



Diabetic Neuropathy

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Structure of this talk



- Diagnosis (differential diagnosis)
- Treatment



Differential Diagnosis

A typical patient with Diabetic Neuropathy



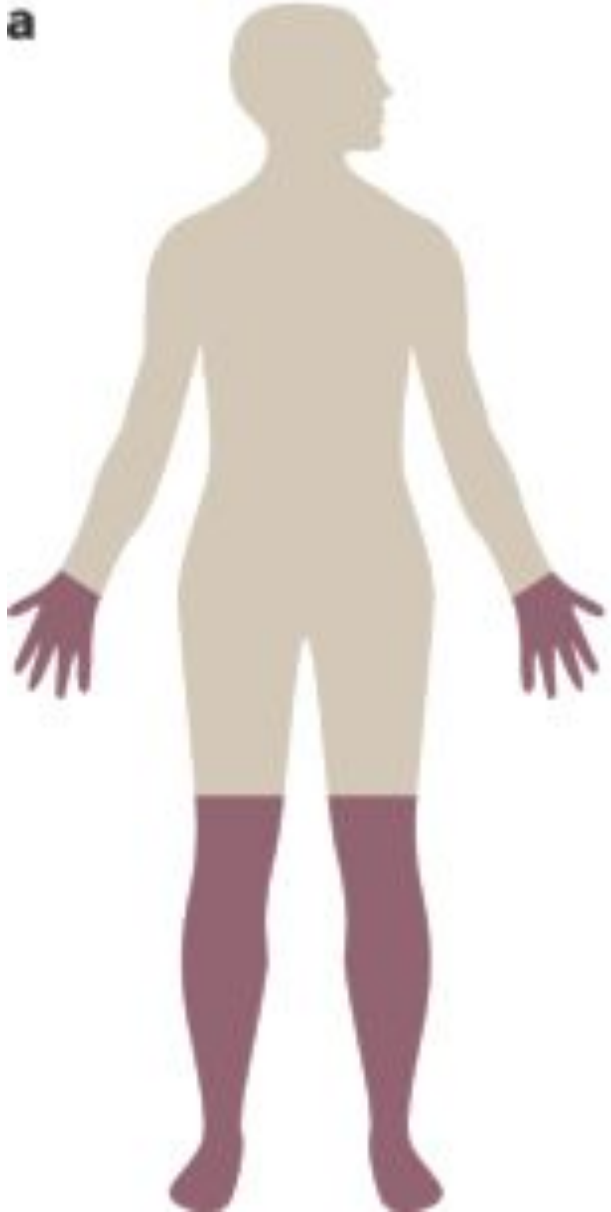
- A patient has diabetes.
- Complains of tingling / burning / numbness in the legs

? = Diabetic neuropathy

Or should you consider other conditions?

A typical patient with Diabetic Neuropathy

a



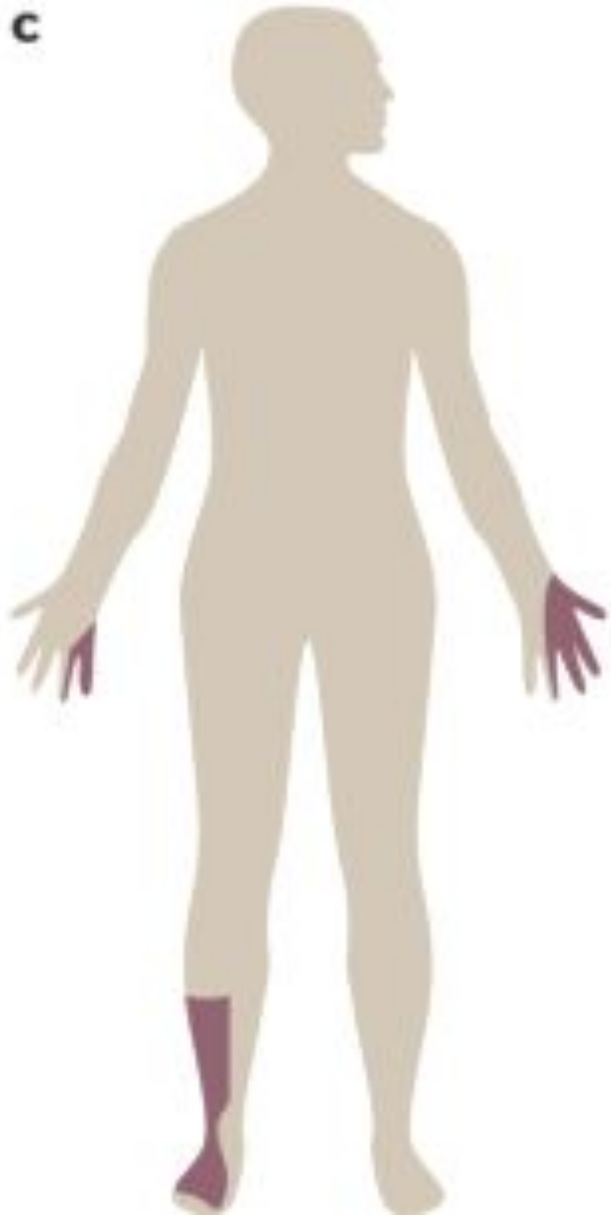
- Symmetric
- Length-dependent
- Small > Large fiber
- Neuropathy (Without s/s of myelopathy)

Warning bell 1

Asymmetric sensations

Symmetric, length-dependent, Small > large fiber Neuropathy

c



What if the sensations are **asymmetric**?

- Radiculopathy
- Diabetic Amyotrophy (LS plexus)
- Entrapment of nerves
- Rare: Vasculitis (Mononeuritis Multiplex), Leprosy (similar but painless) etc...

