NYU School of Medicine
NYU LANGONE MEDICAL CENTER

BOSTON UNIVERSITY
SCHOOL of Medicine

Nerves and Neuropathy

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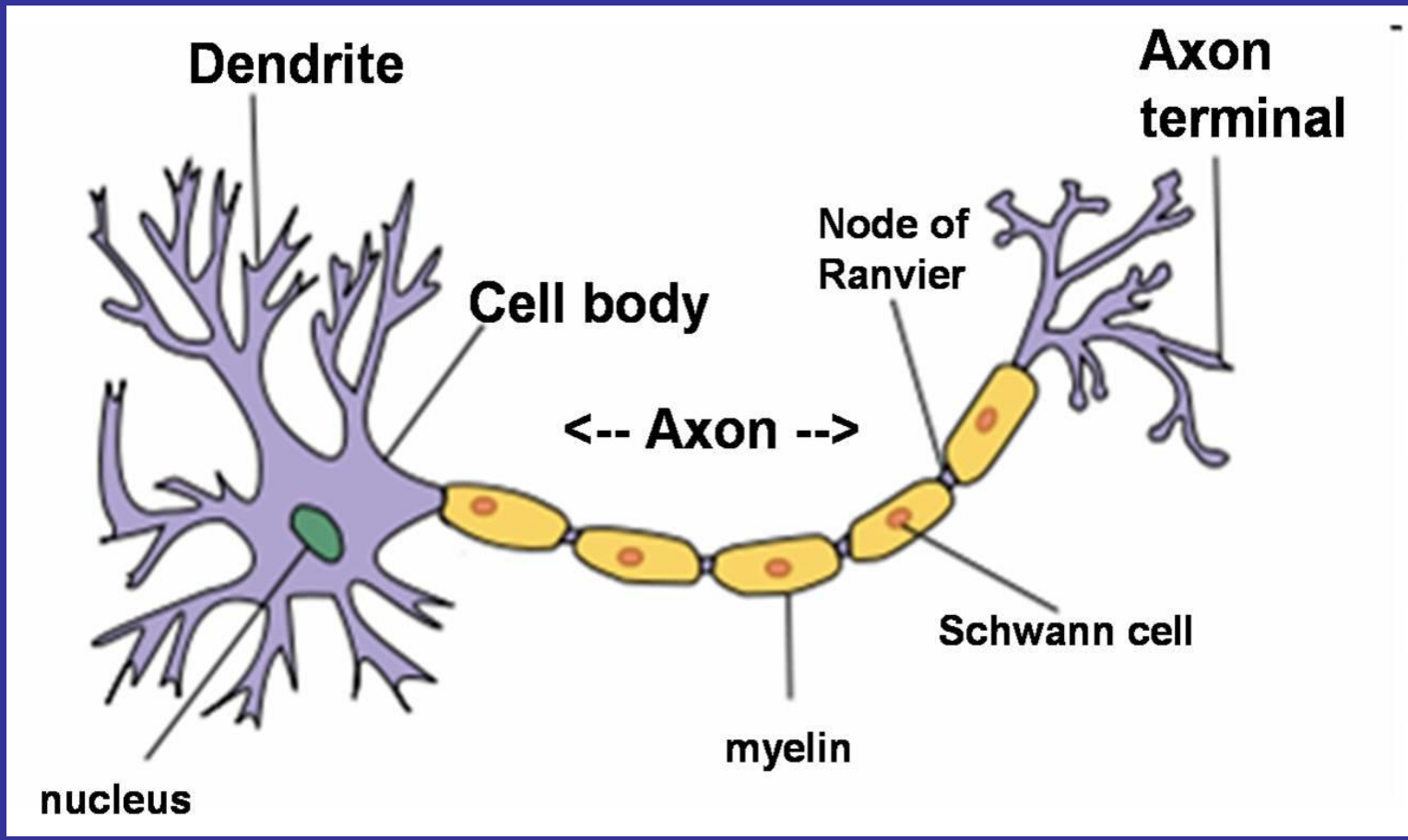
Structure of a neuron



