



# Nerves and Neuropathy

Janice Wiesman MD, FAAN

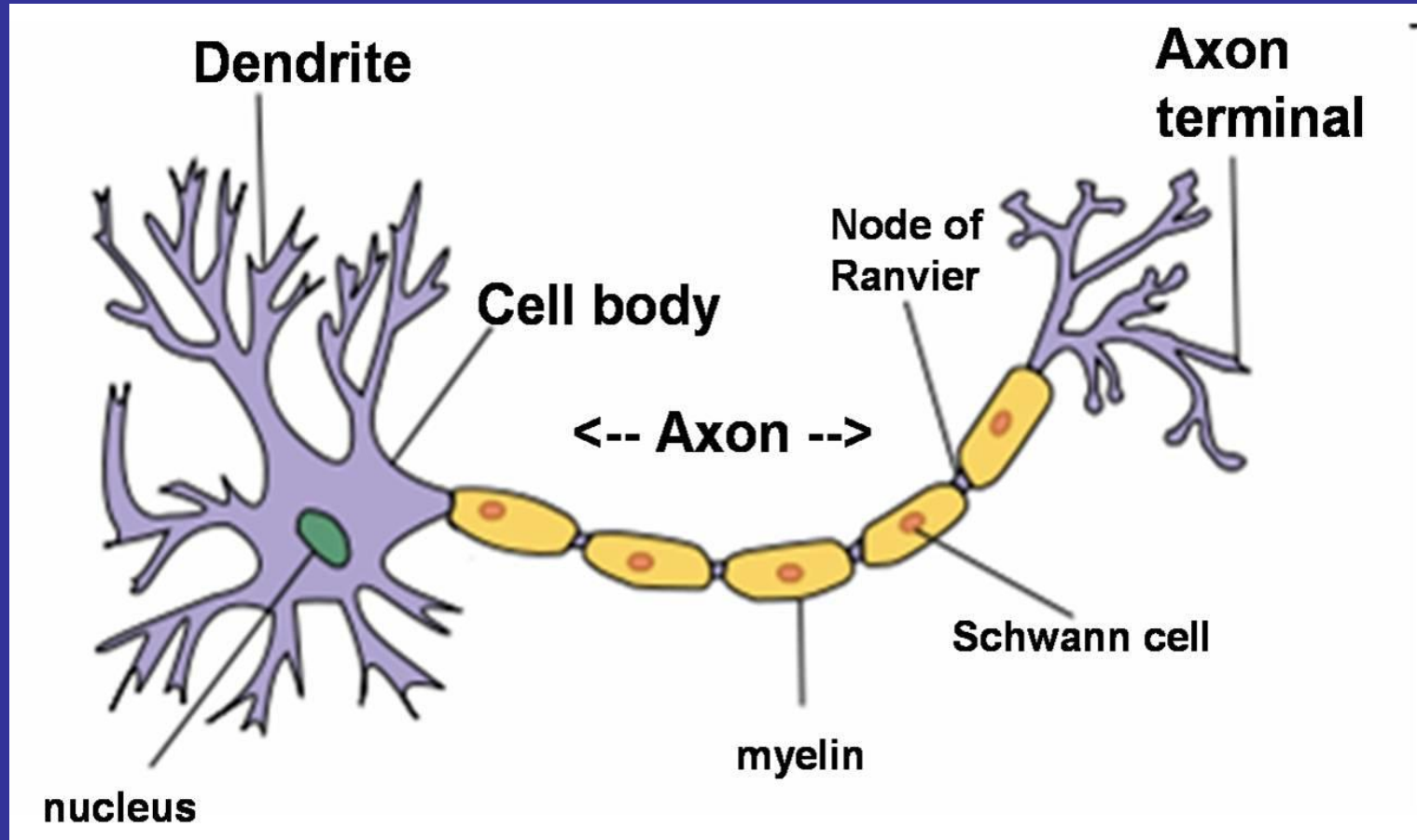
Associate Clinical Professor of Neurology

New York University School of Medicine

Adjunct Assistant Professor of Neurology

Boston University School of Medicine

# Structure of a neuron



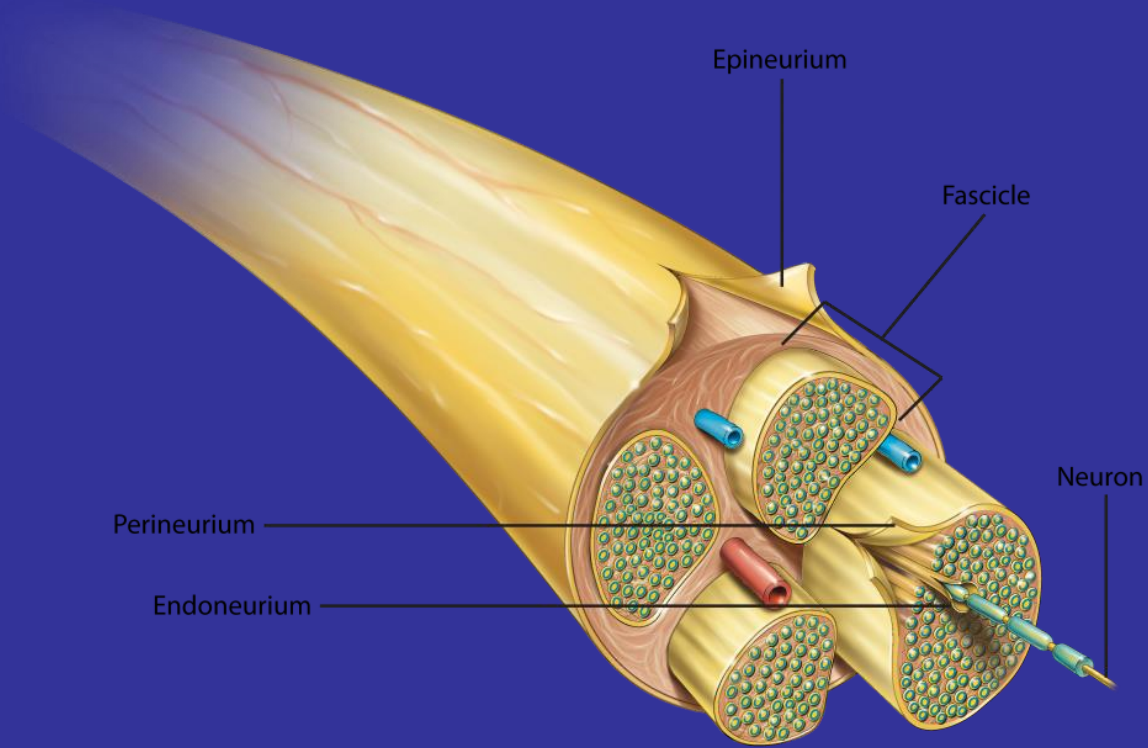
# What is an Axon?

