

The Internist's Approach to Neuropathy

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RELEVANT DECLARATIONS

- **Financial disclosures: None**
- **Unlabeled Use of Products disclosure: This presentation will mention medications that are very commonly used in peripheral neuropathy that are not FDA – labeled**

Why talk about neuropathy?

- Prevalence in general population about 2.4%
- 8% in those above age 55
- About 8% of patients with type 2 diabetes at the time of diagnosis
- Depending on definition 30-60% in long disease duration.
- Impairment of life quality
- Late complications (cardiac autonomic neuropathy, Charcot Neurorhopathy) are predictors of mortality

Case 1 - History

- 66 year-old man with 14 months of a sensation of “cotton” under his toes and ball of feet. He has some paresthesias and pins and needles sensation, as well as some numbness.
- He denies subjective weakness.
- He has no back pain
- He was diagnosed with type 2 diabetes 3 years ago, in addition to his several year history of hyperlipidemia, hypertension and obesity

What is the most likely diagnosis ?

- A) Plantar fasciitis
- B) Onychomycosis
- C) Diabetic peripheral neuropathy
- D) Amyotrophic lateral sclerosis
- E) Guillain-Barré syndrome

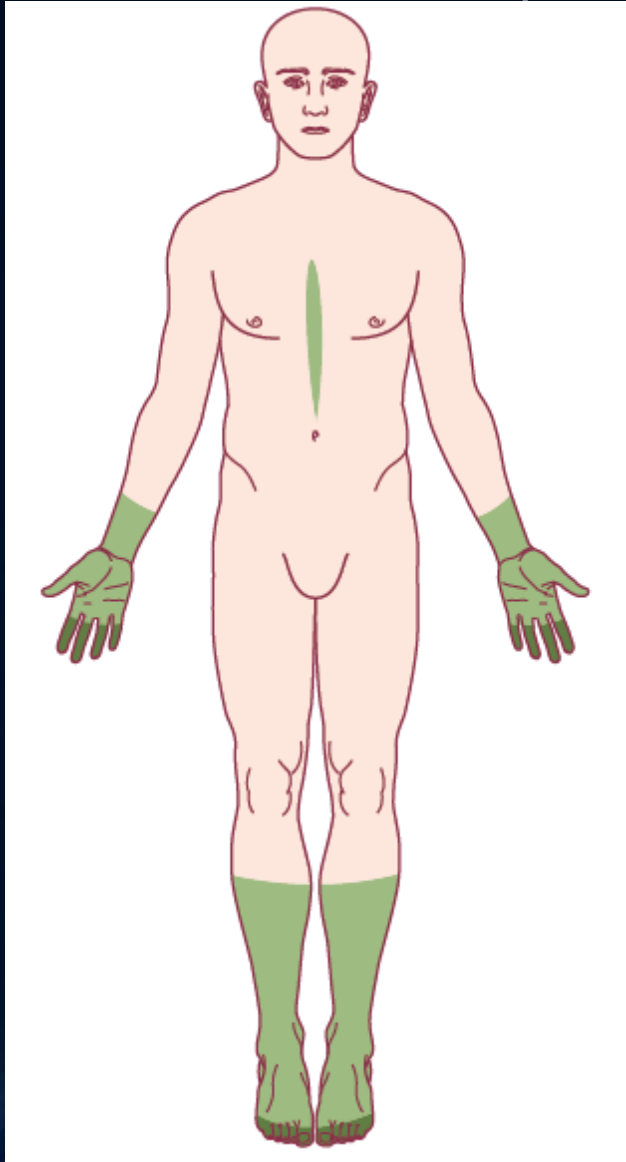
Stepwise evaluation of neuropathic symptoms

- Spatial Distribution
- Involved nerve fibers
- What is the tempo
- Risk factors based on personal and family history

What is the likely spatial distribution described in Case 1?

