



Chapter 107 – Peripheral Nerve Disorders

Episode overview

THIS IS GOING TO BE A BEAST!!!!

1. Describe a neuropathy classification system (7 total) and list the prototypical condition for each
2. List 8 causes of acute emergent weakness and possible respiratory compromise
3. List 4 demyelinating polyneuropathies
4. Describe the pathophysiology of GBS, and list common precipitating organisms
5. What is Miller-Fisher Syndrome?
6. Describe the clinical presentation of GBS, diagnostic tests, and management
7. List 6 distal symmetric polyneuropathies
8. Describe the clinical progression of Diabetic polyneuropathy
9. List 5 causes of an isolated mono neuropathy and 5 causes of a plexopathy
10. What are two other names of a radial mononeuropathy? How does it present?
11. Describe the motor and sensory innervation of the ulnar nerve. How can you discern between a ulnar nerve lesion at the elbow or at the wrist?
12. Describe the motor and sensory innervation of the medial nerve.
13. List 3 physical findings of carpal tunnel syndrome. What are 6 RFs?
14. What are the findings in a lateral femoral cutaneous mononeuropathy?
15. What are the findings of a common peroneal mononeuropathy?
16. List 3 causes of a mononeuropathy multiplex
17. What are the characteristics of Amyotrophic Lateral Sclerosis
18. What is a Ganglionopathy?

No wisecracks: just way too much in this chapter already!!!

Rosen's In Perspective

Nervous System = Central Nervous System + Peripheral Nervous System

PNS divided into

- ❑ 12 cranial nerves
 - ❑ (Remember episode 105?)
- ❑ 31 spinal nerves
 - ❑ (8 cervical, 12 thoracic, 5 lumbar, 5 sacral, and 1 coccygeal).
- ❑ Almost all of these nerves have Sensory, Motor and autonomic function

Anatomically / functionally speaking the autonomic nervous system is divided into:

1. Sympathetic (thoracolumbar) component
2. Parasympathetic (craniosacral) component.



Note: Autonomic dysfunction may cause systemic abnormalities (e.g., Orthostasis), or a local issue, e.g., atrophic, dry skin.

Refer to figure 97.2 in Rosen's 9th Edition for schematic representation of the anatomy of the peripheral nervous system and its interface with the central nervous system

When something goes wrong with the PNS, 1 of 3 issues may develop:

1. **Myelinopathies**, in which the primary site of involvement is limited to the myelin sheath surrounding the axon;
2. **Axonopathies**, in which the primary site of involvement is the axon, with or without secondary demyelination
3. **Neuronopathies**, in which the cell body of the neuron itself is the primary site of involvement, ultimately affecting the entire peripheral nerve.

Note: *“Although overlap occurs, each of these prototypes has a distinctive clinical presentation, electrophysiologic profile, and microscopic appearance.”*

8% of the population over 50 years of age have a peripheral neuropathy. The most common etiology is Diabetes. Like the CNS, the basic approach is to ask yourself: focal or nonfocal?

Focal is then broken down into:

- Single lesion = simple mononeuropathies

versus

- Multiple lesions = multiple mononeuropathies = mononeuropathy multiplex

Nonfocal = Polyneuropathies

Refer to figure 97.1 in Rosen's 9th Edition for the cardinal 7 categories of peripheral neuropathies

Focus your History and physical to answer the following 3 questions:

1. Are the sensorimotor signs and symptoms symmetrical or asymmetrical?
2. Are the sensorimotor signs and symptoms distal or both proximal and distal?
3. Is the modality involved exclusively motor, sensory, or mixed sensorimotor?

How do you workup suspected polyneuropathies?

See box 97.2 in Rosen's 9th Edition for ancillary diagnostic testing in suspected peripheral neuropathy

*** See questions 2 for the emergent causes of polyneuropathies with resp failure that WE NEED TO KNOW***



[1] Describe a neuropathy classification system and list the prototypical condition for each

Remember the RIP!!! Again, let us review...