- An axon is the arm-like extension of a nerve cell (neurons)
- There are motor, sensory and autonomic neurons which send out axons
- The neurons are located in or near the spinal cord

# What is a Nerve?

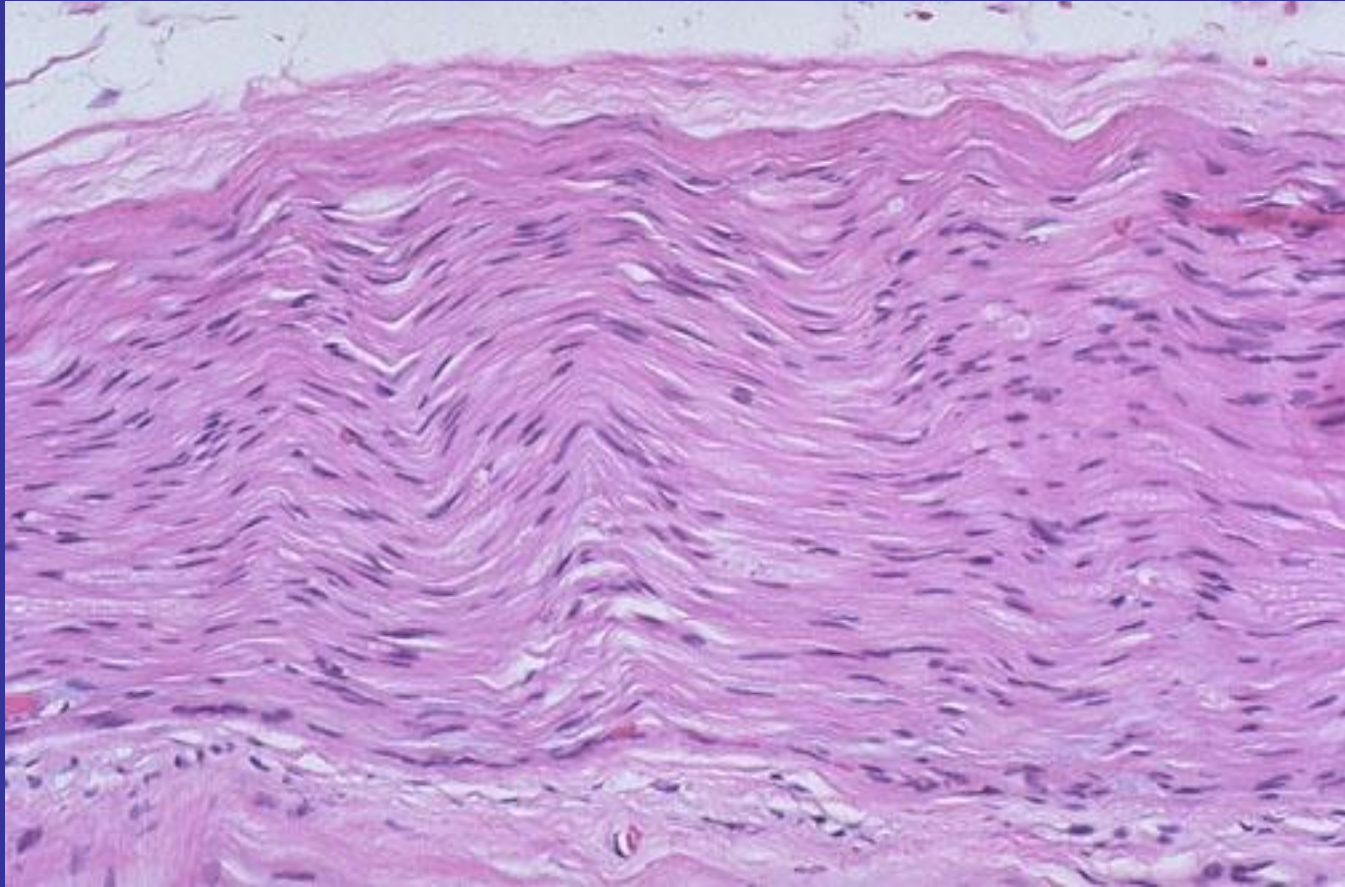
- A nerve is a cable-like bundle of axons that runs between the spinal cord and the periphery
- Axons transmit information by an electrical current that runs along the axon like a wire in your home
- The axons are each surrounded by a fatty coating, called myelin, that acts like insulation on a wire