- A) Mononeuropathy
- B) Mononeuropathy Multiplex
- C) Radiculopathy
- D) Distal symmetric polyneuropathy
- E) Sensory neuronopathy

Distal Symmetric Polyneuropathy

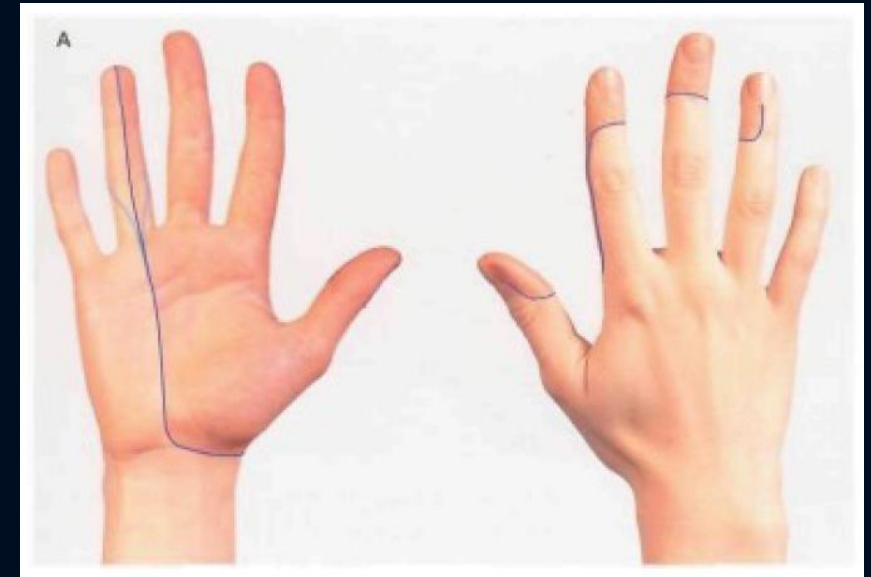


- Primarily sensory complaints
- Motor symptoms occur late
- Slowly progressive

• From Preston DC, Shapiro BE. Electromyography and neuromuscular disorders : clinical-electrophysiologic correlations. 3rd ed. London ; New York: Elsevier Saunders; 2013.

Neuropathy – Other Anatomic Patterns

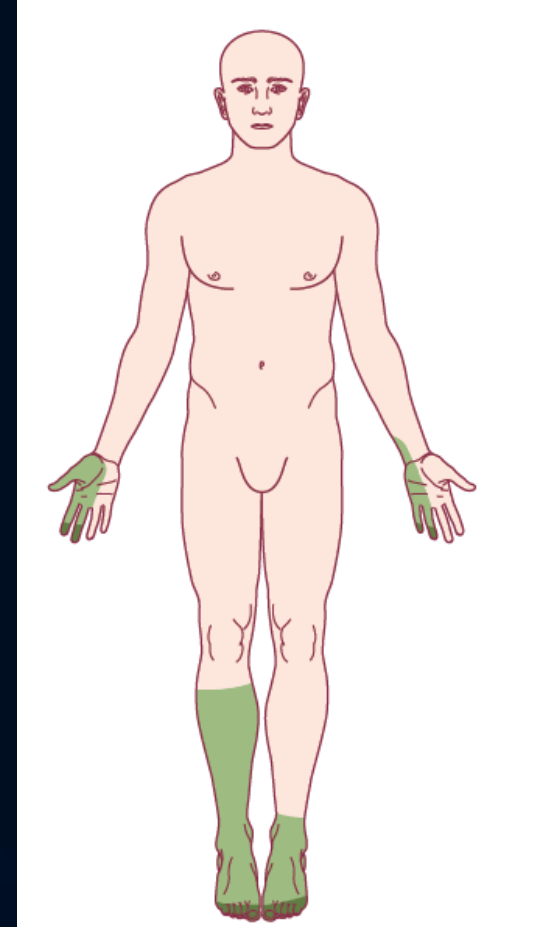
- Mononeuropathies



Compston A. Aids to the investigation of peripheral nerve injuries. Medical Research Council: Nerve Injuries Research Committee. His Majesty's Stationery Office: 1942; pp. 48 (iii) and 74 figures and 7 diagrams; with aids to the examination of the peripheral nervous system. By Michael O'Brien for the Guarantors of Brain. Saunders Elsevier: 2010; pp. [8] 64 and 94 Figures. Brain : a journal of neurology 2010;133:2838-44.