users.tamuk.edu

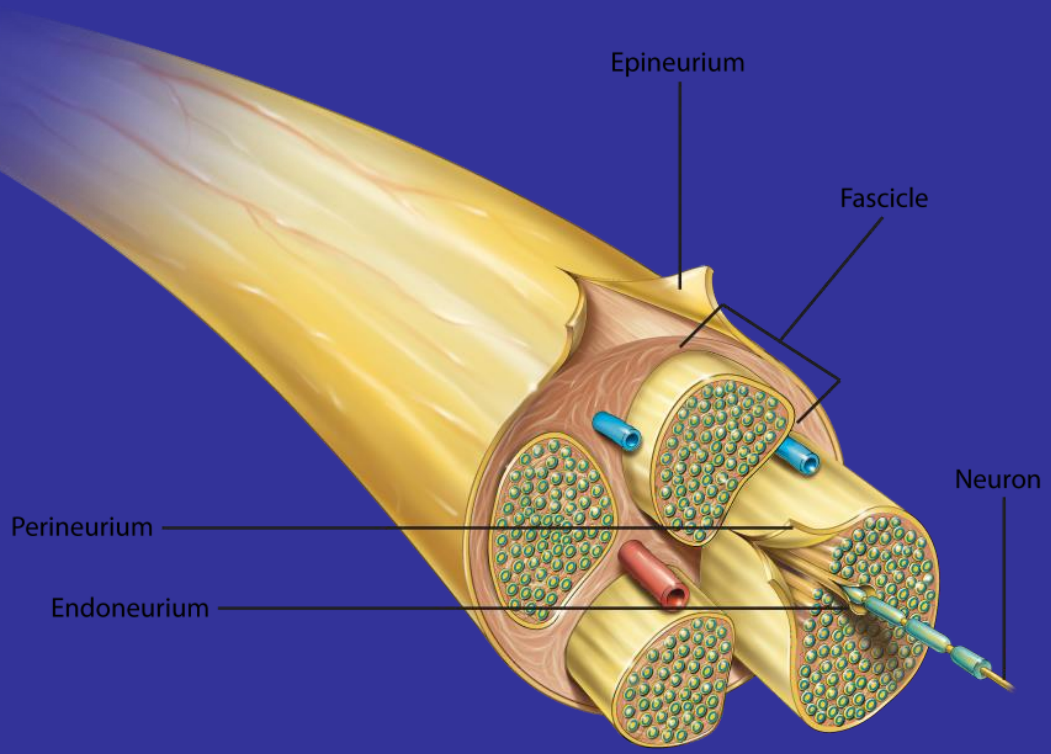
What is an Axon?

- 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

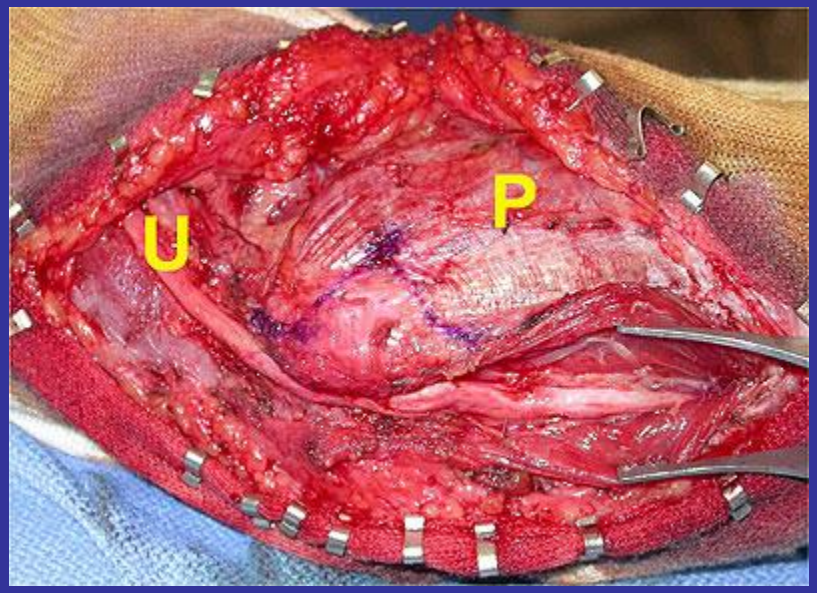
What is a Nerve?