Symmetric, length-dependent, Small > large fiber Neuropathy



- Diabetic Amyotrophy (LS plexus)
 - Type-2 DM, recently started Rx
 - Sudden pain on the side, radiating to one leg
 - Imaging is normal (e.g. no psoas hematoma)
 - Proximal weakness > distal
 - Improves, but significant atrophy

Symmetric, length-dependent, Small > large fiber Neuropathy

Entrapment of nerves



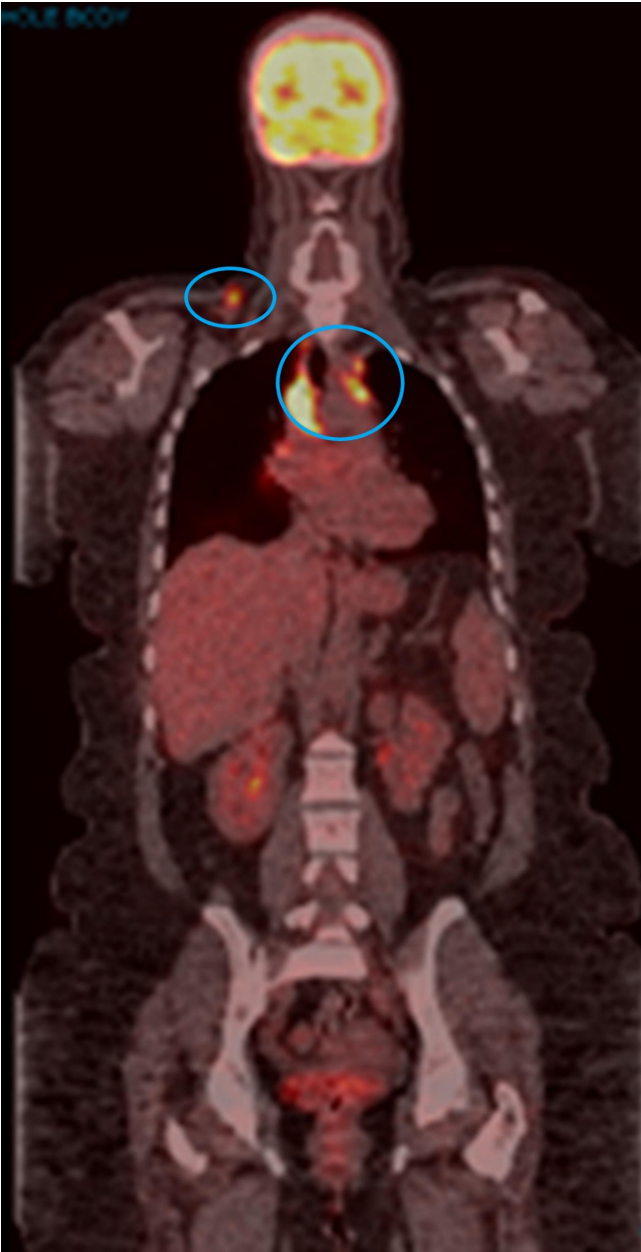
- Meralgia Parasthetica (Fat, tight clothes)
- Peroneal at the fibular neck
- Others: Tarsal Tunnel, Lateral plantar entrapment in flat footed people...



Warning bell 2

Sensations more in the hands

Symmetric, **length-dependent**, Small > large fiber Neuropathy



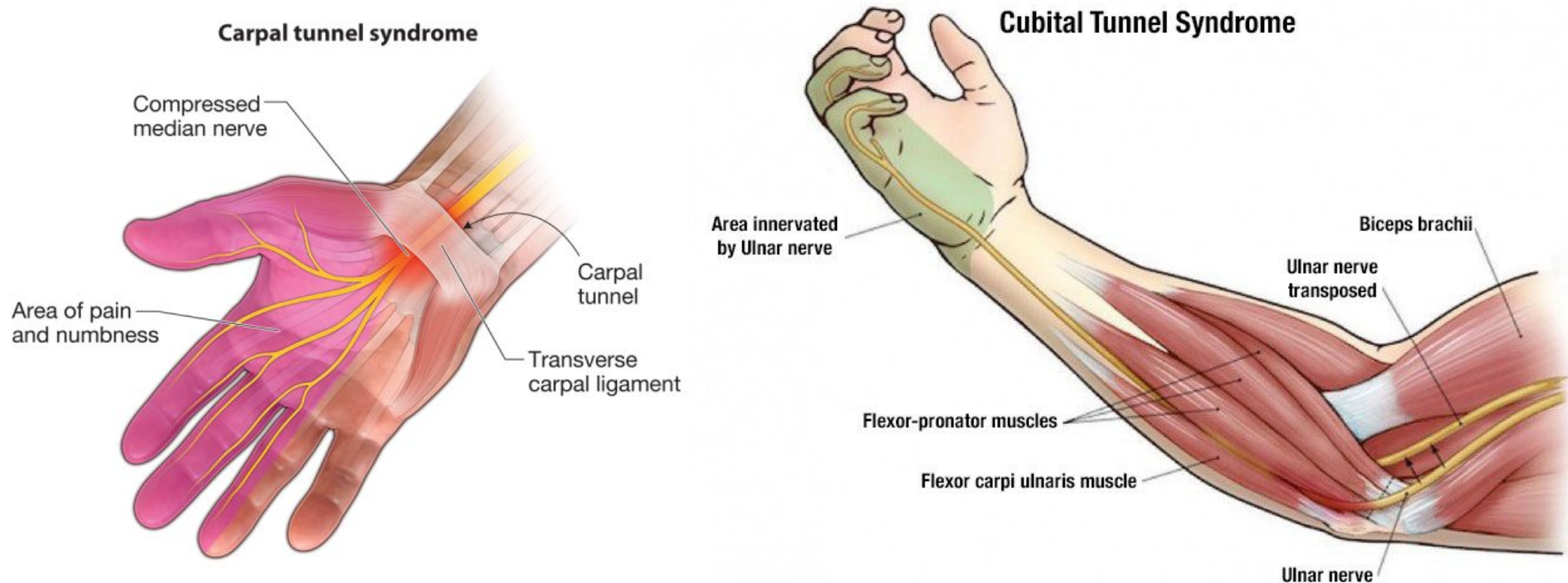
What if the sensations are **more in the hands**?