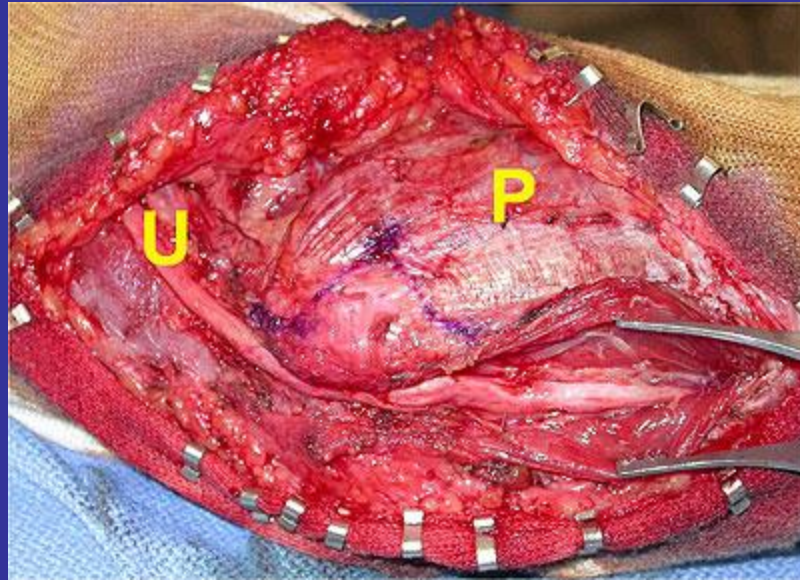
# Cross Section of a Nerve

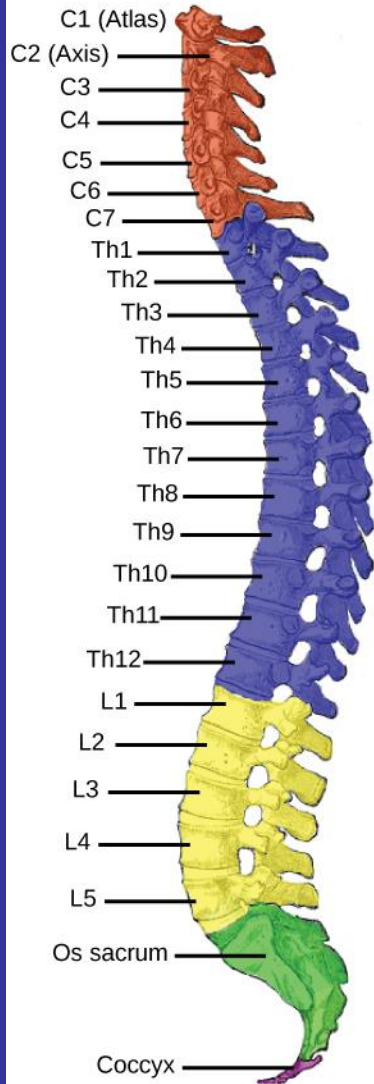


**Nerve**

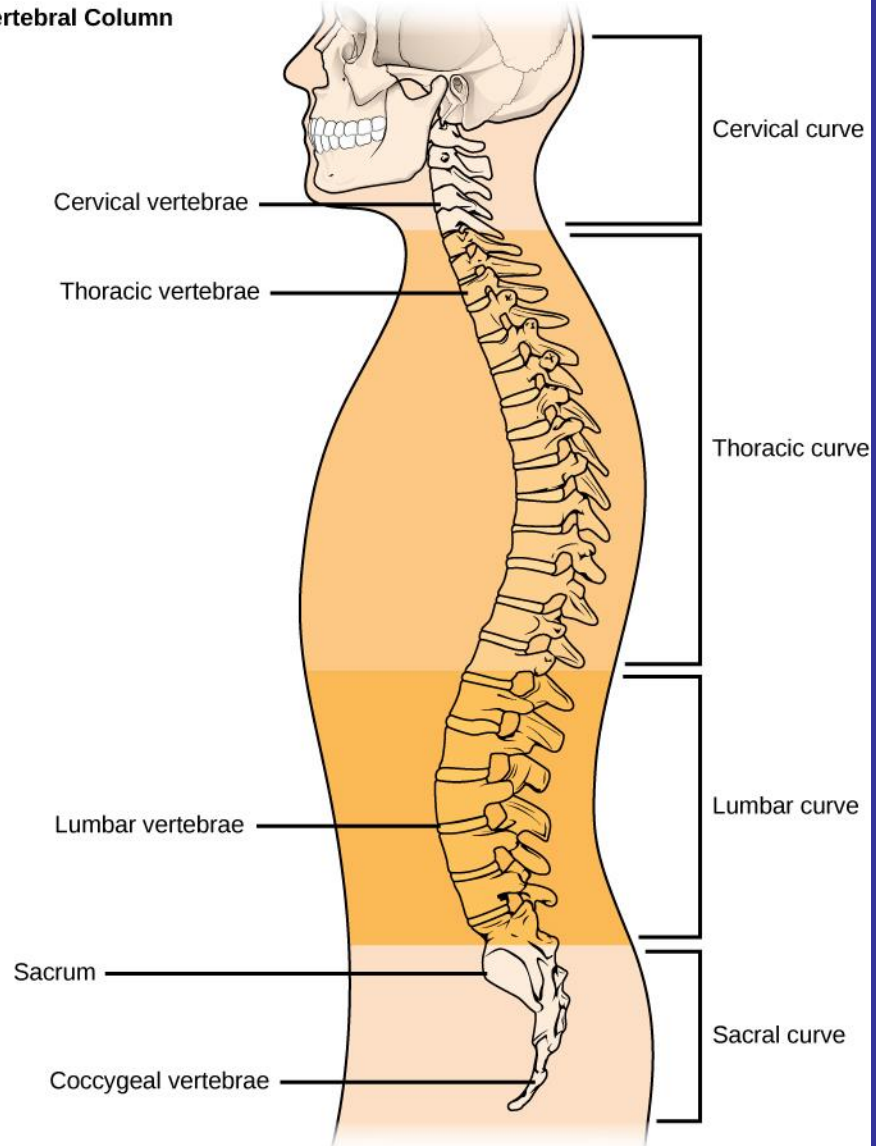
# Normal Nerve – Longitudinal Section







### Vertebral Column





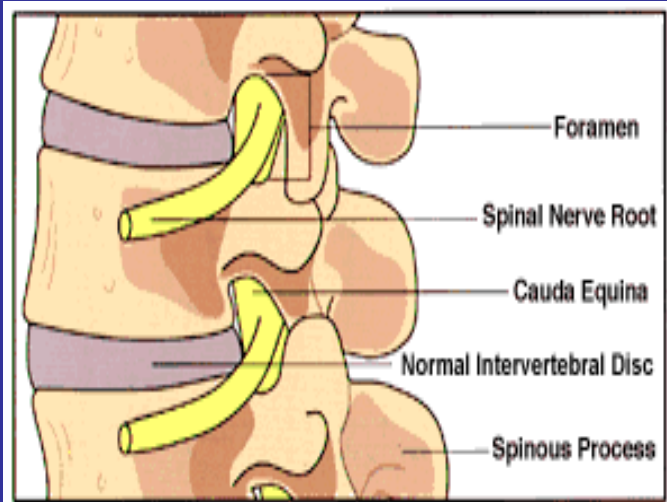
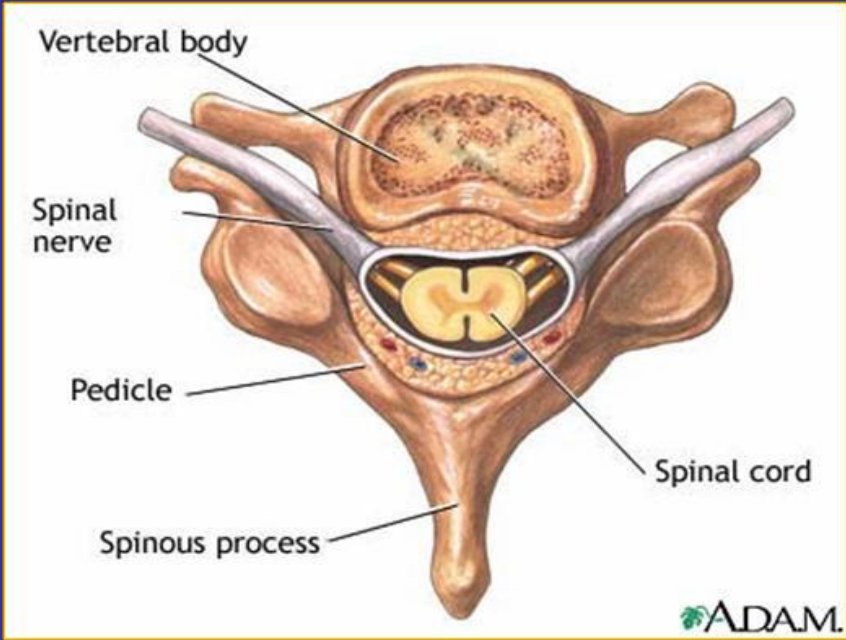
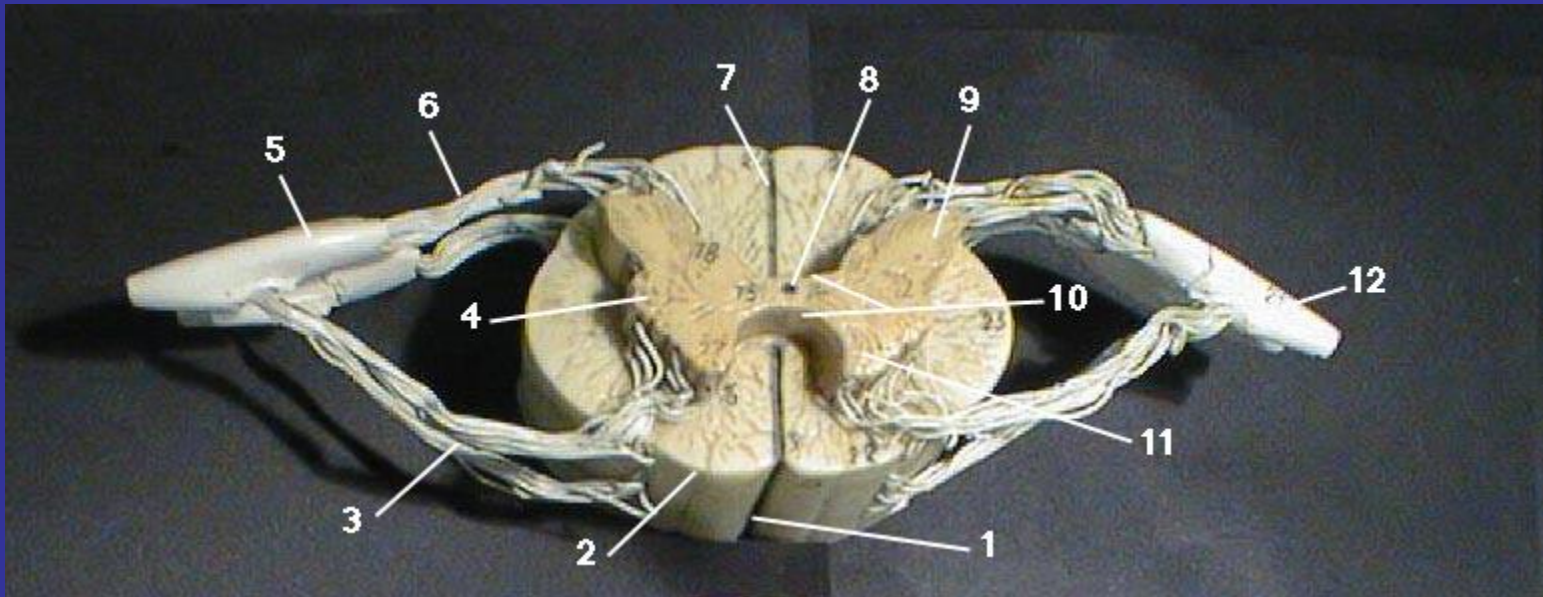