Refer once again to figure 97.1 as well as to box 97.1 in Rosen’s 9th Edition for an approach to peripheral neuropathy, and for the patterns and prototypes of peripheral neuropathies, respectively

Patterns and Prototypes of Peripheral Neuropathies:

Type	Pattern Distribution	Prototypical disease modalities
1	Proximal and distal, symmetrical, sensorimotor polyneuropathy Proximal and distal Motor > sensory	GBS Symmetrical
2	Distal, symmetrical, sensorimotor polyneuropathy Distal Sensory > motor	Diabetic DSPN Symmetrical
3	Proximal and distal, asymmetrical, sensorimotor neuropathy Proximal and distal Sensory and motor	Brachial plexopathy Asymmetrical
4	Distal, asymmetrical, sensorimotor mononeuropathy Distal Sensory and motor	CTS (median mononeuropathy) Asymmetrical
5	Distal, asymmetrical, sensorimotor mononeuropathy multiplex Distal Sensory and motor	Vasculitic mononeuropathy multiplex Asymmetrical
6	Distal, asymmetrical, pure motor neuropathy Distal Motor	ALS Asymmetrical
7	Distal, asymmetrical, pure sensory neuronopathy Distal Sensory	Pyridoxine toxicity Asymmetrical



[2] List 8 causes of acute emergent weakness and possible respiratory compromise

See box 97.1 in Rosen's 9th Edition for causes of acute, emergent weakness and possible respiratory compromise

- Autoimmune
 - Demyelinating
 - Guillain-Barré syndrome (GBS)
 - Chronic inflammatory demyelinating polyneuropathy
 - Myasthenia gravis
- Toxic
 - Botulism
 - Buckthorn
 - Seafood
 - Paralytic shellfish toxin
 - Tetrodotoxin (puffer fish, newts)
 - Tick paralysis
 - Metals
 - Arsenic
 - Thallium
- Metabolic
 - Dyskalemic syndromes
 - Acquired (especially with thyrotoxicosis)
 - Familial
 - Hypophosphatemia
 - Hypermagnesemia
 - Porphyria
- Infectious
 - Poliomyelitis
 - Diphtheria

[3] List 4 demyelinating polyneuropathies

See box 97.3 in Rosen's 9th Edition for a list of demyelinating polyneuropathies

Demyelinating polyneuropathies:

- Guillain-Barré syndrome (GBS)
 - Acute inflammatory demyelinating polyradiculoneuropathy
 - Acute motor axonal neuropathy
 - Acute motor and sensory axonal neuropathy
 - Miller Fisher syndrome
- Chronic inflammatory demyelinating polyradiculoplexoneuropathy



- Malignant disease
- Human immunodeficiency virus (HIV) infection
- Hepatitis B
- Buckthorn
- Diphtheria

[4] Describe the pathophysiology of GBS, and list common precipitating organisms

According to UpToDate: *“GBS is thought to result from an immune response to a preceding infection that cross-reacts with peripheral nerve components because of molecular mimicry. The immune response can be directed towards the myelin or the axon of peripheral nerve, resulting in demyelinating and axonal forms of GBS.”*

“The pattern of symmetrical weakness, usually worse distally, accompanied by variable sensory endings is characteristic of acute Guillain-Barré syndrome (GBS).” - Rosen’s

Broken down into

- Acute inflammatory demyelinating polyradiculoneuropathy
- Acute motor axonal neuropathy
- Acute motor and sensory axonal neuropathy
- Miller fisher syndrome
- Bickerstaff encephalitis
- Pharyngeal-cervical-brachial weakness
- Paraparesis
- Others

“Areflexic paralysis with albuminocytologic dissociation, with marked variation in latency between antecedent infection and symptom onset. Up to 20% of patients remain disabled from this disease process, and about 5% will die despite therapy.”

Most common form of GBS = acute inflammatory demyelinating polyneuropathy (90% of the cases seen in North America).

Risk factors:

- Asian descent
- Increasing age
- Male > Female

Most commonly associated infectious agents:

- Campylobacter jejuni (up to 30% of cases)**
- Cytomegalovirus (CMV)
- Epstein-Barr virus (EBV)
- Mycoplasma pneumonia



[5] What is Miller-Fisher Syndrome?

Miller Fisher Syndrome (MFS) is a rare form of GBS...