- 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



www.axogeninc.com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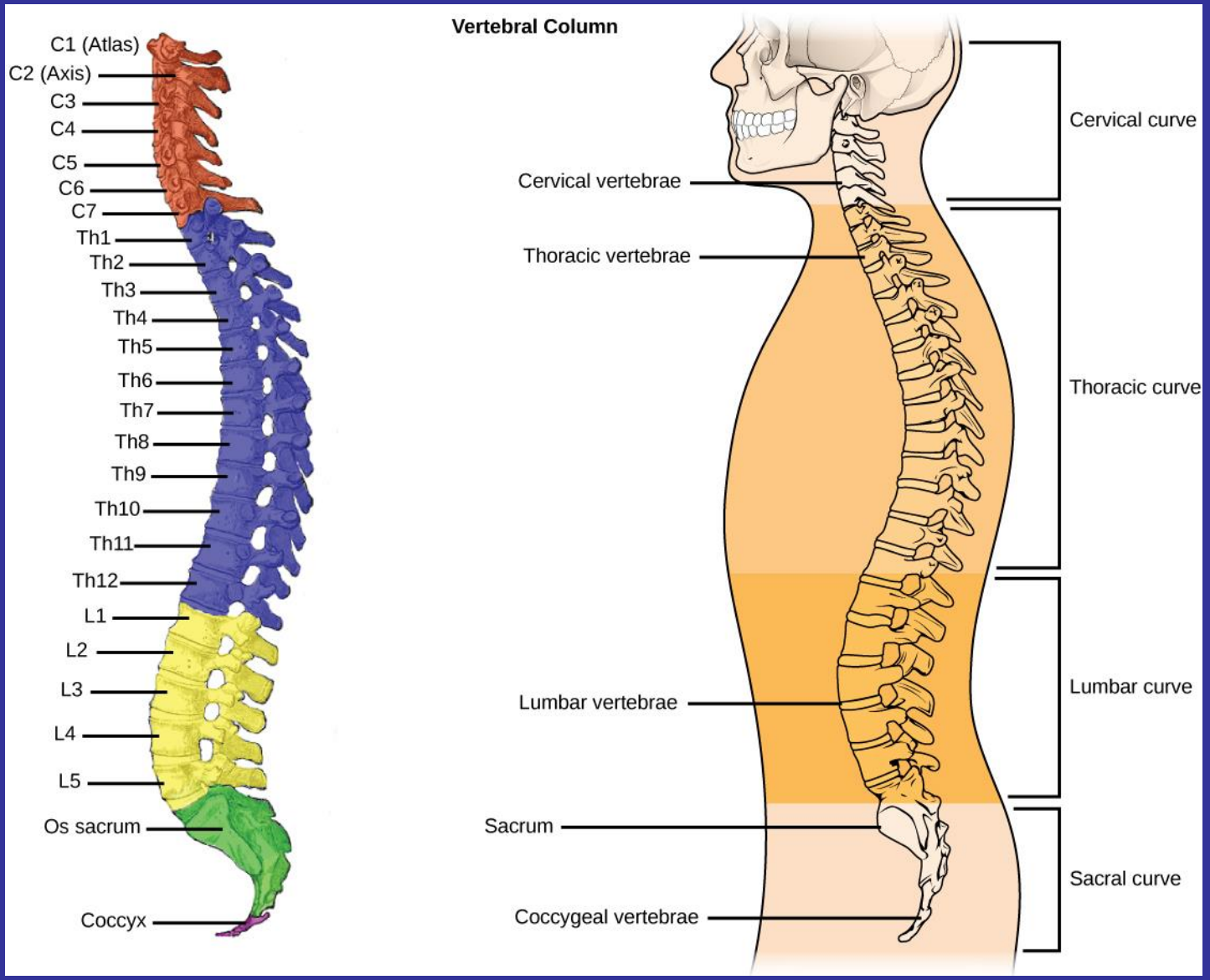
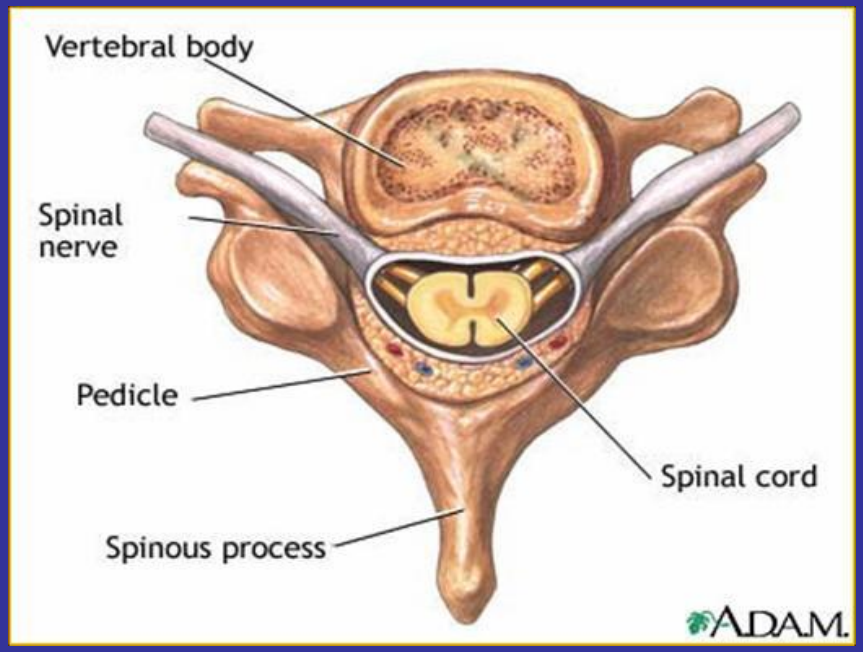