- Could be radiculopathy
- Could be entrapment
- Rarely can be Diabetic Amyotrophy
- Could be Leprosy
- Could be Vasculitis
- But, also could be Paraneoplastic.
 - **B-symptoms: Unexplained weight loss, fever...**
 - **Anti-Hu, Anti-CV2/CRMP-5**
 - **Consider a PET scan**

Symmetric, **length-dependent**, Small > large fiber Neuropathy

What if the sensations are **more in the hands**?

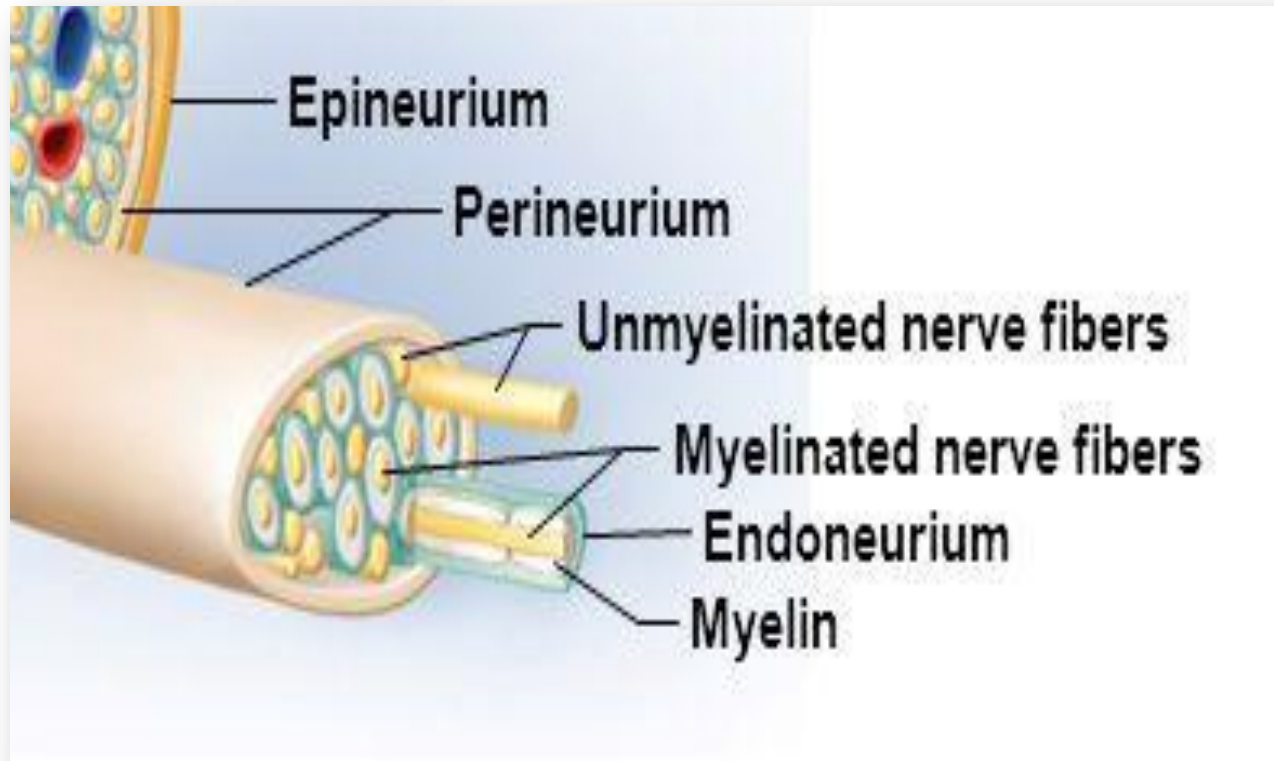
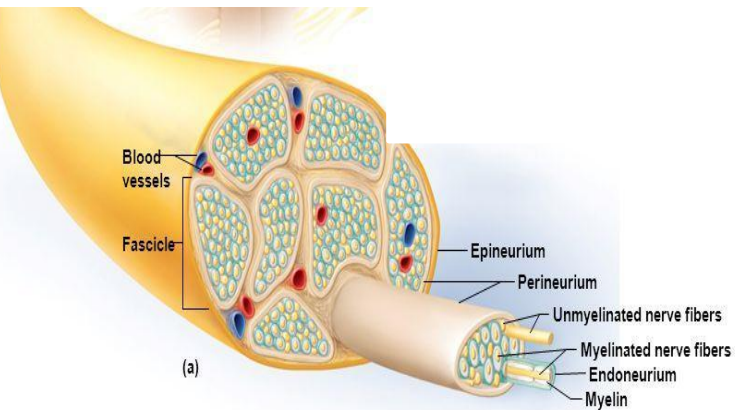
- Entrapment
 - **Carpal Tunnel (Computer operators, knitting)**
 - **Ulnar Neuropathy at the elbow (Executives, Local trains)**