Characterized by the triad of

- Ophthalmoplegia
- Ataxia
- Areflexia

1/4 of patients who present with MFS get extremity weakness

Incomplete forms include:

- Acute ophthalmoplegia without ataxia
- Acute ataxic neuropathy without ophthalmoplegia

Note: Some patients with MFS develop fixed, dilated pupils !!!

[6] Describe the clinical presentation of GBS, diagnostic tests, and management

Usually present post-infectious illness (URTI or GI), upper respiratory or gastrointestinal illness, with progressive, symmetrical, distal (and usually to a lesser extent proximal) weakness.

- Symptoms can progress over ~28 days
- Lower extremities >> Upper extremity weakness
- Decreased or loss of DTRs
- Variable sensory findings
- Sparing of the anal sphincter

According to Uptodate:

- Weakness usually starts in the legs, but it begins in the arms or facial muscles in about 10% of patients
- Severe respiratory muscle weakness requiring ventilatory support develops in 10% - 30%
- Facial nerve palsies occur in more than 50%, and oropharyngeal weakness eventually in 50%
- Oculomotor weakness occurs in about 15%
- Decreased or absent reflexes in affected arms or legs are found in approximately 90% of patients at presentation and in all patients with disease progression
- Paresthesias in the hands and feet accompany the weakness in more than 80% of patients, but sensory abnormalities on examination are frequently mild.



- Pain due to nerve root inflammation, typically located in the back and extremities, can be a presenting feature and is reported during the acute phase by two-thirds of patients with all forms of GBS
- Dysautonomia occurs in approximately 70% of patients
 - Diarrhea/constipation
 - Hyponatremia
 - Bradycardia
 - Urinary retention
 - Tachycardia
 - Reversible cardiomyopathy
 - Horner syndrome
- SIADH

Pearls:

1. The presence of distal paresthesias increases the likelihood of GBS
2. Tongue weakness is associated with the development of respiratory compromise and the need for mechanical ventilation
3. Compared with adults, children have neuropathic pain more often but require mechanical ventilation less often
4. Progression for more than eight weeks is consistent with the diagnosis of chronic inflammatory demyelinating polyradiculoneuropathy (CIDP)
5. GBS and PRES (posterior reversible encephalopathy syndrome) are associated - likely related to acute hypertension from dysautonomia

The following should make you reconsider your diagnosis (from UpToDate)!!!

- Sensory level (decrement or loss of sensation below a spinal cord root level as determined by neurologic examination)
- Marked, persistent asymmetry of weakness
- Bowel and bladder dysfunction at onset
- Severe and persistent bowel and bladder dysfunction
- Severe pulmonary dysfunction with little or no limb weakness at onset
- Severe sensory signs with little or no weakness at onset
- Fever at onset
- CSF pleocytosis with a white cell count $>50/\text{mm}^3$

Diagnosics:

- Imaging - MRI spine (can add brain if mixed picture)
- EMG
- CSF: may be normal, or classically they will have **Albuminocytologic dissociation** = markedly elevated protein with only a mild pleocytosis



Management:

AIRWAY and BREATHING should be your #1 priority!!!

Clinical diagnosis here, but a FVC <15cc/kg, or Negative Inspiratory force (NIF) of <20-30% should make you drop the tube.

Other options, with consultation of neurology:

- Plasma exchange
- Intravenous immune globulin (IVIG) 400 mg/kg per day for 5 days
- Corticosteroids are not recommended**; oral steroids have been shown to delay recovery, and intravenous steroids alone have shown no benefit

Note: The combination of intravenous steroids and IVIG appears to decrease recovery time but no clinical improvement of long term outcomes

[7] List 6 distal symmetric polyneuropathies

Refer to box 97.4 in Rosen's 9th Edition for an extensive list of distal sensorimotor polyneuropathies

Broad categories of distal sensorimotor polyneuropathies include:

- Diabetes mellitus
- Alcoholism
- Neoplastic or paraneoplastic
- Hereditary motor and sensory neuropathies (Charcot-Marie-Tooth)
- Cryptogenic sensorimotor polyneuropathies
- HIV infection
- Toxins
- Nutritional
- End-organ dysfunction
- Paraproteinemias
- Porphyria

[8] Describe the clinical progression of Diabetic Polyneuropathy

First up, although this is the most common cause of distal symmetric peripheral polyneuropathy (DSPN), don't forget the differential diagnosis here!