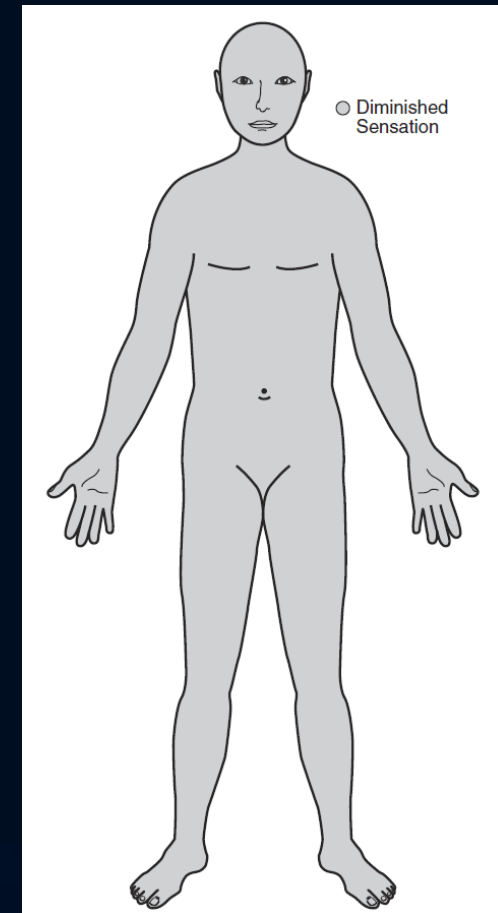
Neuropathy – Other Anatomic Patterns

- Mononeuropathies
- Mononeuropathy multiplex



Neuropathy – Other Anatomic Patterns

- Mononeuropathies
- Mononeuropathy multiplex
- Neuronopathy
- Other causes of neuropathic symptoms
 - Radiculopathies
 - Brain and spinal cord lesions