Warning bell 3

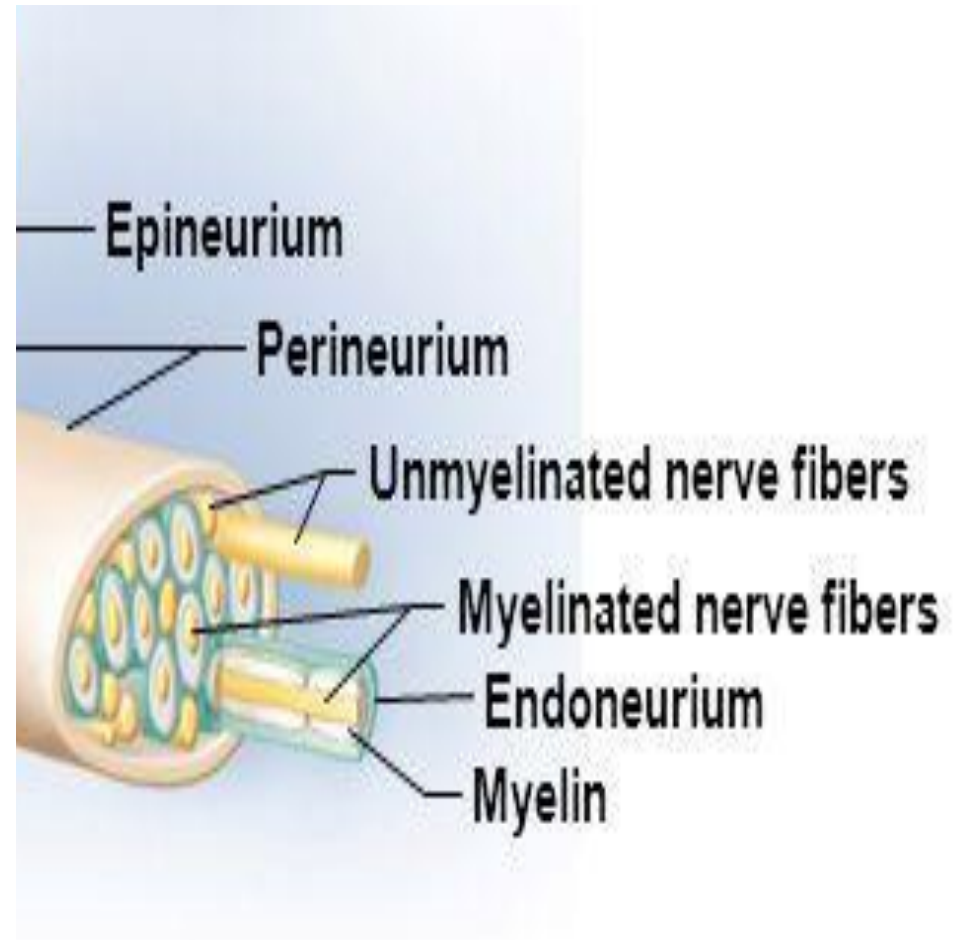
“Large Fiber” neuropathy

Symmetric, length-dependent, **Small > large fiber** Neuropathy



- What are small & Large fibers?
- What are the typical complaints of each?
- How do you test them?
- What if the large fibers are affected more?

Symmetric, length-dependent, **Small > large fiber** Neuropathy

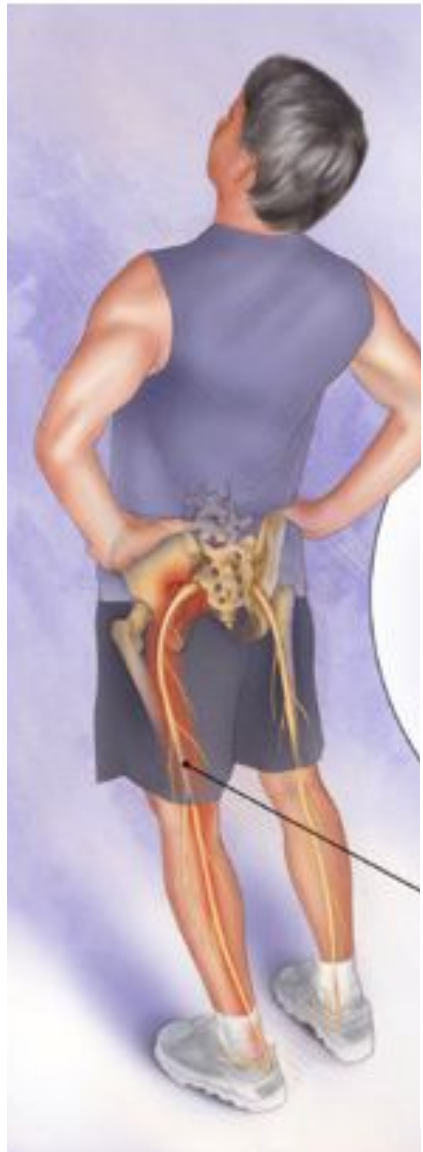


Each NERVE has many fibers.

Some are small in diameter, and some are large.

- **Small sensory fibers – Pain & Temperature**
- **Large sensory fibers – Vibration & Position sense**

Symmetric, length-dependent, **Small > large fiber** Neuropathy



- **Small fibers = BURNING PAIN**
 - Tingling / Numbness “walking on cotton”
 - not able to feel temperature of the floor
- **Large fibers = LANCINATING PAIN**
 - Unsteadiness

Symmetric, length-dependent, **Small > large fiber** Neuropathy



- How do you test them?
 - **Small fibers = With a pin & a metal object**
 - **Large fibers = Toe position & Tuning fork**

Symmetric, length-dependent, **Small > large fiber** Neuropathy



- How do you test them?
 - **Small fibers = With a pin & a metal object**
 - **Large fibers = Toe position & Tuning fork**

Symmetric, length-dependent, **Small > large fiber** Neuropathy

What if the large fibers are affected more?

Don't rule out diabetes, but rule out other things:

- **B12, Folic acid**
- **VDRL (Syphilis)**
- **Paraneoplastic / Autoimmune**
- **Hereditary**
- **Rarely - Vitamin E / Copper deficiency**



Warning bell 4

Signs & Symptoms of a myelopathy
instead!

