggest effective and rational treatments for the causes and symptoms of neuropathy.**

# My Background

## EDUCATION:

University of Illinois at Urbana-Champaign

1991 Bachelor of Science (B.S.)

Biology

1996 Doctor of Philosophy (Ph.D.)

Neuroscience - Brainstem Neurophysiology

1999 Doctor of Medicine (M.D.)

2000 Medical Internship

University of Michigan Hospitals, Ann Arbor

2000-3 Neurology Resident Physician

2003-4 Neuromuscular Disease Fellow

## CURRENT POSITION:

Austin Diagnostic Clinic, Austin Texas

2004-Present

General Neurology with Specialty Interest in Neuromuscular Disease

(Parkinson's Disease, Dementia, Multiple Sclerosis, Stroke, Epilepsy, Peripheral Neuropathy, Migraine and other Headaches, Back and Neck Pain, Nerve and Brain Injury, ALS, etc.)

Member of Board of Directors for Austin Diagnostic Clinic

# Is Neuropathy a Big Problem?

20 Million people in the US are affected (Population 300 million)

Most peripheral neuropathies hurt

Burning, stinging, tingling, throbbing

Most neuropathies affect the feet first (Longest nerves)

Limits our ability to function

Limits independence

Promotes falls and affects wound healing - bloodflow

Pain is usually worse at night

Causes problems with sleep

# Central and Peripheral Nervous System

Central Nervous System

Peripheral Nervous System

- Motor Nerves
- Sensory Cell Bodies and Nerves
  - Large Fibers
  - Small Fibers

# The Autonomic Nervous System is also Part of the Peripheral Nervous System

## Autonomic Nervous System

- Blood pressure control
- Sweating
- Tearing of eyes
- Salivation
- Sexual function
- Bladder, colon and gut motility
- Sensation of hypoglycemia

# Anatomy of a Peripheral Nerve

## Motor Nerve Fibers

- Cell body lives inside spinal cord (Inside Blood Brain Barrier)
- Axon can be 1 cm (muscles in neck) to 5 feet long (toe muscles)

## Sensory Nerve Fibers

- Cell body lives in sensory ganglia ~1 inch lateral to spinal cord
- The Ganglia is leakier than the blood-brain barrier
  - Sensitive to toxins and metabolic control

## Autonomic Nerve Fibers

- Also live in ganglia outside blood brain barrier
- Very, very small fibers

# Why Does a Sick or Dead Nerve Often Cause Pain?

- My first word.

## Large Sensory Nerve Fibers

- Large diameter, myelinated, very metabolically active.
- More resistant to toxins/stress, sensitive to low energy stores.
- Convey vibration and position sense to neo(new)cortex
- Loss of these nerves does not result in typical "neuropathy pain"

## Small Sensory Nerve Fibers

- Small diameter, nonmyelinated, less metabolically active.
- More sensitive to toxins/stress
- Convey burning, pain sense to paleo(old)cortex
- Loss of fibers does not disconnect pain sensation (phantom limb)
- Instead - it amplifies the signal of the fibers that remain

## Autonomic Nerve Fibers

- Smallest diameter, nonmyelinated, less metabolically active.
- Not as sensitive as small fibers to toxins/stress
- Smallest blood vessels - sensitive to atherosclerosis



# What Makes a Nerve Sick?

Metabolic Problems (**Big Nerves** - not too painful)

- Starvation

- Metabolism problems

Poisons (**Small Nerves** - painful)

Immune Attack

Infectious Attack

Waste Removal Problems

# The Most Common Cause of Neuropathy

## Diabetes and Impaired Glucose Tolerance

At levels higher than metabolic needs, SUGAR IS A POISON

- Diabetes affects 18.2 Million People in USA (7%)
- Total of 20 million people with peripheral neuropathy
- >50% of Diabetics will be affected with neuropathy (DPN)
- In developed countries, DPN is responsible for 50-75% of amputations
- The mortality for diabetic autonomic neuropathy is 25-50% in 10 years of onset.

The severity of neuropathy is directly related to how long the nerve cell body and nerve fiber are exposed to hyperglycemia.

# But My Doctor Says I Don't Have Diabetes!

## Diabetes and Impaired Glucose Tolerance

The severity of neuropathy is directly related to how long the nerve cell body and nerve fiber are exposed to hyperglycemia.

10 -20% of all Americans will Develop Type II Diabetes (Insulin resistance)

Twice as many will have Impaired Glucose Tolerance

People with IGT have a 2-5x higher risk of heart attack and stroke

Exercise and diet changes are more effective than our best medications for preventing IGT to move to diabetes

Exercise increases the number of insulin receptors - makes muscles better able to store toxic glucose

Decreasing fat stores makes body rely on muscle glycogen stores for energy

# Organs Affected by High Sugars

Three organs cannot stop the flow of glucose from the blood into their cells...

- **Kidney** (Nephropathy leads to renal failure and eventually requires dialysis)
- **Eye** (Retina cells are also Sensory Nerves outside of the brain)
- **Sensory Nerves** (Sensory Ganglia are Leaky)
  - Nerve damage begins in everyone once HbA1c passes 9%
  - Great variability in sensitivity
    - Type I diabetics with long history
    - Some people with mild IGT

# Treating Diabetic Neuropathy

Aggressive management of:

blood sugars, weight loss and exercise can  
**REVERSE** neuropathy in impaired glucose tolerance.

