Approach to Neuropathies

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Goals and objectives

- Obtain informative history from a patient with peripheral neuropathy.
- Use clinical information to recognize different patterns of peripheral neuropathy
- Provide differential diagnosis for each pattern

History

- Symptoms
  - Tingling, burning, stabbing, throbbing, prickling, dead, icy, hot, clumsy, wooden
  - Weakness
  - Distal leg
    - Tripping, stepping over curbs, uneven ground
  - Proximal
    - Standing from sitting, walking up or down stairs
    - Shaving, combing hair, brushing teeth
  - Upper extremity predominant
    - Turning keys, opening jars, doing up buttons
  - Autonomic: anhydrosis, excessive sweating, orthostatic light-headedness, impotence, dry mouth, early satiety.
- Onset
  - <4 weeks, 4-8 weeks, >8 weeks
- Duration
- Were you a reasonable athlete as a child? Did you finish last in foot races? Were you able to skate or play soccer?
- Progression
  - Chronic progression
  - Acute deterioration to nadir then stability or improvement

Past Medical History

- Diabetes (glucose intolerance)
- Thyroid disease
- Renal failure / hepatic failure
- Malignancies
- Connective tissue disease
  - SLE
  - Rheumatoid arthritis
- Previous cervical or lumbar disc disease
- Previous entrapment neuropathies
  - Multiple entrapments (consider HNPP, amyloidosis)
- Orthopedic procedures on feet and ankles
- Exposure to toxin

Family History

- Detailed family history
  - Walking difficulty, use of cane or wheelchair
  - Postural or foot deformities
- Probe history of disabled or possibly affected individuals
- Do not necessarily accept what diagnoses other individuals have

Social History

- Exposure to alcohol
- Occupation
- Tobacco
- Recreational drugs
- Vitamin and herb use

Occupation	Neuropathy
Dentists	Nitrous oxide
Painters	Hexacarbons
Farmers	Organophophates
Welders	Lead
Jewelers	Arsenic
Plastic industry	Acrylamide

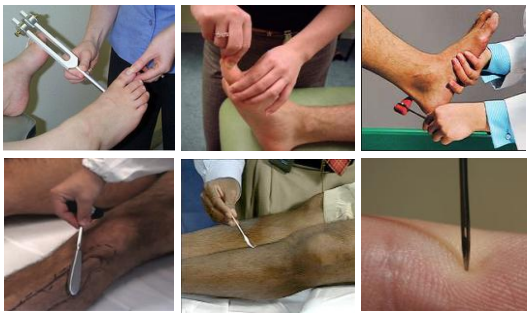
Review of Systems

- Joint pain, stiffness and swelling
- Fever
- Skin rash
- Other systems

Neurological examination

- Confirm localization (LMN vs UMN, myopathy vs neuropathy)
- Recognize pattern of neuropathy
  - Motor vs sensory vs sensorymotor
  - Proximal vs distal
  - Symmetric vs asymmetric
- Recognize features of hereditary neuropathy
- Recognize features that narrows the differential diagnosis.
  - Purpura and levido reticularis
- Autonomic features
  - BP & HR supine and standing
  - Pupillary reaction to light and accommodation
- Other
  - Skin: trophic changes (such as thin, shiny, and discolored skin)
  - ulcerations or amputations.
  - peripheral pulses.

Neuro exam…



Approach

1. Recognition of a clinical pattern.
2. There are 6 key questions the clinician should consider in arriving at the pattern that fits the patient best.
3. Most neuropathy and neuronopathy patients can be placed into one of 10 patterns.

Approach – 6 questions

1- What systems are involved?

2- What is the distribution of weakness?

3- What is the nature of the sensory involvement?

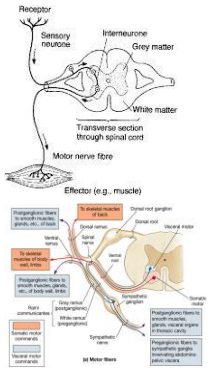
4- Is there evidence of upper motor neuron involvement?

5- What is the temporal evolution?

6- Is there evidence for a hereditary neuropathy?