Neuropathy versus Myelopathy



- ONE thing in symptoms?
- ONE thing in examination?
- ONE special thing you can do?

Symmetric, length-dependent, Small > large fiber **Neuropathy**

Neuropathy versus Myelopathy

- ONE thing in symptoms?

Bladder urgency/incontinence = Myelopathy
Rare in neuropathy

- ONE thing in examination?

- ONE special thing you can do?



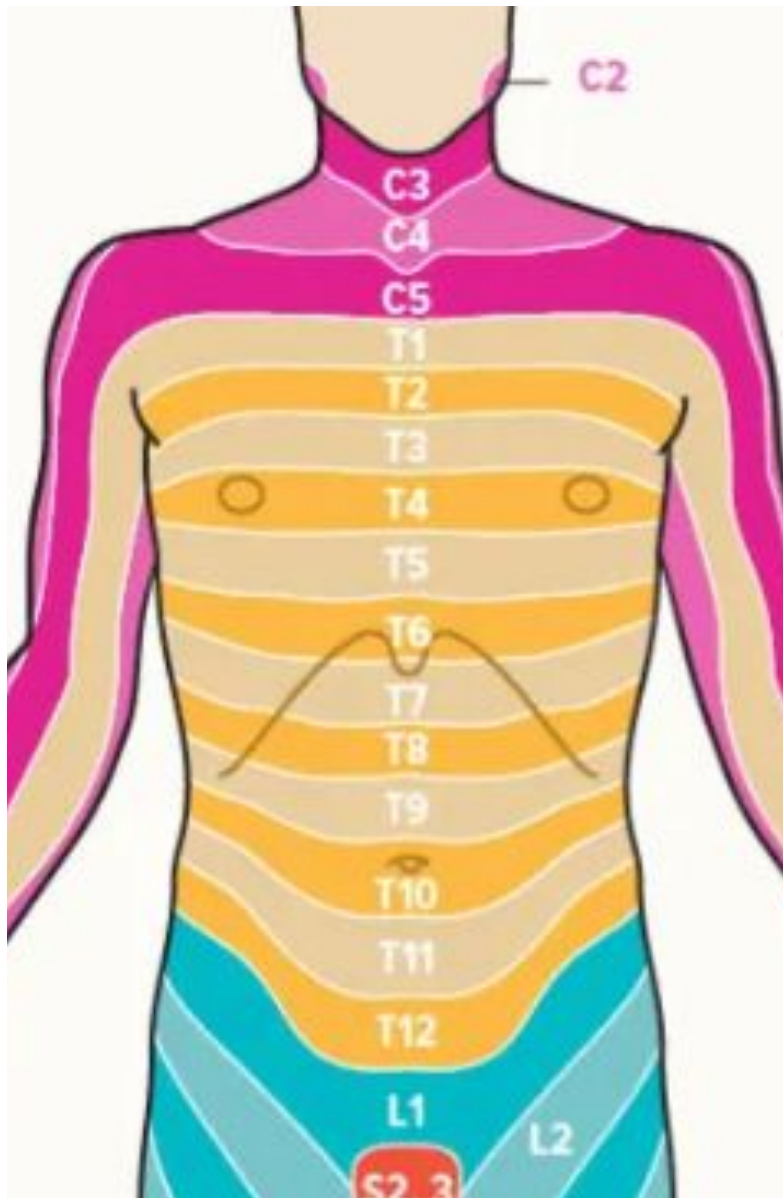
Symmetric, length-dependent, Small > large fiber **Neuropathy**



Neuropathy versus Myelopathy

- ONE thing in symptoms?
Bladder urgency/incontinence
- ONE thing in examination?
Brisk reflexes.
“Upgoing plantars → Not reliable”
- ONE special thing you can do?

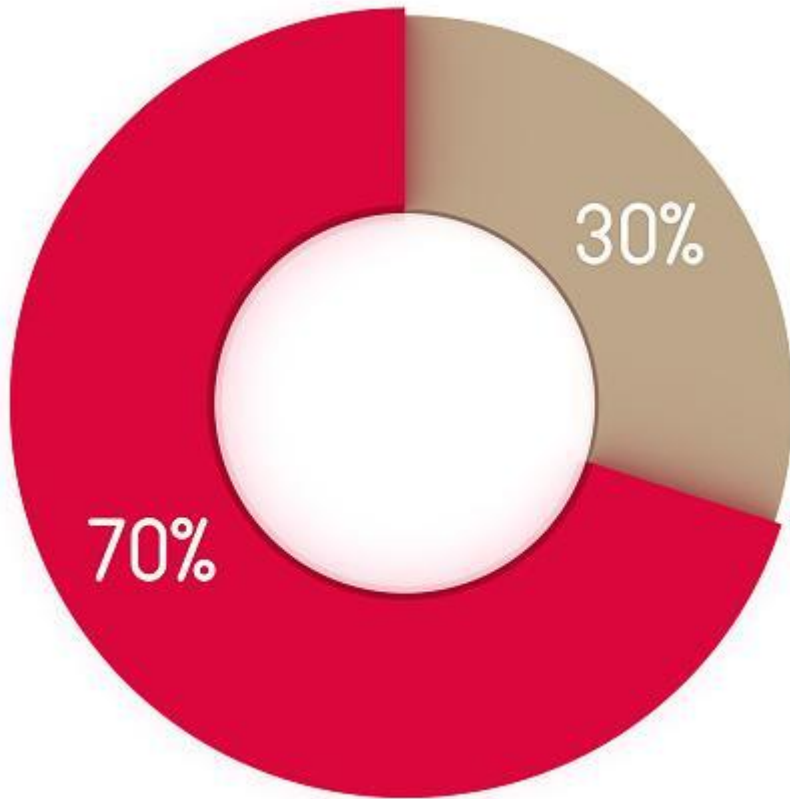
Symmetric, length-dependent, Small > large fiber **Neuropathy**



Neuropathy versus Myelopathy

- ONE thing in symptoms?
Bladder urgency/incontinence
- ONE thing in examination?
Brisk reflexes.
“Upgoing plantars → Not reliable”
- ONE special thing you can do?
 - Check for a “Sensory Level” using a pin

Symmetric, length-dependent, Small > large fiber Neuropathy



In a patient with diabetes = we blame Diabetes!