Figure #4: Side view of vertebral (spinal) column.



# 3 Types of Axons

## 1. Motor

- Information runs from cell bodies in the spinal cord to muscle
- These axons are thick with a heavy fatty coating

## 2. Sensory

- Information runs from nerve endings in the skin and organs to the spinal cord and up to the brain
- These axons are thin with less fatty coating

# 3 Types of Axons

## 3. Autonomic (“automatic”)

Information runs out from the spinal cord to:

- Salivary glands in the mouth
  - Tear glands in the eye
  - Muscle in the walls of blood vessels
  - Muscle in the walls of the stomach and intestine
  - Sweat glands in the skin
  - Blood vessels in the genitals
- These axons are the thinnest, with almost no fatty coating

# What is Neuropathy?

- Neuropathy is a general term meaning damage to a nerve
- One nerve = mononeuropathy
  - Example carpal tunnel syndrome
- Many nerves = polyneuropathy
  - Also called peripheral neuropathy

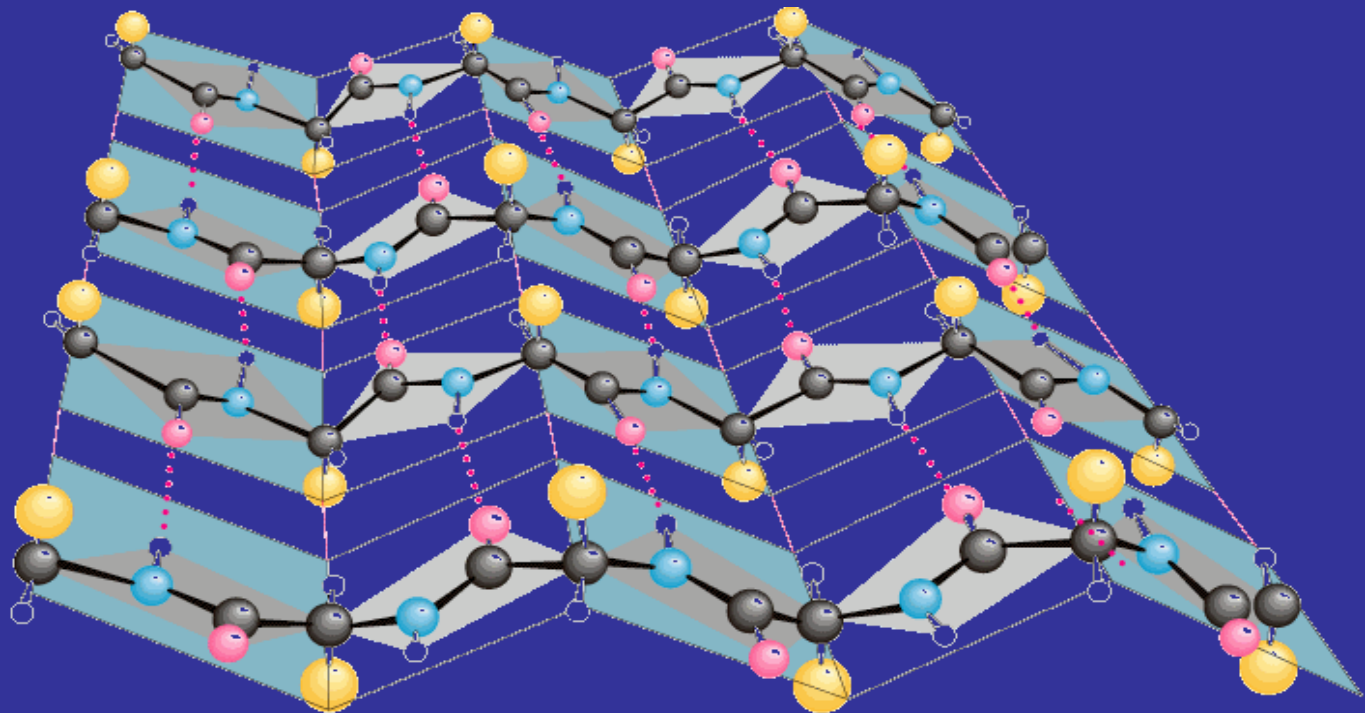
# Nerve Damage in Amyloidosis

- Seen in two types
  - Primary (AL, problem in bone marrow)
  - Inherited
    - TTR – also called Familial Amyloid Polyneuropathy
    - Gelsolin
    - ILE122 (though not common)
  - Not typically seen
    - AA amyloid
    - Focal amyloid

# What the heck is amyloidosis?

- A general term that refers to a number of diseases that result from extracellular deposition of insoluble proteins in tissues and organs.
- The diseases are a subset of disorders caused by misfolding of protein.
- Many different proteins can make amyloid fibrils
- All have a  $\beta$ -pleated sheet conformation which confers unique staining properties