C1 (Atlas)
C2 (Axis)
C3
C4
C5
C6
C7
Th1
Th2
Th3
Th4
Th5
Th6
Th7
Th8
Th9
Th10
Th11
Th12
L1
L2
L3
L4
L5
Os sacrum
Coccyx
Vertebral Column
Cervical vertebrae
Thoracic vertebrae
Lumbar vertebrae
Sacrum
Coccygeal vertebrae
Cervical curve
Thoracic curve
Lumbar curve
Sacral curve



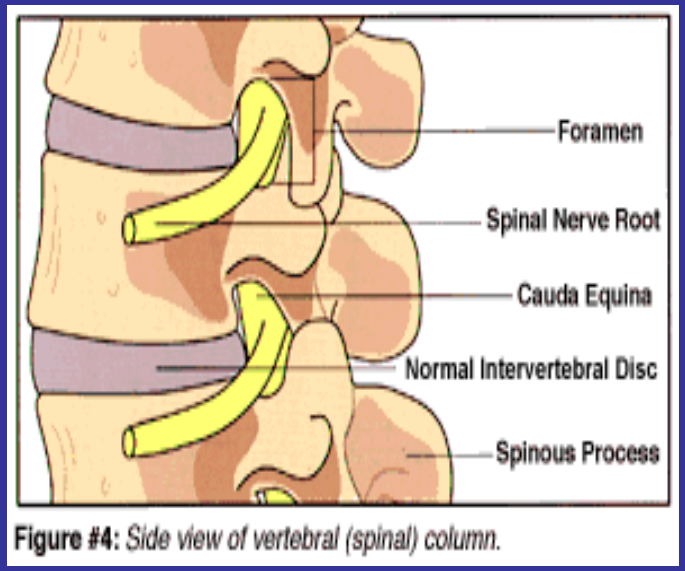
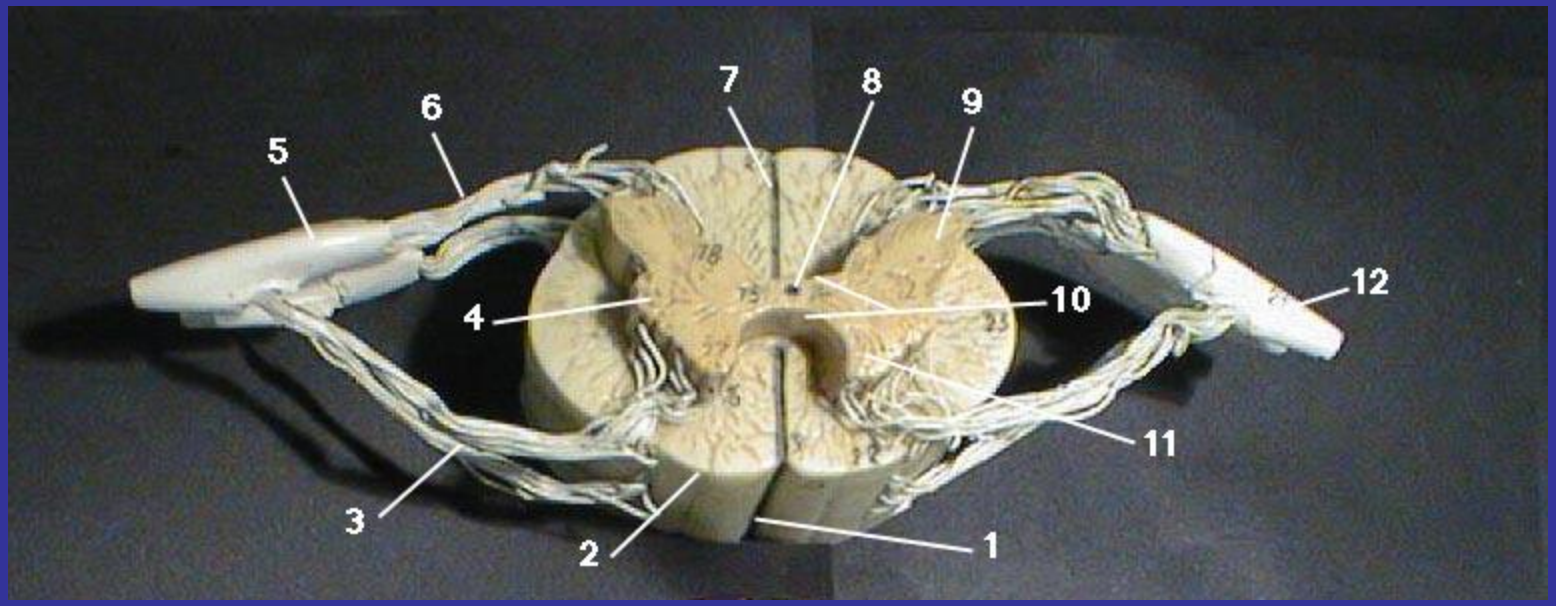


Figure #4: *Side view of vertebral (spinal) column.*

Espine.com



Homes.bio.psu.edu

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

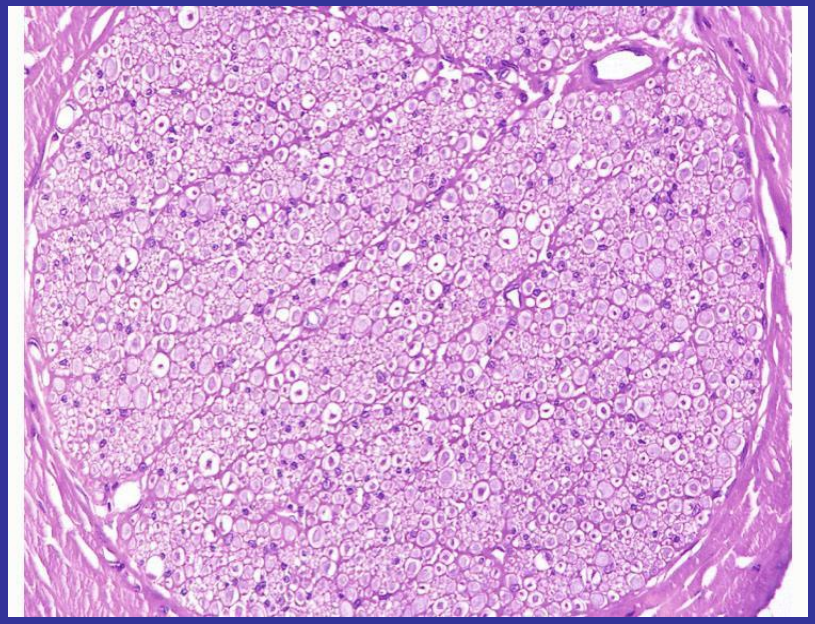
What is Neuropathy?