- Diabetes
- Alcoholism
- HIV
- Toxic metabolic

These are the most common. Many more as stated in question 7.



As with most DSPN, diabetic neuropathy presents as:

- ❑ Pattern of distal, symmetrical sensorimotor findings
- ❑ LE > UE
- ❑ stocking-glove distribution of sensory abnormalities that gradually diminishes as one moves proximally
 - ❑ Early sensory complaints like burning or tingling
- ❑ Motor weakness and loss of DTRs (lag behind the sensory features)
 - ❑ Loss of big toe dorsiflexion usually first motor sign
 - ❑ “Steppage gait,” in which footdrop causes the toes to point downward and scrape the ground while walking, requiring the patient to lift the leg higher than normal when walking.
- ❑ Eventual ataxia
- ❑ Diabetic foot ulcers ranging from 2% to 10% of the population.
 - ❑ Mechanism: Unperceived trauma

[9] List 5 causes of a plexopathy & 5 causes of an isolated mononeuropathy

So here we are talking about category 3: asymmetric proximal and distal peripheral neuropathies aka radiculopathies and plexopathies, and category 4: isolated mononeuropathies

Refer to boxes 97.5 and 97.6 in Rosen’s 9th Edition for asymmetrical proximal and distal peripheral neuropathies, and isolated mononeuropathies, respectively

Asymmetrical proximal and distal peripheral neuropathies:

- Brachial plexopathy
 - Open
 - Direct plexus injury (knife or gunshot wound)
 - Neurovascular (plexus ischemia)
 - Iatrogenic (central line insertion)
 - Closed
 - Traction injuries
 - “Stingers”
 - Traction neurapraxia
 - Partial or complete nerve root avulsion
 - Radiation
 - Neoplastic
 - Idiopathic brachial plexitis
 - Thoracic outlet
- Lumbosacral plexopathies
 - Open
 - Closed



- Traction injuries
 - Pelvic double vertical shearing fracture
 - Posterior hip dislocation
 - Retroperitoneal hemorrhage
- Vasospastic (deep buttock injection)
- Neoplastic
- Radiation
- Idiopathic lumbosacral plexitis
- Infectious
 - Herpesvirus (sacrocoxygeal)
 - Herpes simplex 2
 - Herpes zoster
 - Cytomegalovirus polyradiculopathy (HIV infection)

Isolated mononeuropathies (broad categories):

- Upper extremity
 - Radial nerve
 - Ulnar nerve
 - Median nerve
- Lower extremity
 - Sciatic nerve
 - Femoral nerve
 - Lateral femoral cutaneous (meralgia paresthetica)
 - Peroneal nerve
 - Tibial nerve
 - Sural nerve
 - Plantar nerve
 - Obturator mononeuropathy

[10] What are two other names of a radial mononeuropathy? How does it present?

Remember your anatomy? Yeah... that is what we thought:

- ❑ Rises from the C5 to T1 nerve roots.
- ❑ *“After exiting the brachial plexus, it passes behind the proximal humerus in the spiral groove and takes a lateral (radial) course down the upper arm (Fig. 97.3). At about the level of the antecubital fossa, it bifurcates into the posterior interosseous (pure motor) and superficial radial (pure sensory) nerves.” – Steward JD 3rd Edition*

Motor: extension of fingers/thumb/wrist/elbow (triceps). All motor function = extrinsic muscles of hand (unlike median and ulnar)



Sensory: cutaneous dorsal area overlying the first dorsal interosseous muscle (sometimes extending part of the way up the dorsa of the thumb, index, and long fingers)

Refer to figure 97.3 in Focal Peripheral Neuropathies, by Steward JD 3rd Edition, for an anatomical diagram of the radial nerve and its major branches

“Saturday night palsies” = radial mononeuropathy, secondary to compressive neuropathy.