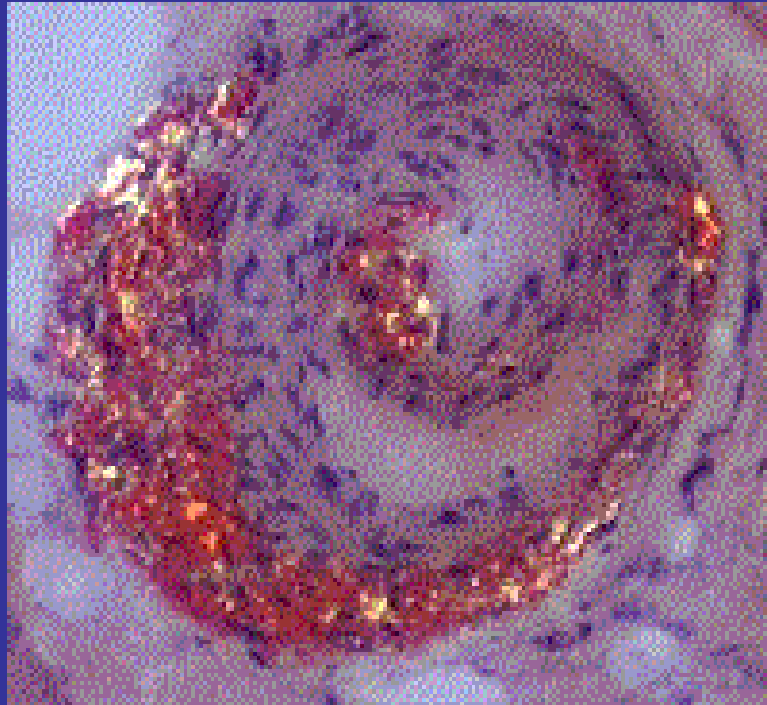
# Beta-Pleated Sheet



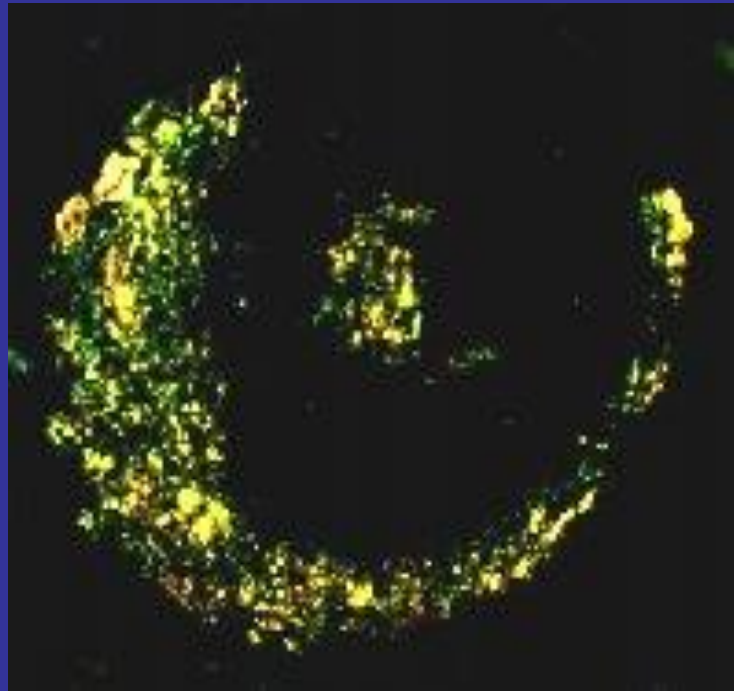
From *Biochemistry* 2nd Ed. by Garrett and Grisham (Harcourt, Brace & Company)



# Birefringence



# Birefringence



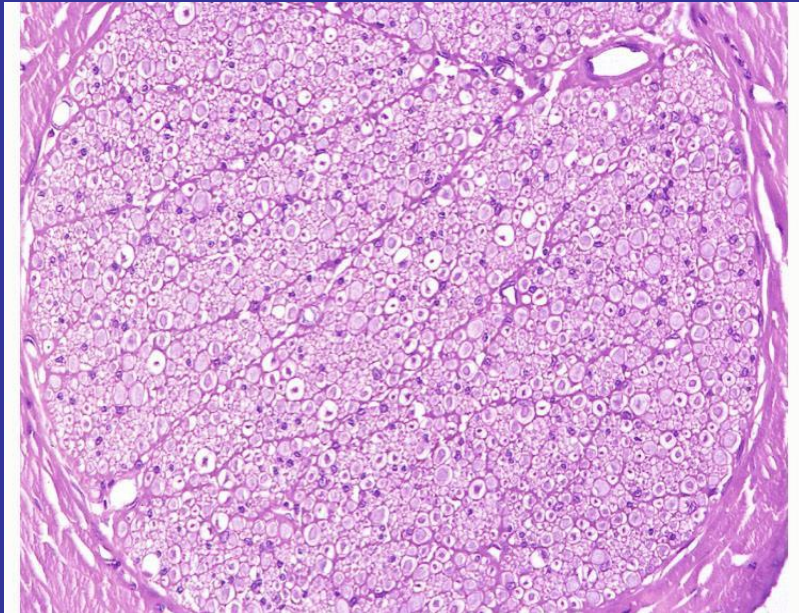
# Nerve Damage in Amyloidosis

- Can be one nerve
  - Carpal tunnel syndrome
- Can be generalized disorder of nerves
  - Amyloid polyneuropathy = peripheral neuropathy

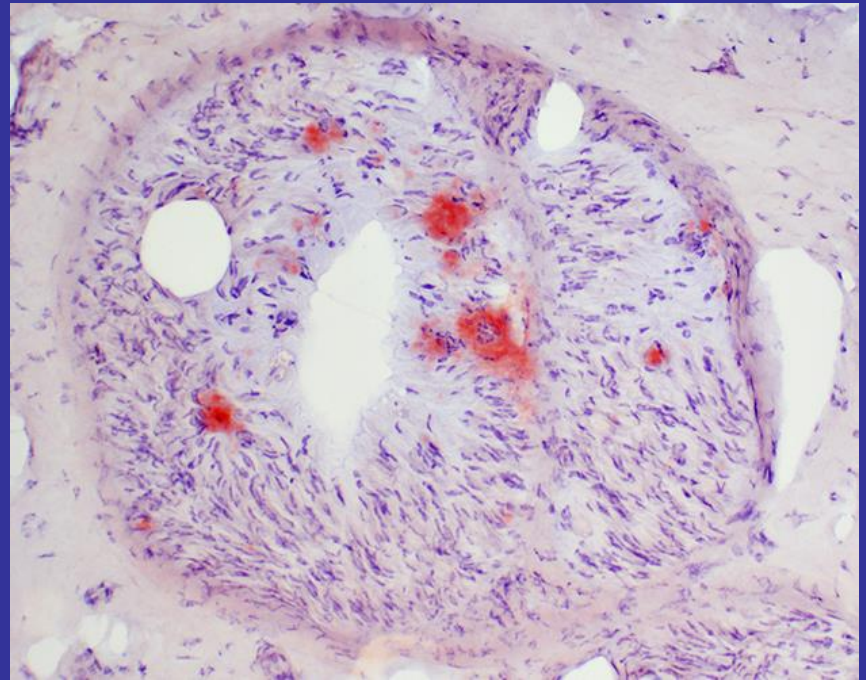
# Amyloid Polyneuropathy

- Axonal, length-dependent, symmetrical, dying-back neuropathy
  - Axon itself is damaged
    - Compression by amyloid deposits
    - Amyloid compresses blood vessels to nerve and prevents blood flow
    - The area that surrounds the dorsal root ganglia, where sensory axons are located, has a poor blood/nervous system barrier and amyloid can infiltrate here and damage sensory neurons and axons