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

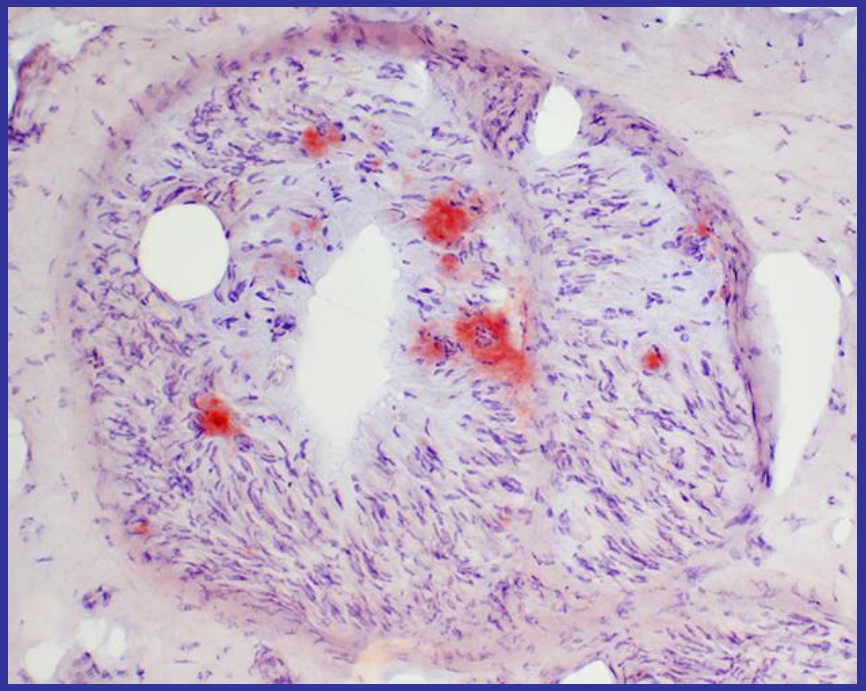
Nerve Damage in Amyloidosis

- Seen in two types
  - Primary (AL, problem in bone marrow)
  - Inherited
    - TTR – also called Familial Amyloid Polyneuropathy
    - ILE122 (though not common)