- Caused when the radial nerve is trapped between the humeral shaft and some hard surface, as seen in deep drunk sleep.

“Bridegroom’s palsy” = radial nerve may be compressed by the bride’s head resting on the groom’s arm during sleep

Rare: Radial neuropathy secondary to improper crutch use causing compressive neuropathy at the level of the axilla!

- Look for wrist +/- finger drop. Also seen is paresthesia of dorsum of 1st digit space.

[11] Describe the motor and sensory innervation of the ulnar nerve. How can you discern between an ulnar nerve lesion at the elbow or at the wrist?

Anatomy: C7 to T1 roots - passes through the brachial plexus to descend medially, without branching, to the ulnar (medial) condylar groove at the elbow. Then goes from cubital canal, it branches to the ulnar wrist flexor and the deep flexors of the fourth and fifth digits. At the wrist it enters Guyon’s Canal between the pisiform and hook of the hamate, after which it bifurcates into the superficial terminal sensory branch and the deep motor branch.

Refer to figure 97.4 in Focal Peripheral Neuropathies, by Steward JD 3rd Edition, for an anatomical diagram of the ulnar nerve and its major branches

Motor: The deep motor nerve supplies

- Hypothenar muscles
- Ulnar intrinsics (e.g., abduction of index finger: all interossei and the ulnar lumbricals of the fourth and fifth digits)

Sensory: The superficial sensory nerve supplies ulnar sensation to the palmar side of the fifth and half of the fourth digit

Localizing lesion: Some compressive lesions just proximal to the elbow can be brought out by prolonged flexion of the elbow, or repetitive flexion-extension. However, the localization gold standard involves electrophysiologic studies.

Wrist vs elbow: Is there sensory splitting of the 4th and 5th digit?



“Although it is difficult to distinguish a condylar from a cubital ulnar mononeuropathy, it is usually possible to localize the problem to the region of the elbow or the wrist. In addition to prior probability heavily favoring the elbow, the presence of sensory abnormalities in an ulnar distribution in the hand and fingers (i.e., usually including the fifth digit and “splitting” the fourth digit) strongly suggests that the lesion is at the level of the elbow rather than the wrist. The ulnar cutaneous innervation to the hand branches off from the main trunk proximal to the nerve entering Guyon’s Canal. Thus a lesion at the wrist should not produce sensory abnormalities, whereas one at the elbow would be expected to do so.” -Rosen’s 9th edition

[12] Describe the motor and sensory innervation of the medial nerve.

Anatomy: C5 to T1 spinal nerve roots and exits the brachial plexus through the lower trunk.
Usually diagnosed as carpal tunnel syndrome (CTS) = most common entrapment neuropathies

Refer to figure 97.6 in Focal Peripheral Neuropathies, by Steward JD 3rd Edition, for an anatomical diagram of the median nerve and its major branches

Motor = Thenar contraction with opposition

Sensory = Index finger sensation

[13] List 3 physical findings of carpal tunnel syndrome. What are 6 risk factors?

Motor dysfunction = median intrinsic involvement = Test the LOAF muscles: “lumbricals (flexion of the metacarpophalangeal joints) and subserve thumb opposition, abduction, and flexion, known as the LOAF muscles.”

The most sensitive finding is abnormal sensation of the distal palmar tip of the index finger

Physical exam (classically taught but not satisfactory sensitive or specific):

1. Tinel’s sign (percussion of the median nerve at the wrist)
2. Phalen’s sign (maximal palmar extension at the wrist) have been classically taught as provocative tests to reproduce the sensory symptoms of CTS
3. Dropping of objects is indicative of severe CTS!!!
4. The best way to examine patients for sensory findings = touch the distal palmar tips very lightly, asking the patient whether the sensation feels “abnormal.”

Refer to box 97.7 in Rosen’s 9th Edition for conditions associated with CTS

Conditions associated with Carpal Tunnel Syndrome:

- Acromegaly
- Amyloid
- Diabetes mellitus
- Hypothyroidism



- Obesity
- Pregnancy
- Renal failure
- Rheumatoid arthritis

[14] What are the findings in a lateral femoral cutaneous mononeuropathy?