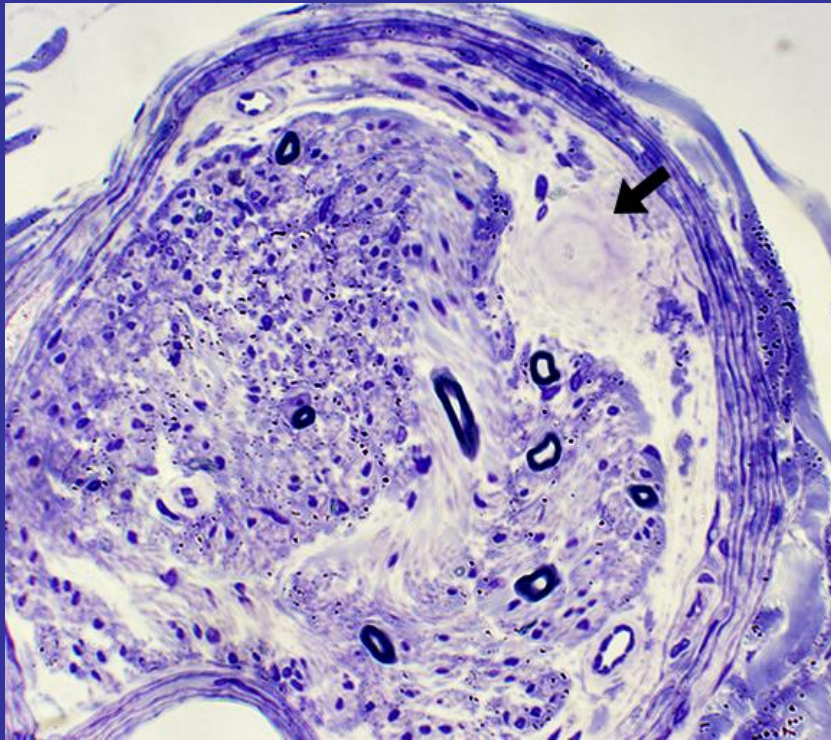
**Normal nerve**



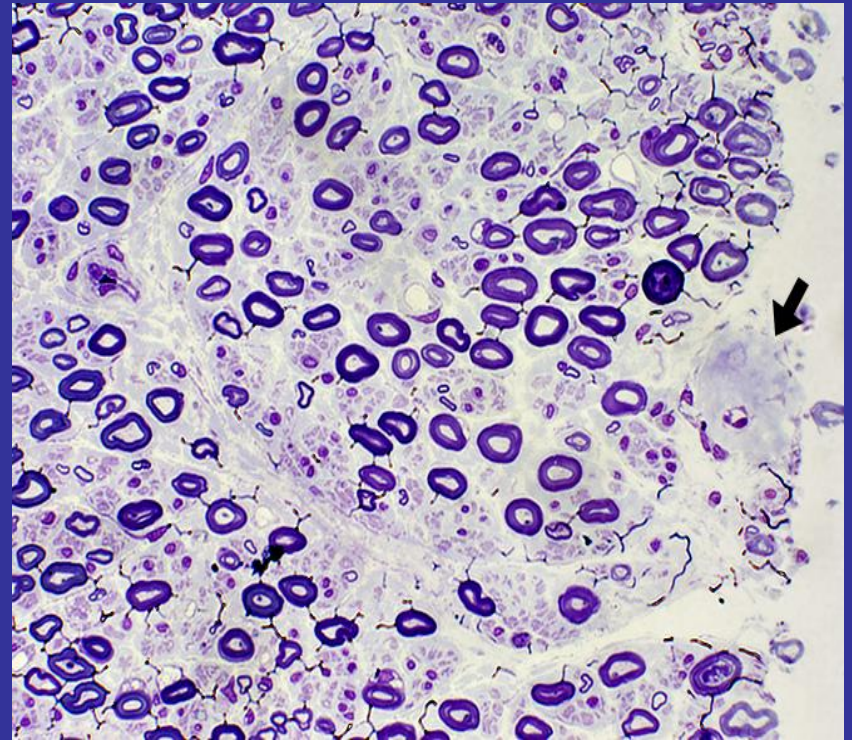
**Nerve with amyloid**



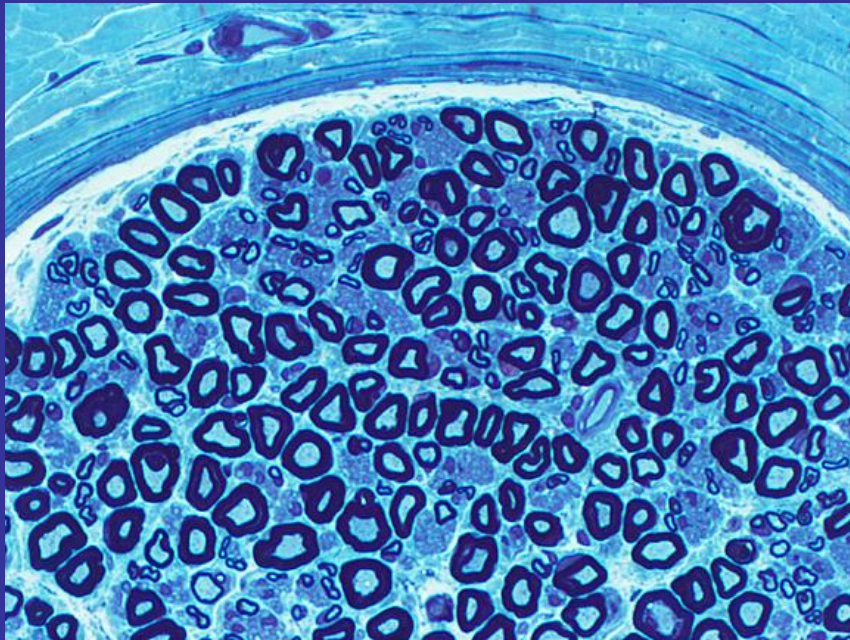
**Nerve with amyloid deposit**



**Amyloid surrounding an artery**

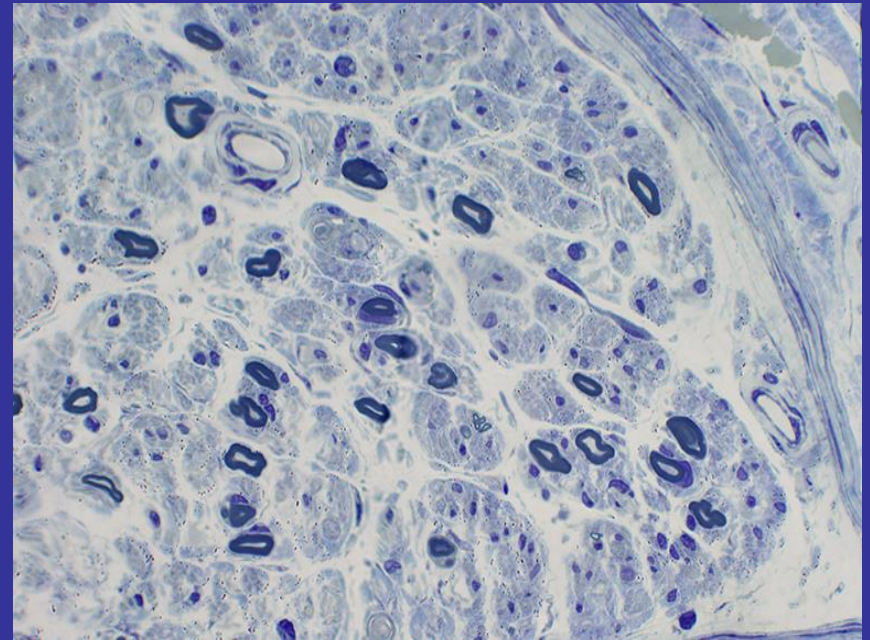


Normal nerve cross-section



[Missinglink.ucsf.edu](http://Missinglink.ucsf.edu)

Nerve with amyloid



Wustl.....