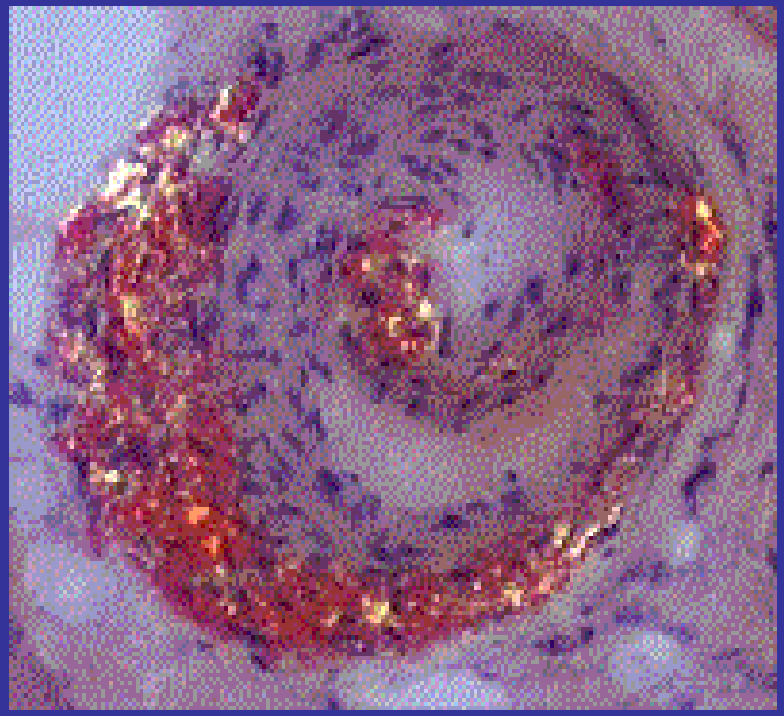
Normal nerve



Nerve with amyloid



Birefringence



www.neuro.wustl.edu/neuromuscular

Birefringence

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

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 Neuropathy

- Tingling
- Burning
- Pain
- Numbness
- Tight feeling
- Feeling like something is in your shoe
- Trouble with balance
- Muscle cramps
- Autonomic symptoms

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

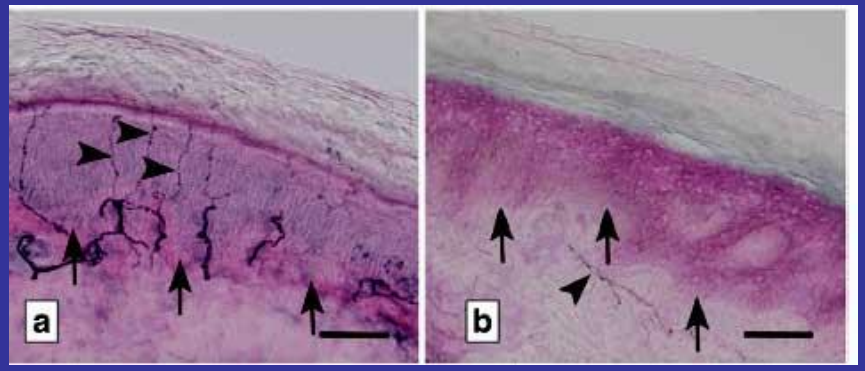
Diagnosis of neuropathy

- History
- Neurological Exam
- Nerve conduction studies and electromyography
- Blood tests
- Nerve biopsy
- Skin biopsy

Skin Biopsy

- Performed to look at the very thinnest nerves which mediate pain
- One sample is taken for the thigh and another from above the ankle
- Done in the office with local anesthetic
- A core is taken and a stitch put in or a steri-strip used to close the wound
- Sample is preserved, cut and stained. The number of axons (fibers) per mm is counted and compared with age-matched healthy controls
- Can be repeated to follow the course of treatment
- Commercial labs and university medical center labs

Skin biopsy



Neuropathy Support Network

https://www.healthrising.org/blog

Treatment of Neuropathy

1. Etioloigic

   Treating the cause of neuropathy

2. Symptomatic

   Treating the symptoms

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 Tx - 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
- The question of opioids
- The question of marijuana

Alternative treatments for nerve pain

1. Spinal modulation of pain
2. Warming the limb
3. Electricity
4. Behavioral
5. Acupuncture
6. Placebo
7. Medications that are not pills
8. Pills that are not medication
9. Weird stuff
10. Treatment of cramps

Electricity

- TRANScutaneous electrical stimulation
  - Stimulation on surface of skin
  - Mixed reports of efficacy
  - Inexpensive
  - Can do at home
  - No side effects

- PERcutaneous electrical stimulation
  - Stimulate via short needles (1-3 cm) under the skin in a band just below the knee
  - Multiple reports of efficacy (Diabetes Care 2000 Mar; 23: 365-370)
    - Decreased pain and dose of analgesic medication, improved sleep
  - Done in a rehabilitation or physical therapy office; can not do at home
  - 30 minutes, 3X/week, effect may last a few weeks
  - Expensive, may be covered by insurance
  - Theoretical risk of infection