Lateral femoral cutaneous mononeuropathy = *meralgia paresthetica*

Pure sensory nerve injury usually at level of inguinal ligament (belt, tight pants, post-surgery, HIV)

O/E = Numbness and dysesthesia over the skin of the upper lateral thigh

[15] What are the findings of a common peroneal mononeuropathy?

Anatomy = continuation of one trunk of the sciatic nerve. Most vulnerable at the fibular neck

Refer to figures 97.7 and 97.8 in Focal Peripheral Neuropathies, by Steward JD 3rd Edition, for an anatomical diagram of the Sciatic and Common Peroneal nerves and their major branches

Motor: Ankle Dorsiflexion, foot eversion

Sensory: (superficial peroneal = lateral dorsal foot, deep peroneal = Dorsal 1st webspace)

O/E

- Foot drop
- Weak foot eversion
- BUT INVERSION SHOULD BE INTACT, if not, think about sciatic mononeuropathy

[16] List 3 causes of a mononeuropathy multiplex

Refer to box 97.8 in Rosen's 9th Edition for a list of etiologies of mononeuropathy multiplex

Mononeuropathy multiplex etiologies:

- Vasculitis
 - Systemic vasculitis
 - Polyarteritis nodosa
 - Rheumatoid arthritis
 - Systemic lupus erythematosus
 - Sjögren's syndrome (keratoconjunctivitis sicca)



- Nonsystemic vasculitis
- Diabetes mellitus
- Neoplastic
 - Paraneoplastic
 - Direct infiltration
- Infectious
 - Lyme disease
 - HIV infection
- Sarcoid
- Toxic (lead)
- Transient (polycythemia vera)
- Cryoglobulinemia (hepatitis C)

[17] What are the characteristics of Amyotrophic Lateral Sclerosis

Refer to box 97.9 in Rosen's 9th Edition for clinical findings of ALS

Objective clinical findings consistent with Amyotrophic Lateral Sclerosis:

- Upper motor neuron signs
 - Hyperreflexia
 - Sustained clonus, especially at ankle
 - Finger flexors and jaw jerk
 - Spasticity, especially of gait
 - Presence of Babinski's sign
- Lower motor neuron signs
 - Positive motor phenomena
 - Fasciculations
 - Cramps
 - Negative motor phenomena
 - Asymmetrical distal weakness
 - Atrophy
- Combined upper and lower motor neuron signs
 - Dysarthria
 - Dysphagia
 - Respiratory compromise

[18] What is a Ganglionopathy?

Last thing to note: The 7th type of peripheral neuropathy (Sensory Neuronopathy, aka Ganglionopathy) can be characterized by a selective/predominant involvement of the dorsal root ganglion. This results in producing a pure sensory syndrome analogous to the pure motor syndrome of ALS.



Clinical features

- Proprioception is profoundly altered = sensory ataxia
- Loss of DTRs without weakness
- Asymmetrical and distal at the outset, severe can progress to symmetrical

Diagnostic Testing:

MRI of the spinal cord and surrounding areas

- Dorsal root ganglion disease localisation

Causes seen here:

Refer to box 97.10 in Rosen's 9th Edition for list of sensory neuropathies

Sensory neuropathies (Ganglionopathies):

- Herpes
 - Herpes simplex 1 and 2
 - Varicella-zoster (shingles)
- Inflammatory sensory polyganglionopathy
- Paraneoplastic
- Primary biliary cirrhosis
- Sjörger's syndrome (keratoconjunctivitis sicca)
- Toxin induced
 - Pyridoxine (vitamin B₆) overdose
 - Metals
 - Platinum (cisplatin)
 - Methyl mercury
- Vitamin E deficiency



AND JUST FOR SPACED REPETITION BEFORE YOU GO:

Refer once again to box 97.1 in Rosen’s 9th Edition for the patterns and prototypes of peripheral neuropathies

Patterns and Prototypes of Peripheral Neuropathies:

Type	Pattern Distribution	Prototypical disease modalities
1	Proximal and distal, symmetrical, sensorimotor polyneuropathy Proximal and distal Motor > sensory	GBS Symmetrical
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