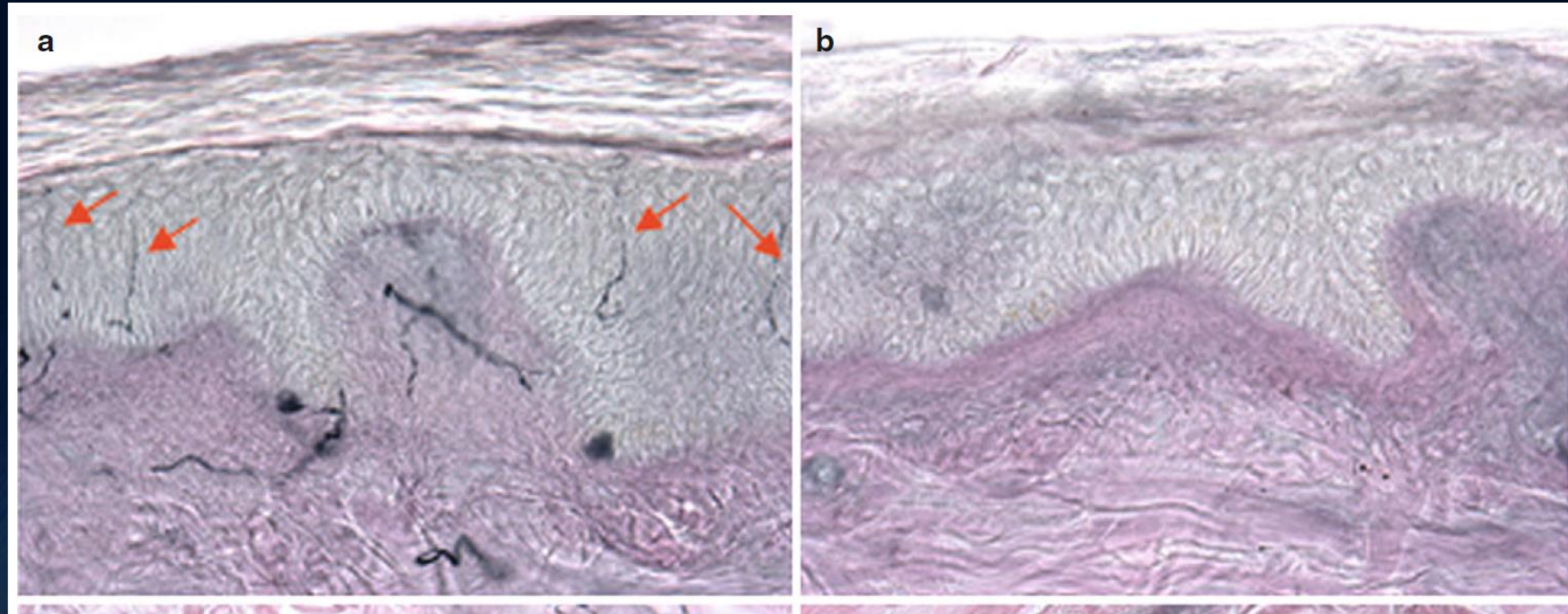
Case

- 55 year old woman with 2-years of dry mouth, dry eyes, joint pains, swollen parotid glands presents with 4 months of severe burning in her feet, thighs and abdomen. She can not tolerate the sheets touching her feet when in bed. She wears loose clothing because tight clothing irritates her.
- On examination she has entirely normal strength, muscle bulk, normal vibration and reflexes. Her gait is unremarkable.
- Her EMG and nerve conduction studies are normal.

Where is the lesion?

- A) Motor neurons
- B) Small sensory fibers
- C) Large sensory fibers
- D) Multiple nerve roots
- E) This presentation is not due to neuropathy

Skin biopsy



Katirji B, Kaminski HJ, Ruff RL. Neuromuscular Disorders in Clinical Practice: Springer New York; 2013.

Signs and symptoms based on fiber type

- Small sensory fibers
 - Symptoms: Burning, allodynia, hyperesthesia, numbness
 - Signs: Decreased pinprick, abnormal temperature sensation
- Large sensory fibers
 - Symptoms: Numbness, paresthesias, poor balance/falls
 - Signs: Loss of vibration and joint position, decreased distal reflexes, abnormal light pressure (monofilament), ataxia, pseudoathetosis

Signs and symptoms based on fiber type

- Autonomic fibers (same diameter as the small sensory fibers)
 - Symptoms: Orthostatic lightheadedness, bladder dysfunction, constipation, erectile dysfunction, early satiety
 - Signs: Resting tachycardia, orthostatic hypotension, hair loss, pale skin, cold or hyperemic feet
- Motor fibers
 - Symptoms: Weakness, cramps
 - Signs: Atrophy, weakness, fasciculations, cramps

What is the typical velocity speed of an upper extremity motor nerve in NCS ?

- A) 20m/s
- B) 50m/s
- C) 80m/s
- D) 100m/s
- E) 200m/s

Useful examination in 2 minutes

- **Motor examination**
 - Remove the shoes and socks
 - Is there atrophy?
 - Weakness in small hand or foot muscles
 - Functional weakness
- **Sensory examination**
 - Tuning fork or monofilament, joint position
 - Pinprick or temperature
 - Romberg sign
- **Reflexes**
- **Gait!**

Examination pictures/video

Back to our diabetic man- Examination

- He has normal strength and bulk
- Diminished vibration at the toes, preserved at the ankles
- Mild dullness to pinprick distal to his ankles
- Normal reflexes except depressed ankle jerks.
- His gait is normal.

Case

- 70 year-old woman with 20 years of diabetes presents with 1.5 years of intolerable paresthesias in her feet and distal legs. She has been feeling off balance and had a few falls. Her hands feel like “sand paper”. She must turn the lights on to be able to walk to the bathroom in the middle of the night. Legs feel stiff and sometimes she has painful spasms as if “the whole leg cramps up in a straight position.”
- On examination, she has normal strength in her arms but mild hip flexion weakness. She can't walk on her heels.
- She has absent vibration at her toes and ankles, and impaired joint position
- Reflexes are 3+ throughout. Her gait is mildly wide based.

What is the best next step

- A) Start symptomatic treatment for diabetic neuropathy. No need for additional workup
- B) Perform additional simple neuropathy workup (Routine labs, B12, Protein electrophoresis)
- C) Perform neuropathy workup and obtain an MRI of her lumbar spine
- D) MRI of the cervical spine and blood work for myeloneuropathy
- E) MRI of the lumbar spine alone

When to refer to a neurologist

- Acute/subacute onset
- Severe symptoms
- Rapidly progressive symptoms
- Non-length dependent presentation
- Focal or multifocal symptoms
- Severe dysautonomia
- Motor predominance