BUT: Other causes e.g. HIV and alcohol can also cause this picture.

What do I do if I find a symmetric, length-dependent polyneuropathy?

- **History of Alcohol** & Factory exposure (lead etc)
- Check Medications
- Family history
- Make sure it is not a myelopathy: Bladder involvement, Reflexes and sensory level.
- Look and test for patchy sensory loss for **leprosy**
- **I don't do an EMG/NC (except entrapment / suspecting demyelination)**
- First line: FBS, B12 – Folic acid, HIV-VDRL
- Second line: Vitamin E, ANA-blot, Serum electrophoresis. IF B-symptoms ☐ PET
- **Third: Refer**



Treatment of Diabetic Neuropathy

Possible medications to use



Alpha-Lipoic acid

Amitriptyline & Nortriptyline

Duloxetine

Pregabalin & Gabapentin

Carbamazepine & Valproate

Topical medications – Capsaicin,
Gabapentin

Alpha lipoic acid

Alpha lipoic acid

“Decreases oxidative stress”

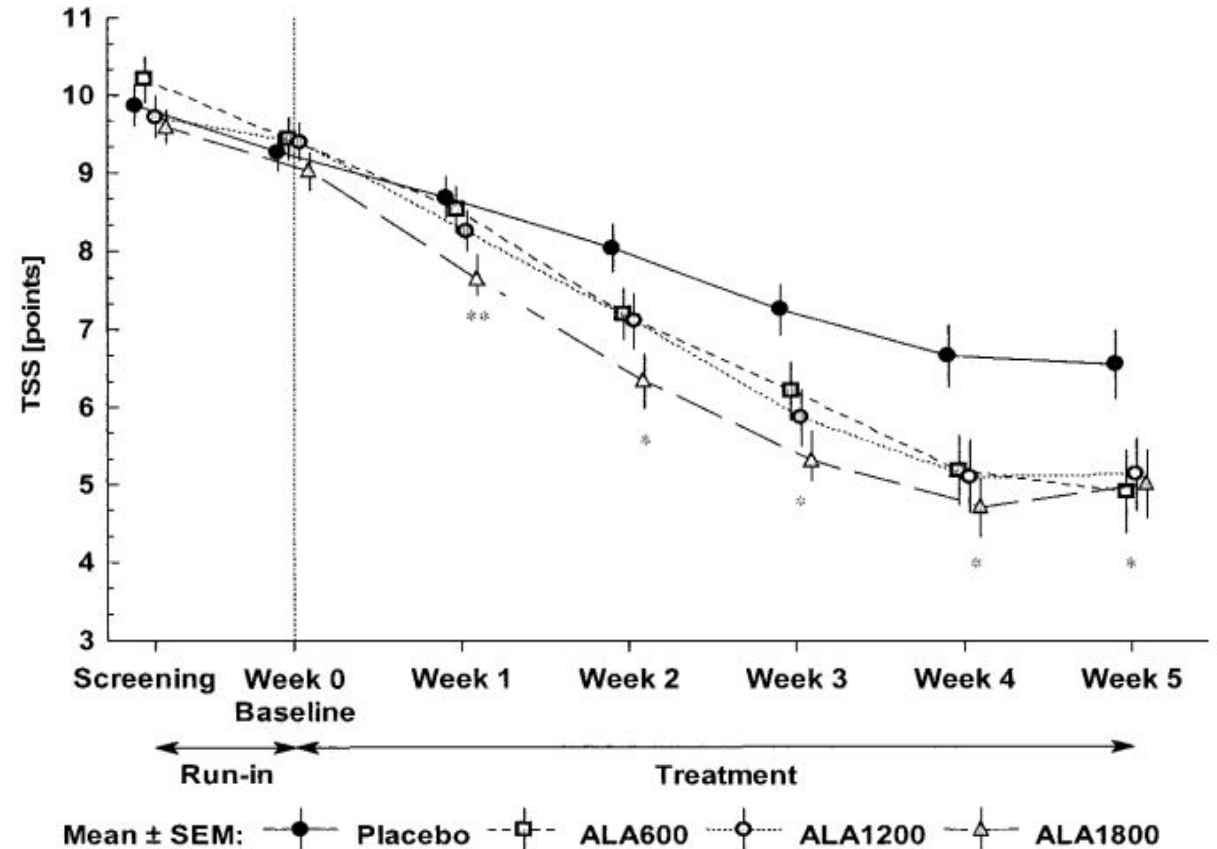
Surprisingly, it does work!
(*SYDNEY-2 TRIAL*)