# Amyloid Polyneuropathy

- Longest nerves affected first – why?
  - High metabolic load
- Symmetrical
- The nerve degenerates from the end, upward
- Thin axons affected first (pain and autonomic)
- Thick axons affected later (to muscle)



# Symptoms of Polyneuropathy

- Tingling, numbness, burning, electrical shocks, feeling cold, feeling like walking on cotton/something in your shoe
- Often feel worse at night
  - Off your feet
  - Not distracted

# Symptoms of Polyneuropathy

- Same in amyloid as in neuropathy due to other causes such as diabetes, kidney failure or alcohol use
- Start in feet, slowly climbs up the legs. When the symptoms are at knee level symptoms start in the hands

# Symptoms of Polyneuropathy

- Why does it feel numb and painful at the same time?
  - Different axons mediate different sensations
  - Thin axons mediate pain sensation
    - When damaged, they fire – brain “feels” it as pain
  - Thick axons mediate touch and pressure sensation
    - When damaged, do not transmit information to the brain – so brain does not “feel” touch

# Diagnosis of Amyloid Polyneuropathy

- History
- Examination
- Nerve Conduction Studies
- Electromyography (EMG)
- Blood work
- Biopsies
- “Rule out” other causes

# Think about other causes of PN

- Are symptoms directly related to amyloid deposition or to something else?
  - Organ damage due to amyloidosis
    - Kidney failure
    - Malnutrition
  - Other medical problems
    - Diabetes
    - Vitamin deficiency
    - Thyroid disease
  - Medications and other toxins
    - alcohol

# Treatment

## 1. Etiologic

Treating the cause of neuropathy

## 2. Symptomatic

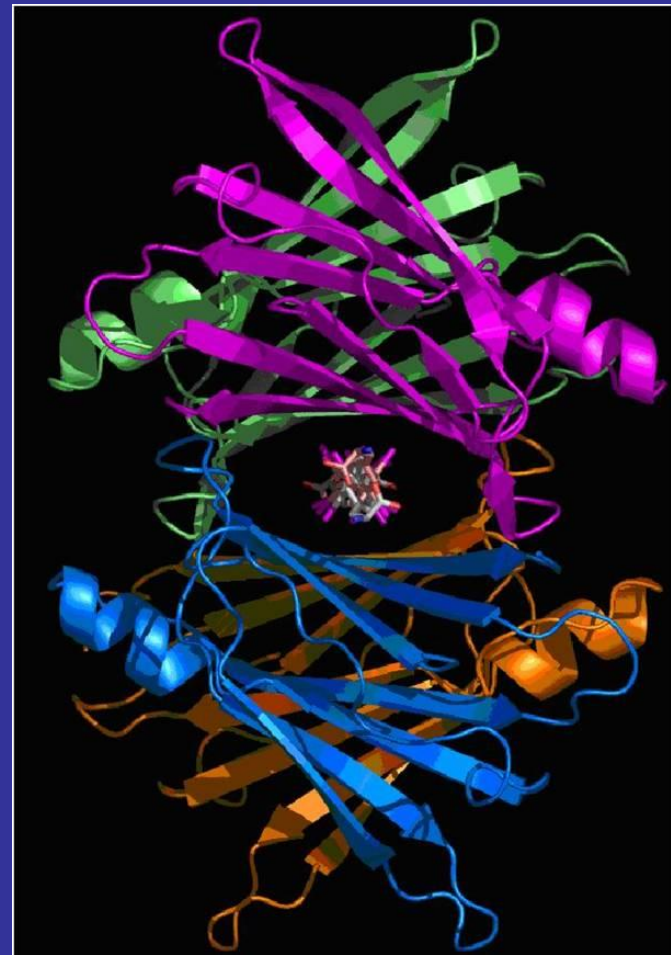
Treating the symptoms

# If the cause is treated will my nerves grow back?

- Maybe
- Nerves regrow best in people who are young and otherwise healthy
- Nerves grow back slowly
  - 1 mm a day = 1 inch a month = 1 foot a year

# Etiologic Treatment of ATTR

- Molecules that stabilize TTR so it does not fall apart, change confirmation and deposit in tissues
  - Diflunisal
  - Tafamidis





# Etiologic Treatment of ATTR

- Preventing the liver from making mutant TTR
  - Liver transplantation
- Medications that prevent liver cells from making TTR
  - RNA antisense/interfering molecules
    - ISIS
    - Alynlam

# Can amyloid be removed from tissues once it deposits?

- Maybe
  - Doxycycline trial
  - Monoclonal antibodies

# Treatment of Polyneuropathy

- First ask – Do I Need To Be Treated?
  - Is underlying disease being treated?
  - No treatment to make nerves grow back
  - Treatment is symptomatic
    - Crazy-making: Yes or No??

# Symptomatic Treatment of Polyneuropathy

- Without Medication
  - Foot rub or warm water foot massage before bed
  - Acupuncture: Anecdotal reports only (but check with your doctor regarding risk of infection!!!)

# Symptomatic Treatment

- Topical Medication
  - Lidoderm patch – topical anesthetic
  - Anesthetic cream
  - Capsacin
    - causes release of Substance P (causes pain)
    - initially increases pain
    - must be used 2-3 times/day

# Symptomatic Treatment Medication

- Anti-seizure medications
  - Lyrica (pre-gabalin)
  - Neurontin (gabapentin)
  - others
- Antidepressants
  - Cymbalta (duloxetine)
  - “tricyclic antidepressants” like Elavil – not typically used in amyloid
- Anti-inflammatory
  - Aspirin-like drugs
  - Tylenol

# Treatments for severe pain

- Narcotics
  - Extended release pill or patch
- Intravenous lidocaine
- Marijuana
- Percutaneous nerve stimulation
- Nerve stimulation (TENS) unclear if effective
- Spinal cord stimulation
  - Very invasive, risk of infection

# Symptoms of Autonomic Dysfunction

- Dry eyes and mouth
  - Nerves to the glands are damaged
- Trouble accommodating to bright light
  - Autonomic nerves control how constriction of the pupil in the eye
- Lightheadedness when standing
  - Blood vessels do not constrict when you stand up
  - Heart rate does not increase when you stand up
- Diarrhea
- Constipation
- Erectile dysfunction
- Talk to your doctor about symptomatic treatment for these symptoms



# Beware

## ReBuilder



\$500-700

## Neuracel

**NEUROPATHY TREATABLE?**



FAST START FORMULA  
**Neuracel**  
The Ultimate  
**Neuropathy**  
Support System  
Neuracel 90 Capsules