Distribution of Causes of Neuropathy

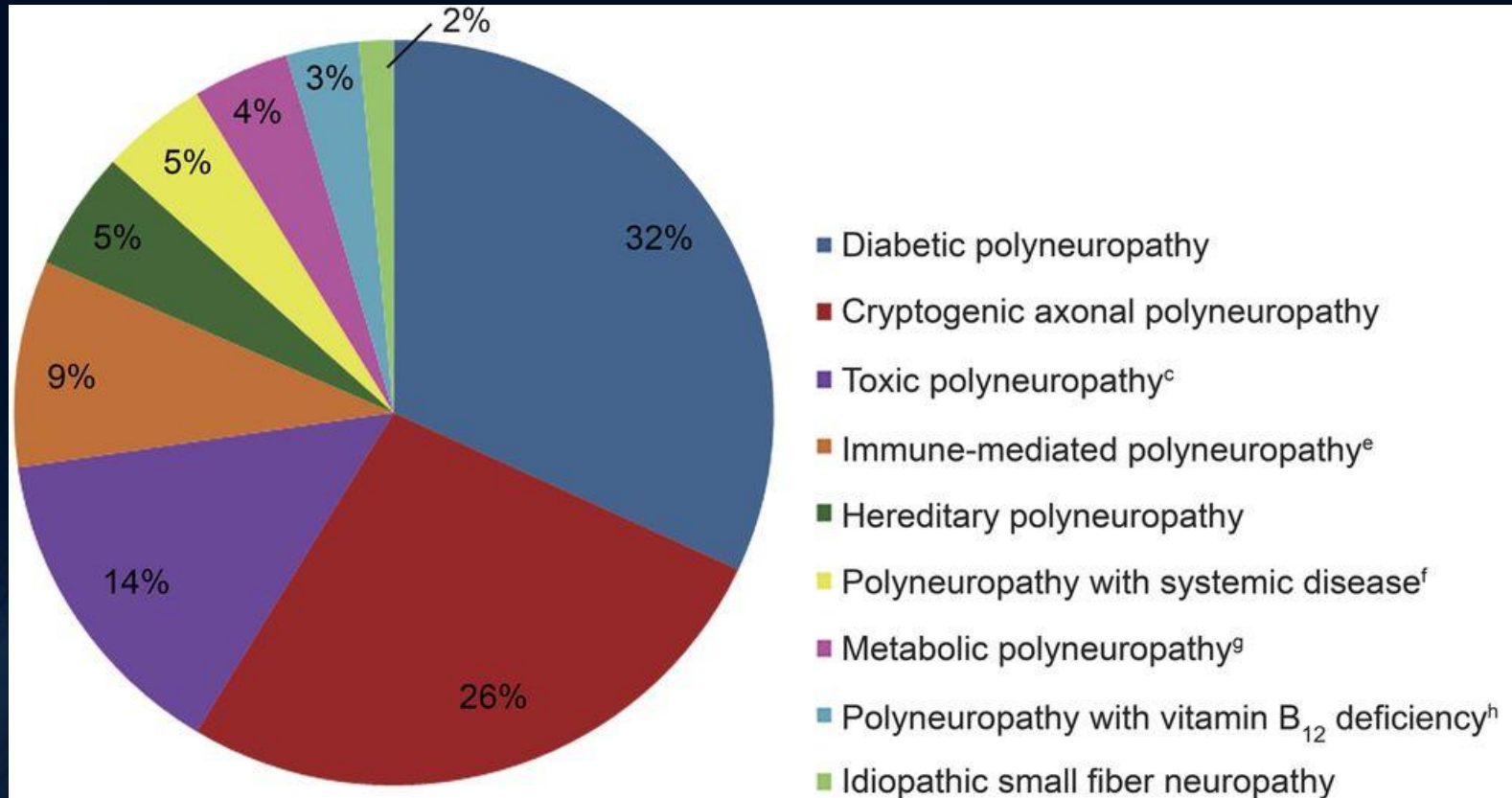