Electricity - Scrambler Therapy

- Principle is to provide transcutaneous electrical stimulation NEAR the site of pain to “re-program” input from the painful area to the brain. Re-programming is thought to replace stimulation that is perceived as painful with stimulation that is perceived as a non-painful.
- Transcutaneous stimulation of C-fibers
- Thought that this change happens at the level of the brain, not the spinal cord.
- Requires professional visit
- Trials of efficacy have been mixed, but favor efficacy
- Variable insurance coverage
  - Support Care Cancer, 2016, Jun; 24:2807-14

1. Simulating electrodes are placed on normal skin around the painful site. The electrodes are not placed at the site of actual pain
2. Electrical stimulation (like a TENS unit) sends “non-pain” information through the nerves and into the spinal cord
3. The intensity of stimulation is adjusted according to patient comfort and pain will be replaced by the Scrambler device sensation, which is described as “pleasant, vibratory, or humming”.
4. Up to five sets of electrodes are used to treat the area(s) of pain.
5. The device runs for 30–45 min
6. After a session’s completion, patients may report a soothing sensation and note that the pain has been reduced or has disappeared.
7. Treatment is given for 10 days and relief may last weeks to months

Symptoms of Autonomic Dysfunction

- Dry eyes and mouth
  - Nerves to the salivary glands are damaged
- Trouble accommodating to bright light
  - Autonomic nerves control constriction of the pupil
- Lightheadedness when standing
  - Autonomic nerves go to the muscles in the wall of blood vessels and to the heart to control heart rate
  - Blood vessels do not constrict when you stand up
  - Heart rate does not increase when you stand up
- Male and female sexual dysfunction
- Constipation and diarrhea
  - Autonomic nerves supply the muscle in the lining of the intestine
  - Infiltration of intestine walls and blood vessel walls with amyloid

Treatment of dry mouth

- Avoid medications that have dry mouth as a side effect – amitriptyline is common
- Short term lubrication with Biotene products and Xylimelts
- Chew sugar-free gum
- Decrease caffeine
- Don’t smoke/chew tobacco
- Stay well hydrated
- Use a humidifier at night
- Good dental hygiene is important

Treatment of dry eyes

- Saline eye drops (preservative free – change often)
- Lacri-lube
- Humidifier
- Tear duct plugs
- Discuss with your ophthalmologist

Accommodating to bright light

- Change location slowly
- Wear sunglasses

Lightheadedness and fainting

- Stand up slowly
- Sleep with the head of the bed up at 30°
- When standing, contract the muscles in your legs – go up and down on your toes
- Stay well hydrated (talk to your doctor if you have heart disease)
- Increase salt intake, if you can
- Compression stockings
- Medications:
  - Fludrocortisone (Florinef)
  - Midodrine (Proamatine)
  - Droxidopa (Northera)

Sexual dysfunction

- Erectile dysfunction in men
  - Referral to a urologist who specializes in this
  - Story of Viagra
- Decreased vaginal lubrication in women
  - Over the counter creams
  - Referral to a gynecologist

Constipation

- Stay well hydrated
- Increase fiber in diet and/or with supplements
- Stay active
- Stool softeners – docusate (Colace etc.)
- Miralax/fiber supplements – increases fluid in the bowel
- Stimulant laxative
  - Bisacodyl (Dulcolax etc.)
  - Senna
  - Magnesium citrate – electrolyte imbalance
- Prescription medications
  - Referral to a gastroenterologist
    - Lubiprostone (Amitiza)
    - Linaclotide (Linzess)
    - Plecanatide (Trulance)

Diarrhea

- Multiple small meals
- Avoid milk products if you are lactose intolerant
- Stay well hydrated
- Oral nutritional supplements
  - Provides calories but can make diarrhea worse
- Medications:
    - Loperamide (Imodium)
    - Diphenoxylate and atropine **(**Lomotil)
    - Tincture of opium
- Parenteral (intravenous) nutrition

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!

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
- Book: *Peripheral Neuropathy: What It Is and What You Can Do To Feel Better, Janice Wiesman MD, FAAN*