Week 1

- Headache Cases #1 & 2
- Coma Case #1
- Leg Weakness Case #1
- Acute Weakness Case #1
- Diplopia Case #1
- Movement Disorders Case #1
Neurological Case Review

Headache Case #1
A 22 y.o. obese female with a 4 months history of headaches arrives to the ED with worsening, positional headaches. Physical examination reveals papilledema, affected abducens nerve and otherwise non-focal examination.
Differential Diagnosis Top Considerations

Toxic/Metabolic: Vitamin A toxicity, Acute lead toxicity, Corticosteroids, OCP’s

Infectious/Post-Infectious/Autoimmune: Aseptic Meningitis, Fungal or Mycobacterial Meningitis, Viral syndromes

Neoplastic/Paraneoplastic: Carcinomatous meningitis, Posterior fossa tumor, Choroid plexus carcinoma

Structural: Hydrocephalus (congenital or acquired),

Vascular: Dural venous sinus thrombosis, SAH, Intracranial Bleed, Hypertensive encephalopathy

Paroxysmal: Migraine or other primary headache disorder with Drusen
Neurological Case Review

Diagnostic Evaluation

- **Blood Work**
  - CMP, PT, PTT, CBC

- **Neuroimaging**
  - CT Brain without contrast (*rule out hemorrhage, mass lesion hydrocephalus*)
  - MRI with MR Venogram (*rule out venous sinus thrombosis*)

- **Lumbar Puncture**
  - Needs to be “cleared” by CT first
Normal or Abnormal?
Normal or Abnormal?
Lumbar puncture

- Clear and colorless
- Protein – 28mg/L
- Glucose - 65
- Cell Count – 2 RBC, 0 WBC Cytology: normal
- **Opening Pressure – 270mm H2O**

What is a normal Opening Pressure?
Diagnostic Evaluation: **Increased Intracranial Pressure**

- **Blood Work**
  - CMP, CBC (Platelets), PT, PTT

- **Neuroimaging**
  - CT Brain without contrast (90% sensitivity for SAH, look in ventricles and cisterns)
  - Ventricles may be normal or Slit-like (suggests elevated pressure without mass lesion)

- **Lumbar Puncture**
  - Needs to be “cleared” by CT first
  - **Elevated Opening pressure** suggests Pseudotumor cerebri

- **Other**
  - MRV to **rule out venous sinus thrombosis** as underlying cause of IIP
Idiopathic Intracranial Hypertension

Acute Medical Therapy:

- Goal is to lower intracranial pressure
  - Acetazolamide: carbonic anhydrase inhibitor, reduces CSF production
  - Topirimate: used if unable to tolerate acetazolamide due to hypotension, dizziness
  - Pain control: sometimes opiate meds used
  - Serial taps: not typically used in adults but may be used in children for pain and symptom relief (though CSF production is 0.5cc/kg/hr)
  - L/P Shunt: surgical treatment for medically refractory cases

Complications:

- Visual Field Deficit/Permanent visual loss
- Optic nerve sheath decompression and fenestration can be done to relieve pressure on optic nerve
- Assess Visual fields with formal ophtho testing initially, then on 6month-1 year basis
**Increased Intracranial Pressure**

**Clinical Pearls/Pitfalls**

- IIH or Pseudotumor Cerebri is a **diagnosis of exclusion** requiring a neuro exam showing **only signs of increased ICP**, normal neuroimaging and CSF studies.

- Obesity is a common underlying factor and **weight loss may improve symptoms significantly**.

- Abducens nerve (CN VI) palsy can occur as a non-localizing sign of raised ICP.

- **Corticosteroids not recommended** for treatment and daily use may cause IIP.

- Endocrine problems (adrenal insufficiency, Cushing’s disease, hypoparathyroidism, hypothyroidism) can cause intracranial hypertension.