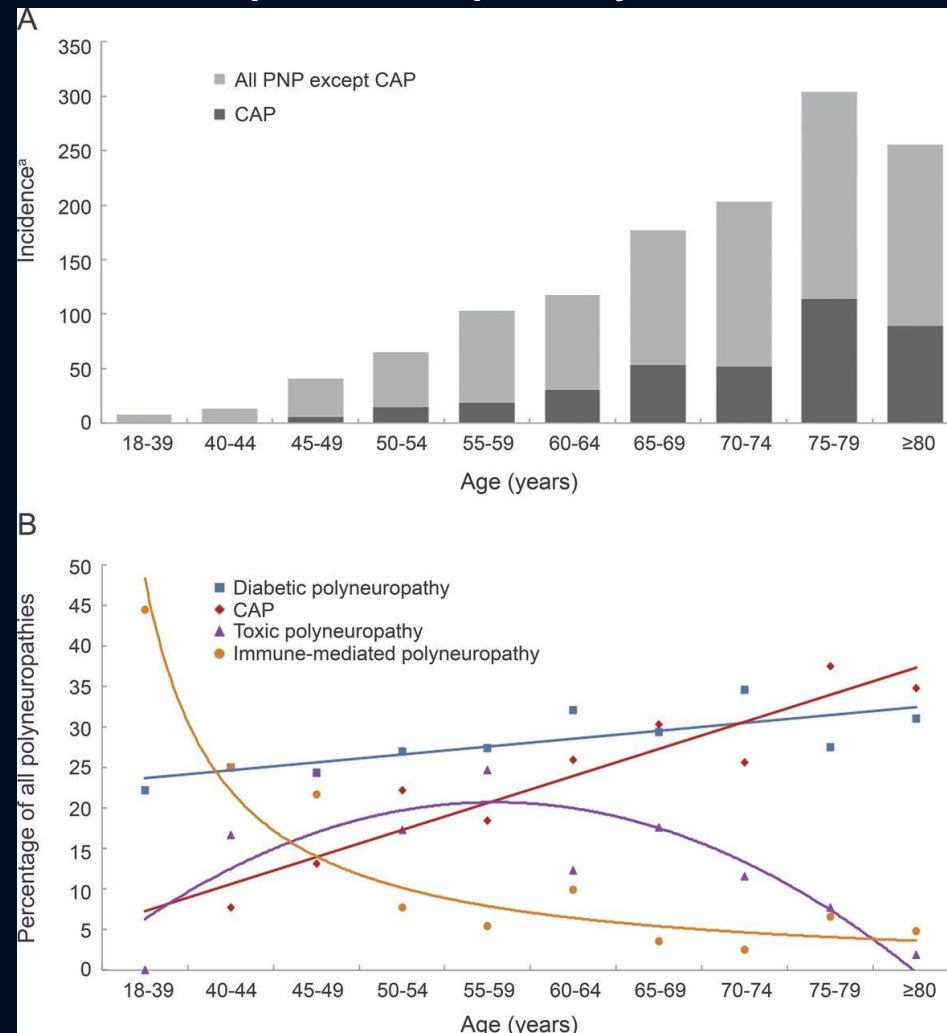