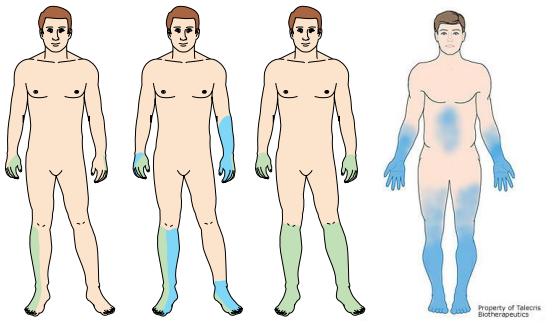
1- What Systems are Involved?

a. Motor: localized to AHC, motor nerve roots, motor nerves.
b. Sensory: DRG, sensory nerve roots, small nerves. Could be central
c. Autonomic: autonomic nerves, gray/white communicants
d. or combinations



2- What is the Distribution of Weakness?

a. Only distal versus proximal and distal
b. Focal/asymmetric versus symmetric



Asymmetric/focal weakness

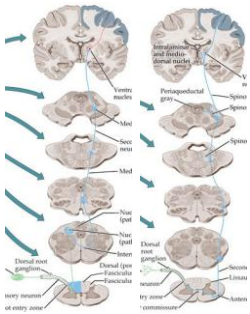
- Motor neuron disease
- Radiculopathy
- Plexopathy
- Mononeuropathy or multiple mononeuropathies
- Compressive/entrapment mononeuropathies

Symmetric weakness

- Represents a huge variety of DDx
- Symmetric **proximal** and **distal** weakness in a patient who presents with both motor and sensory symptoms → CIDP and GBS.
- Symmetric sensory and motor findings involving only the **distal** lower and upper extremities → the disorder generally reflects a primarily axonal peripheral neuropathy and is much less likely to represent a treatable entity.

3- What is the Nature of the Sensory Involvement?

- Pain (burning or stabbing) and temperature → small fiber
- Vibration and proprioception→ large fiber
- Most neuropathies involve both small and large fibers.
- Severe proprioceptive loss
  - Central: dorsal column
    - Generally less profound proprioceptive loss
    - UMN signs
  - Ganglionopathy: loss of all sensory modalities and reflexes



4- Is there evidence of upper motor neuron involvement?
   a. Without sensory loss (ALS,PLS)
   b. With sensory loss (B12 def, copper, vit E, etc)

5- What is the temporal evolution?
   a. Acute (days to 4 weeks)
   b. Subacute (4–8 weeks)
   c. Chronic (>8 weeks)
   d. Preceding events, infections, drugs, toxins

6- Is there evidence for a hereditary neuropathy?
   a. Family history of neuropathy
   b. Skeletal deformities
   c. Lack of sensory symptoms despite sensory signs

Ten patterns of neuropathic disorders

	Weakness								
	Proximal	Distal	Asymmetric	Symmetric	Sensory Symptoms	Severe Proprioceptive Loss	UMN Signs	Autonomic Symptoms/ Signs	Diagnosis
Pattern 1: symmetric proximal and distal weakness with sensory loss	+	+		+	+				GBS/CIDP
Pattern 2: distal sensory loss with/ without weakness		+		+	+				CSPN, metabolic, drugs, hereditary
Pattern 3: distal weakness with sensory loss		+	+		+				Multiple: vasculitis, HNPP, MADSAM, infection Single: mononeuropathy, radiculopathy
Pattern 4: asymmetric proximal and distal weakness with sensory loss	+	+	+		+				Polyradiculopathy, plexopathy
Pattern 5: asymmetric distal weakness without sensory loss		+	+				±		LMN and UMN – ALS Pure UMN – PLS Pure LMN – MMN, PMA, BAD, LAD, MAMA
Pattern 6: symmetric sensory loss and upper motor neuron signs		+		+	+	+	+		B_{12} deficiency, copper deficiency, Friedreich ataxia, adrenomyeloneuropathy
Pattern 7[A]: symmetric weakness without sensory loss	±	+		+					Proximal and distal SMA Distal Hereditary motor neuropathy
Pattern 8[A]: focal midline proximal symmetric weakness	+ Neck/extensor + Bulbar			+ +			+ +		ALS
Pattern 9: asymmetric proprioceptive loss without weakness			+		+	+			Sensory neuronopathy (ganglionopathy)
Pattern 10: autonomic dysfunction								+	HSAN, diabetes, GBS, amyloid, porphyria, Fabry

What is the pattern?