- Medicines (Tetracycline, Minocycline, Bactrim, Corticosteroids, Tamoxifen, Lithium, Levothyroxine, Vitamin A) may all be associated with increased intracranial pressure.
Neurological Case Review

Headache Case #2
Neurological Case Review

Headache Case #2

A 20 y.o. female college student presents to the ED for evaluation of a severe headache. Her symptoms began 7 days previously with a sudden-onset headache that was maximal in severity at the onset, with associated nausea. She was seen at an outside ED, diagnosed with migraine headaches, and sent home on sumatriptan. Her headache eventually resolved 2 days later. On the day of admission, she was brought in unconscious by EMS after her roommate found her unconscious, lying on the floor of her bathroom.

Physical examination showed T = 98.7, P = 125, BP = 160/110, R = 18

HEENT: Nuchal rigidity with + Kernig’s and Brudzinski signs

Neuro: MS: Unarousable to deep noxious stimuli

CN: Pupils 6mm OU and equally reactive to 2mm, Fundus shows subhyaloid hemorrhages around flat optic discs, EOMI, face symmetric, reduced gag reflex

Motor: Intermittent decerebrate posturing. DTR’s brisk symmetrically, extensor plantar responses.

Sensory: Postures to painful stimuli in all 4 ext’s
Neurological Case Review

Headache Case #2

Summarize Case

A 20 y.o. female with a history of headaches 5 days prior who arrives to the ED unconscious in a coma. Physical examination reveals nuchal rigidity, coma, and an otherwise non-focal examination.
Neurological Case Review

Localization
- Central vs. Peripheral Nervous System
  - Spinal Cord, Brainstem, Cerebellum, Basal Ganglia, Subcortical Structures, Cortex

Differential Diagnosis Top Considerations

Infectious/Post-Infectious/Autoimmune:
- Acute Bacterial Meningitis, Encephalitis, ADEM

Neoplastic/Paraneoplastic:
- Posterior Fossa Tumor (with hydrocephalus)

Structural:
- Acute Hydrocephalus

Vascular:
- SAH, Stroke (Ischemic or Hemorrhagic), Hypoxic-Ischemic Injury
Neurological Case Review

Diagnostic Evaluation

- Blood Work
  - CMP with STAT Serum Glucose, PT, PTT, CBC

- Neuroimaging
  - CT Brain without contrast (rule out hemorrhage, or hydrocephalus)

- Lumbar Puncture
  - Needs to be “cleared” by CT first

- Neurophysiology
  - ? EEG for non-convulsivie status epilepticus if other testing fails to reveal cause

- Other
Your Diagnosis?
Neurological Case Review
Diagnostic Evaluation: **Subarachnoid Hemorrhage**

- **Blood Work**
  - CMP with STAT Serum **Glucose** (look for hyponatremia due to SIADH and/or Cerebral Salt Wasting), CBC (Platelets), PT, PTT

- **Neuroimaging**
  - **CT Brain without contrast** (90% sensitivity for SAH, look in ventricles and cisterns)
  - Once SAH confirmed, Non-invasive **CT Angiography** or MR angiography to identify any vascular abnormalities (such as aneurysms)
  - May need conventional cerebral angiography to define and/or treat aneurysm or AVM

- **Lumbar Puncture**
  - Needs to be “cleared” by CT first (would only do if SAH suspected but CT normal. Need to rule out traumatic tap with RBC count in tubes #1 and #4 and look for xanthochromia (“rule of 2’s”))

- **Other**
  - EKG may show arrhythmias, Q-T prolongation, S-T elevation or depression
Acute Medical Therapy:
- ABCD’s
  - Intubation for GCS < 9
  - Treat HTN: SBP 90-140 prior to aneurysm treatment, < 200 mmHg after Rx
  - Glucose between 80 and 120 mg/dl
  - Euvolemia (CVP 5-8 mmHg unless vasospasm, then CVP 8-12 mmHg)
- Temperature
- Quiet Room / Sedation
- GI (H2 blocker, stool softener, NPO)
- Vasospasm
  - Nimodipine 60 mg po q 4 hrs for 21 days
- Seizures (Phenobarbital or Lorazepam)