Improving blood sugars in diabetes:

Slowed retinopathy, kidney disease and **IMPROVED** neuropathy by electrical testing

The best exercises are aerobic

- Swimming, Elliptical trainer, stationary bike
- Not treadmill, walking, running

Treat other Risk Factors

- Smoking and high lipids speed atherosclerosis
- Magnesium 250-750 mg at bedtime (metabolic effect?)
- Alpha Lipoic Acid supplements
- Get the Right shoes and supports

# Treat the Pain

## Neuropathic Medications

gabapentin/Neurontin, pregabalin/Lyrica, duloxetine/Cymbalta  
amitrptiline and nortriptiline  
antiepileptic medications

Works on nerves that are left

Acts on the subcortical brain pain processing regions

## Opiates

Not as helpful

Can lead to tolerance, dependency and addiction

## Topical Ointments

Lidocaine turns off nerve signals

Capsaicin drains a transmitter that causes pain

## Transcutaneous Electrical Stimulation (TENS)

## Acupuncture

## Photo Therapy

# Other Causes and Treatments of Peripheral Neuropathy

## o Genetic Causes

- o Charcot-Marie Tooth (CMT) (Motor and Sensory Nerves Affected)
  - o Most common inherited neurological disorder (36/100,000)
- o Friedrich's Ataxia (Large Sensory Fibers and Brain)
  - o Error in Metabolism
- o Porphyria (Motor Nerves)
- o Amyotrophic Lateral Sclerosis (ALS)
  - o (Only Motor Nerves)
  - o Unknown Cause

## Treatment

CMT - Supportive Care

Friedrich's - Clinical Trials underway

Porphyria - diet, IV medications and avoiding sunlight exposure

ALS - Supportive Care



# Other Causes & Treatments of Peripheral Neuropathy

## o Immune System Causes

- o Guillain Barre' GBS (Sensory and Motor Nerves)
- o Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)
- o Monoclonal Gammopathy of Unknown Significance (MGUS)
- o Lupus/Vasculitis (Any and All Nerves)
- o Sjogren's Syndrome (Sensory Nerves)
- o Rare Cancers - Paraneoplastic Syndromes
  - o (Sensory Nerves)
  - o Ovarian Cancer
  - o Small Cell Lung Cancer
  - o Pancreatic Cancer

## Treatment

GBS - Acute IV medications and support

CIDP, Lupus and Sjogren's -

Steroids, Immunosuppressants

MGUS - Monitor and treat symptoms

Paraneoplastic Syndromes - Treat the Cancer

# Other Causes and Treatments of Peripheral Neuropathy

## o Infectious Causes

- o Leprosy (The Ends of Long and Short Nerves- not length dependant)
  - o Beware the armadillo (Illegal to sell, state mammal)
  - o Used to be #1 in the world (1 million now)
- o HIV (Any and All Nerves)
- o Syphilis and Lyme Disease (Any and All Nerves)
- o Herpes Zoster (Shingles) (Sensory Nerves)
- o Polio (Motor Nerves)

## Treatment

Leprosy- Antibiotics for 24 months \*

HIV - Antivirals very effective

Syphilis/Lyme Disease - Antibiotics

Shingles - Antivirals

Polio- Vaccinate Population

# Other Causes & Treatments of Peripheral Neuropathy

## oToxins

### o Alcohol (**Large Fiber Sensory Nerves and Brain First**)

- o Don't have to be an alcoholic

### o Chemotherapy

- o (Paclitaxel/Taxol, Docetaxel/Taxotere, Abraxane, Vincristine/Onkovin, Vinorelbine/Navelbine, Cisplatin/Platinol, Carboplatin/Paraplatin, Oxaliplatin/Eloxatin)

### o Arsenic and some heavy metals (**Small fiber Sensory Nerves**)

- o Bangladesh, well water in the USA

### o Vitamin B6 (**Small Fiber Sensory Nerves**)

- o More than 200 mg a day should be avoided

### o Uremia

### o Amyloidosis

- o Can also be genetic

## Treatment

Alcohol - Abstinence

Chemotherapy - Vitamin E for some

Heavy Metal Exposure - stop exposure, Rare Chelation Therapy

Uremia - Minimize uremia levels (Dialysis)

Amyloidosis - Supportive Care, Liver Transplant

# Other Causes and Treatments of Peripheral Neuropathy

## o Deficiency States

- o **Vitamin B12 (Large Fiber Sensory Nerves first and Brain)**
  - o Fairly common
- o **Vitamin E**
- o **Thiamin**

CHANGES IN THE NEURONAL CENTRES IN  
BERI-BERIC NEURITIS.  
By HAMILTON WRIGHT, M.D.,  
Director of the Pathological Institute, Federated Malay States.

- 1901

## Treatment

**B-12 - IM replacement**  
**Occasionally oral**

**Vitamin E - may require IV therapy**

**Thiamin - Regular Diet**

# Another Way to Classify Neuropathy

## **Axonopathies (Most)**

**Diabetes (High Sugars)**

**Most infections, toxins and drugs**

## **Neuronopathies**

**B6 Toxicity**

**Paraneoplastic Cancers**

**Herpes Zoster/Shingles**

**Lou Gehrig's Disease (ALS)**

**Polio**

## **Myelinopathies**

**Autoimmune (CIDP, Guillain Barre')**

**Charcot Marie-Tooth**

**Some Toxins**

# A Third Way to Classify Neuropathy

**“When you hear hoofbeats- think horses, not zebras”**

*- Common medical school teaching point*

**Diabetes/Impaired Glucose Tolerance**

**B-12 deficiency**

**CIDP/Guillain Barre’**

**Alcohol**

**Chemotherapy**

**Herpes Zoster/Shingles**

**Charcot Marie Tooth + Something else**

**B6 toxicity**

**Syphilis/Lyme Disease**

**ALS/paraneoplastic neuropathies**

# Selected References

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