ALA 600 mg 1-0-0

*Higher doses cause nausea,
and don't have any additional
benefit.*

Oral Treatment With α -Lipoic Acid Improves Symptomatic Diabetic Polyneuropathy

The SYDNEY 2 trial

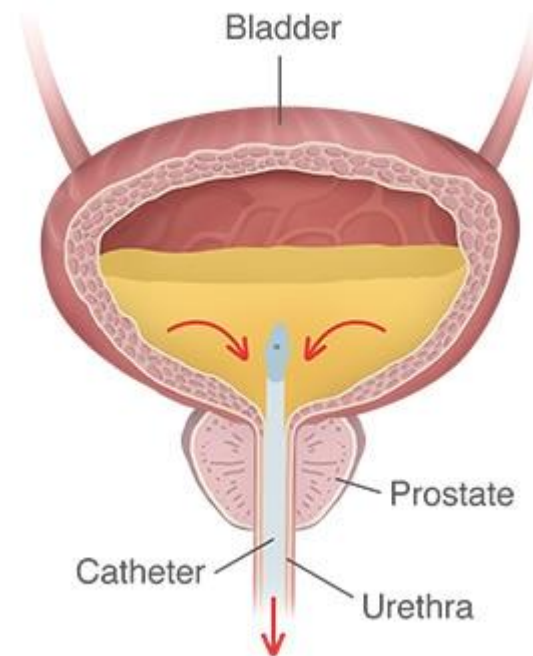
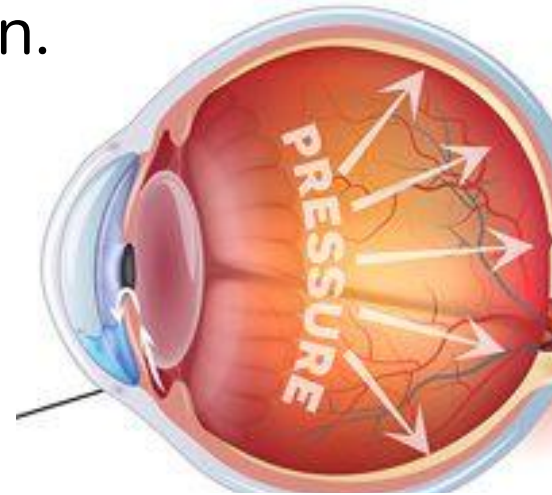


Amitriptyline?

- As effective as any other medication.
- Anticholinergic side-effects
 - Dry mouth
 - Glaucoma
 - Constipation
 - Urinary retention

Solution:

- Use NOR-triptyline!
- Also, make sure you remember many brand names...



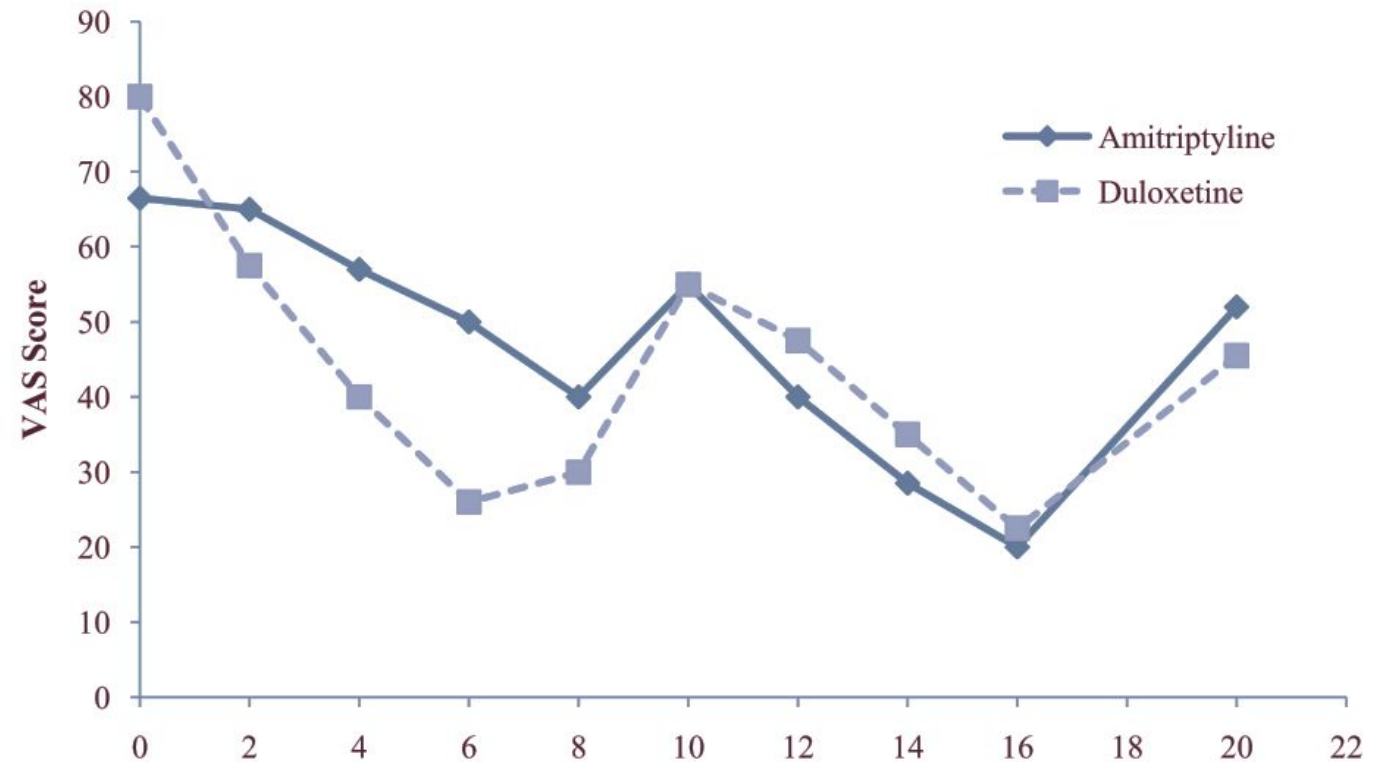
Duloxetine?

- Equally effective
 - Fewer anticholinergic s/e
- Although I have seen 1 patient with acute glaucoma.

-
- Fluoxetine
 - Escitalopram
 - Venlafaxine
- are **NOT** effective.