Figure 2 Age-stratified incidence of polyneuropathy (A) and percentage of incident patients of the etiologic subgroups of polyneuropathy compared with all polyneuropathies (B) a Incidence per 100,000 person-years.



Nora A. Visser et al. Neurology 2015;84:259-264



Initial workup

- Hemoglobin A₁C / Fasting glucose/ Oral glucose tolerance test
- Serum immunofixation electrophoresis
- Vitamin B₁₂ (Methylmalonic acid for vitamin B₁₂ levels 200-400)
- CBC
- Metabolic Panel
- +/- TSH
- Review of medical and family history!

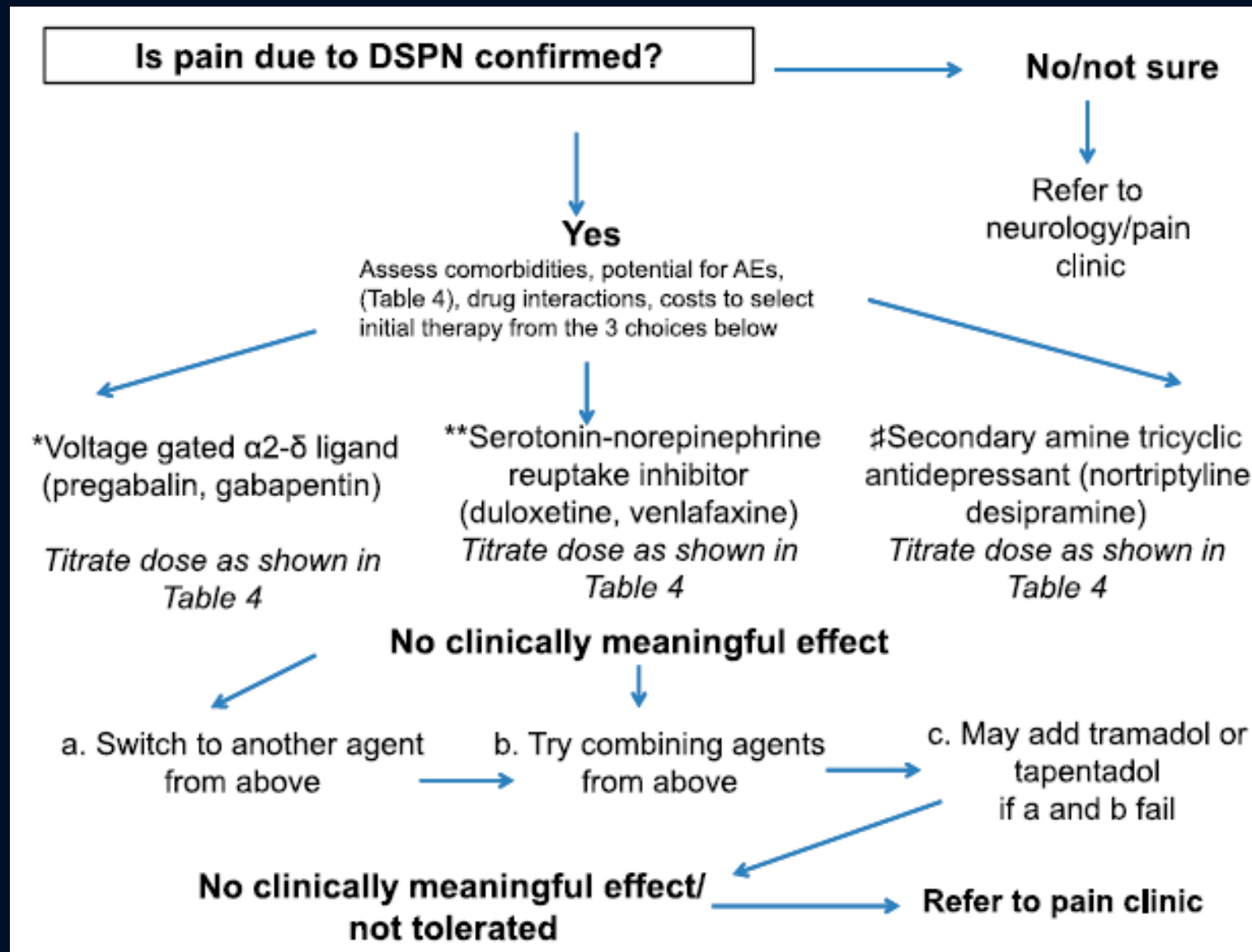
Management

- Symptomatic treatment
- Treatment of underlying disorder
- Fall prevention
- Foot ulcer prevention

Table 6 Pharmacologic Agents for the Management of Neuropathic Pain in Patients with Neuropathy

Name	Instructions for Starting	Goal Dose	Maximum Dose	Good for Patients with:	Consider Alternatives if:	Common Side Effects
Gabapentin	100 mg TID or 300 mg at bedtime	300 mg TID	3600 mg/d	Seizure disorder	Renal insufficiency	Dizziness, sedation, gait disturbance, confusion, peripheral edema
Pregabalin	75 mg BID	150 mg BID	600 mg/d	Seizure disorder	Renal insufficiency	Dizziness, sedation, gait disturbance, confusion, peripheral edema
Amitriptyline/ Nortriptyline	10-25 mg at bedtime	50-100 mg at bedtime	150 mg/d	Insomnia Migraine	Cardiac disease, arrhythmia, other serotonergic medications	Dry mouth (more common with amitriptyline), sedation, dizziness, confusion, QT-prolongation, orthostatic hypotension
Duloxetine	30 mg/d	60 mg/d (daily or split BID)	120 mg/d	Depression, anxiety, fibromyalgia	Hepatic failure, other serotonergic medications, anticoagulants	Nausea, dyspepsia, constipation, sedation, dry mouth, dizziness, hyperhidrosis, sexual dysfunction
Venlafaxine	37.5 mg/d (XR)	150 mg/d (XR)	225 mg/d	Depression, anxiety	Uncontrolled hypertension, other serotonergic medications	Nausea, dyspepsia, sedation, dizziness, nervousness, insomnia, hypertension, sexual dysfunction

BID = 2 times per day; TID = 3 times per day; XR = extended release.



Wrapping it up