FIND OUT WHAT YOUR PEERS VOTED AS THEIR  
**#1 SUPPLEMENT**  
TO HELP REDUCE  
**NEUROPATHY PAINS...**

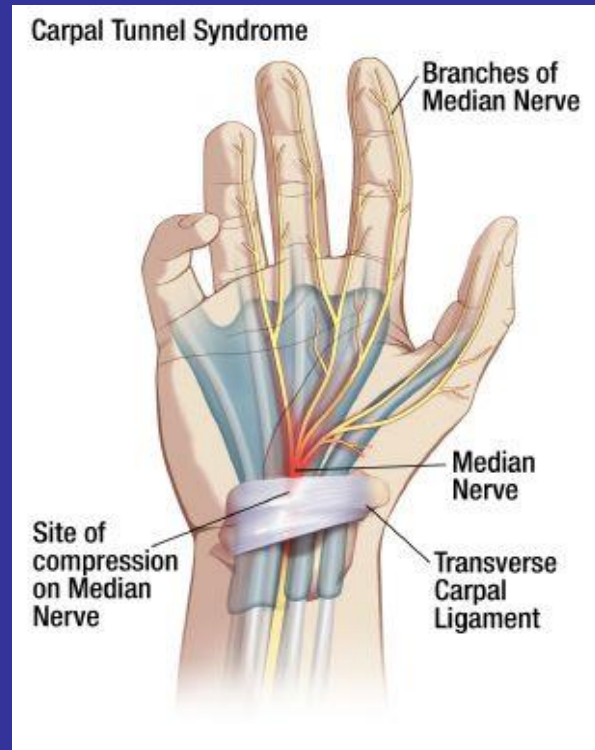
**WATCH VIDEO SUCCESS**  
[STORIES HERE...](#)

\$70 for one month

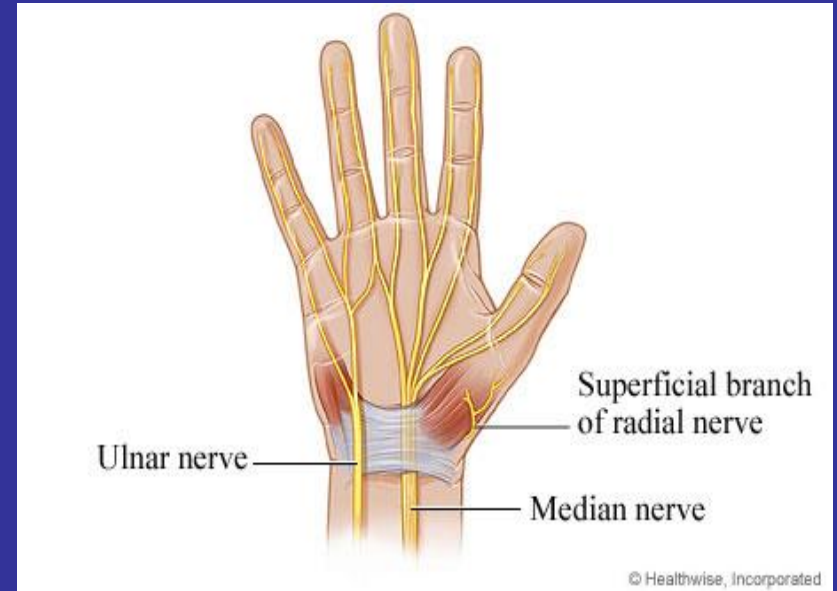
# A word about foot care

- Foot care is important
- If you can't feel your feet you can't feel cuts or sores that can become infected.
- Foot care tips
  - Look between and under your toes every day
  - Wear soft, well fitting shoes
  - Do not walk barefoot, particularly outside
  - Keep feet soft and well moisturized
  - Have nails filed rather than cut
    - A podiatrist or specialized pedicurist can help
    - Don't cut your own nails
- We want you have all 10 toes, all of the time!

# Carpal Tunnel Syndrome



[www.carpal-tunnel-syndrome.com](http://www.carpal-tunnel-syndrome.com)



webMD

# Carpal tunnel syndrome (CTS)

- Common in the general population over age 50 and common in TTR amyloidosis
- Also seen with diabetes and low thyroid function
- May have this many years before diagnosis is made.
- The median nerve runs down from the neck into the hand
- At the wrist, the nerve runs under a band of connective tissue that encircles the wrist
- Amyloid deposits in the connective tissue and compresses the nerve

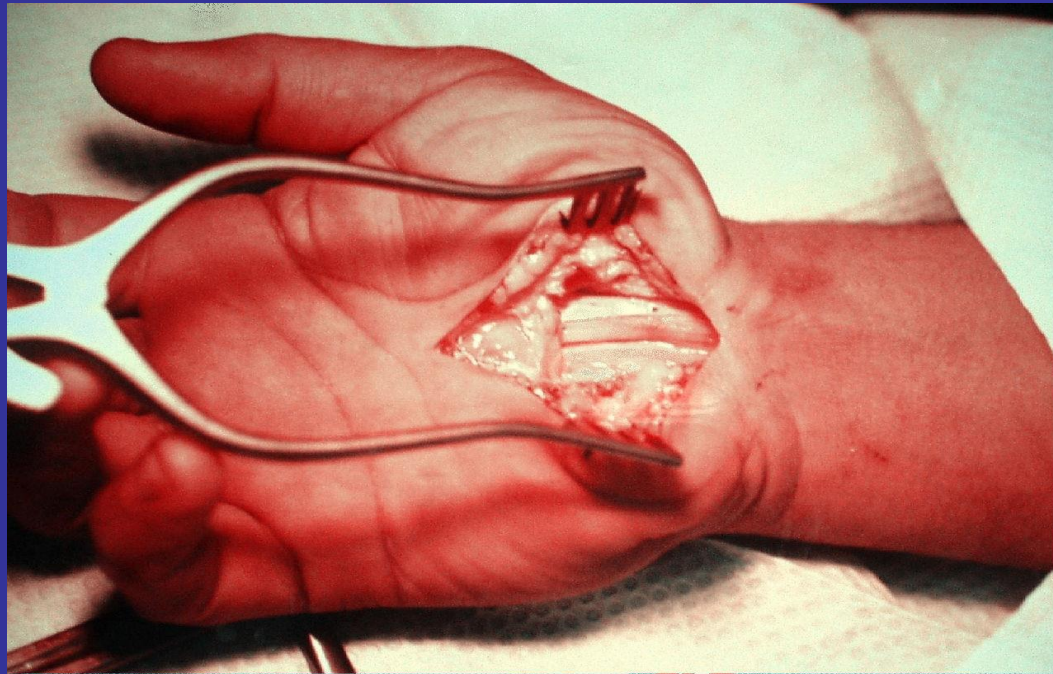
# CTS Symptoms

- Tingling, pain ,numbness in the thumb, forefinger and middle finger
- Weakness of the thumb and of grip
- Trouble opening jars and buttoning
- Worse at night, with driving, typing

# CTS Treatment

- Ergonomic adjustment
- Wrist brace
- Local injection of steroid
- Surgery
  - Always make sure the surgeon sends a sample of the connective tissue band to pathology!!

# Carpal Tunnel Syndrome



wikipedia

# What you can do for healthy nerves

1. CUT DOWN ON ALCOHOL – IT IS DIRECTLY TOXIC TO NERVES
2. STOP SMOKING – WITH EVERY PUFF YOU CAUSE CONSTRICTION OF THE BLOOD VESSELS THAT NOURISH NERVES
3. EAT A LOT OF FRUITS AND VEGETABLES, ESPECIALLY DARK GREEN LEAFY VEGETABLES WHICH CONTAIN B VITAMINS (but not if you are taking coumadin)
4. MUSCLES DEPEND ON THEIR NERVE SUPPLY TO STAY HEALTHY – USE THEM BOTH



# Resources

- Healthy Nerves pamphlet on ASG website
- Boston University Amyloid Treatment and Research Website
  - Podcasts
  - Healthy Nerves pamphlet

<http://www.bu.edu/amyloid/resources/patient-resources/>