- A 65-year-old woman presented with a 3-month history of right-hand numbness, grip weakness, and vague elbow pain. Examination demonstrated diminished sensation of the medial hand and fourth and fifth digits, and weakness of finger abduction and adduction, associated with intrinsic hand muscle atrophy. Froment and Wartenberg signs were evident

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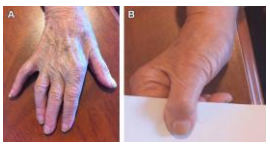

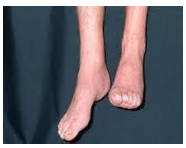

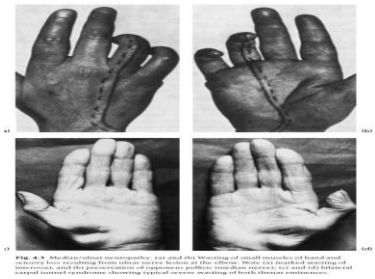

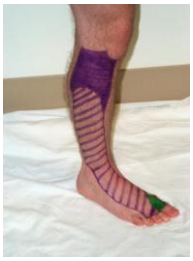

What is the pattern?

- A 25-year-old man with no family history of neuropathy had been weak early childhood. He remembers he was unable to keep up with his peers when running. He is currently only able to walk if wearing ankle-foot orthosis. He denied sensory symptoms.
- Neurological examination showed symmetric severe weakness in distal leg muscles with power of 1-2/5 with bilateral drop feet. proximal leg muscles were 4/5 as well as intrinsic hand muscles. Proximal upper limb muscles were normal.
- Reflexes were absent.
- Vibration and proprioception sensation were absent over the toes bilaterally and Pinprick and temperature were decreased to the knees and wrists

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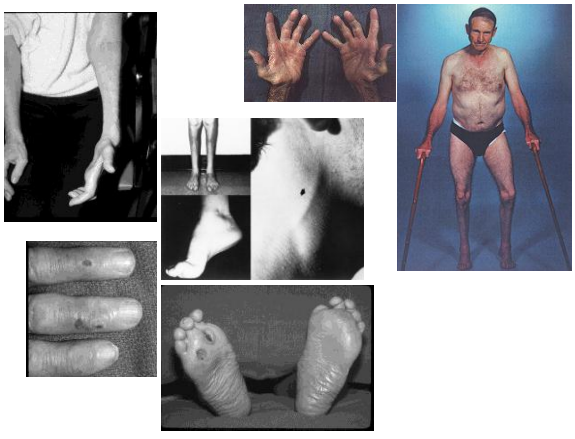

What is the pattern in this case?

- A 25 year-old woman developed numbness and tingling of the feet and hands followed by progressive leg more than arm muscle weakness over the last week. She experienced a diarrheal illness 3 weeks ago that had resolved within 10 days.
- Examination showed marked bifacial weakness and absent muscle stretch reflexes. She had normal pinprick, light touch and proprioception but vibration was reduced at the toes.
- Muscle power in the lower limbs was 2/5 and in the upper limbs 3/5, with equal proximal and distal weakness. She could not stand up or walk with assistance.

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- Laboratory studies including vitamin B12 level and 2 hour glucose tolerance test were normal and there was no serum monoclonal protein.
- Forced vital capacity was 2.0 liters.
- Cerebrospinal fluid evaluation showed no white cells but protein was 82 mg/dl.
- Nerve conduction studies showed 50% delay in tibial and median F wave latencies. Sensory conductions showed normal sural and absent median potentials.

What is the pattern here?

- A 42-year-old man developed numbness and tingling in the toes, progressing up to the ankles over 2 years. He describes burning pain in his feet, mainly at night. He recently started noticing symptoms of numbness and tingling in distal fingers. He denies any weakness.
- Examination showed normal strength, with decreased pinprick and light touch sensations to the ankles and distal fingers. Vibration was absent at the toes and decreased at the ankles, and proprioception is normal at the toes. Reflexes are normal in the arms and at the knees but ankle reflexes are absent. Gait is normal

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What is the pattern in this case?

- A 36-year-old man
- Eight weeks ago, he had bent down to lift a chair and developed acute pain in the right back and buttock with radiating paresthesias into the calf and lateral foot.
- Neurologic examination:
  - normal muscle bulk and tone in the lower extremities.
  - Straight-leg raising elicited pain and paresthesias into the right leg at 45 degrees.
  - Power: weakness in right **hip extension**, **knee flexion**, and **ankle plantar flexion**
  - Sensory examination: mild sensory loss on the right sole and lateral foot.
  - DTR: right ankle reflex was absent, other DTRs were normal

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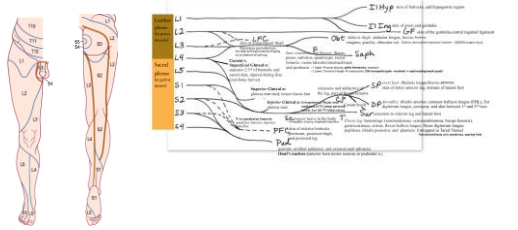

- thanks