A Comparative Evaluation of Amitriptyline and Duloxetine in Painful Diabetic Neuropathy

A randomized, double-blind, cross-over clinical trial



Pregabalin? Gabapentin? Valproate? Carbamazepine?

Pregabalin and Valproate have been proven to be effective.

It is UNCLEAR if Gabapentin really helps DM pain!

Carbamazepine can be used in refractory cases.

The NEW ENGLAND JOURNAL of MEDICINE

SPECIAL ARTICLE

Outcome Reporting in Industry-Sponsored Trials of Gabapentin for Off-Label Use

CONCLUSIONS

We identified selective outcome reporting for trials of off-label use of gabapentin. This practice threatens the validity of evidence for the effectiveness of off-label interventions.

Also a uniquely Indian problem: Pregabalin Enantiomers

S

More effective
Less dizziness

R

Less effective
More dizziness

Because of patent and possibly technical/cost issues, most Indian brands contain a 50-50 blend of S and R- enantiomers...

What medications work the best? Local applicants

Capsaicin gel

I don't use it!

Gabapentin + Lidocaine gel

*Zero evidence but I use it
sometimes in many acutely
painful sensory conditions (e.g.
trigeminal Neuralgia)*



What medications work the best? **Combinations**

The following combinations have been studied:

1. Gabapentin + Nortriptyline
2. **Pregabalin + Duloxetine**
3. Gabapentin + Morphine

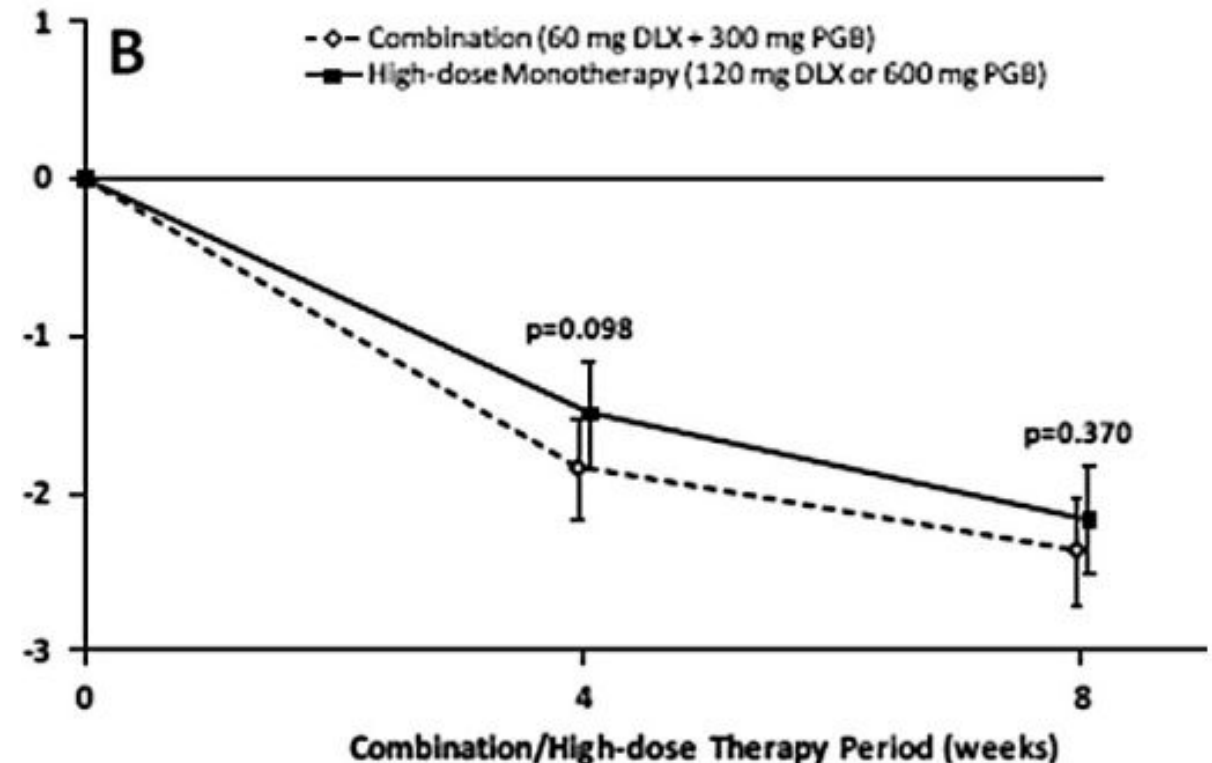


PAIN® 154 (2013) 2616–2625

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www.elsevier.com/locate/pain

Duloxetine and pregabalin: High-dose monotherapy or their combination? The “COMBO-DN study” – a multinational, randomized, double-blind, parallel-group study in patients with diabetic peripheral neuropathic pain



What dose should we use?

AAN (American Academy of Neurology) recommended doses are too high for Indian patients.

	Recommended	What I use
Alphalipoic Acid	-	600 mg OD
Amitriptyline	25 - 100 daily	12.5 - 25 HS
Duloxetine	60 - 120 daily	30 Hs - 60 BD
Pregabalin	300 - 600 daily	75 HS - 75 BD
Carbamazepine	-	300 HS - 300 BD
Sodium Valproate Gabapentin Venlafaxine Capsaicin	variable	I don't use these

What do I do?



- **ALA 600 mg 1-0-0**
- Occasionally, Progaba gel

First line:

- If anxious, insomnia □ **Amitriptyline**
- If not □ Duloxetine
- If glaucoma, prostate, constipation, cardiac □ Pregabalin

Second line:

- Pregabalin + Duloxetine
- Carbamazepine

Refractory:

- Refer to pain management: Opioids, Nerve stimulation etc