Complications:
- Rebleeding (uncommon in first 48 hours)
- Cerebral Vasospasm (day 4 to 14 after SAH). Increased CVP and Nimodipine
- Post-Hemorrhagic Hydrocephalus (Obstructive or Communicating)
- SIADH and/or Cerebral Salt Wasting
- Cerebral Edema
Oculomotor nerve (CN III) palsy may be due to a posterior communicating artery aneurysm; bilateral leg weakness with an ACA aneurysm; aphasia with an MCA aneurysm.

Coma without lateralizing signs may be due to SAH.

Abducens nerve (CN VI) palsy may be due to raised ICP.

Sentinel bleeds may cause “Thunderclap Headache” (worst headache ever and of maximal intensity at onset).

Nuchal rigidity may be due to subarachnoid blood or meningitis.

Lumbar puncture is only necessary if SAH is suspected but CT is normal.

Xanthochromia “rule of two’s”: First presents 2 hours after SAH, peaks at 2 days, and resolves by 2 weeks.

Hydrocephalus is a later finding following subarachnoid hemorrhage.
Neurological Case Review

Coma Case #1
Neurological Case Review

Coma Case #1

A 57 y.o. right handed female is found comatose in bed by her son. Her past medical history is remarkable only for some mild hypertension and metabolic syndrome. She is divorced and was recently caring for her father prior to his passing 3 weeks earlier.

She is unresponsive as she arrives in the ED.

Physical Exam: T= 96.5, BP = 110/50, P = 56, R = 12

HEENT: No signs of trauma, neck is supple

Neurological Exam:

MS: Patient is unarousable to deep noxious stimulation. GCS score = 4/15

CN: Pupils 1mm OU but still slightly reactive to light. No EOM movements to Doll’s maneuver, corneal blink reflex absent, absent gag reflex

Motor: Demonstrates bilateral flexion/adduction posturing of the arms and extension of the legs to deep noxious stimulation. DTR’s are absent, plantar responses are non-reactive

Sensory: Decerebrate posturing to painful stimuli applied to either the right or left leg
Neurological Case Review

Coma Case #1

Decorticate posturing

- Flexion
- Plantar flexion
- Extension
- Flexion
- Adduction

Decerebrate posturing

- Flexion
- Pronation
- Adduction
- Extension
A 57 y.o. female brought in comatose with small, reactive pupils, absent EOM's, corneal blink, and gag reflexes, and decerebrate posturing.
Neurological Case Review

Localization
- **Central** vs. Peripheral Nervous System
  - Spinal Cord, Brainstem, Cerebellum, Basal Ganglia, Subcortical Structures, Cortex

Differential Diagnosis
Diagnostic Evaluation and Management
Neurological Case Review

Localization
- Central vs. Peripheral Nervous System
  - Spinal Cord, Brainstem, Cerebellum, Basal Ganglia, Subcortical Structures, Cortex

Differential Diagnosis
- Toxic/Metabolic:
- Infectious/Post-Infectious/Autoimmune:
- Neoplastic/Paraneoplastic:
- Structural:
- Trauma:
- Vascular:
- Paroxysmal:
- Degenerative/Neurogenetic:
- Psychiatric:

Diagnostic Evaluation and Management
Neurological Case Review

Differential Diagnosis Top Considerations

- **Toxic/Metabolic**
  - Carbon Monoxide, chemotherapy, radiation, EtOH, sedative/hypnotic medications and drugs, heavy metals, hyper/hypoglycemia, DKA, hyponatremia, IEM’s, renal failure, liver failure, hypercapnea, hypoxia, porphyria, hypothyroidism

- **Structural**
  - Herniation syndromes, hydrocephalus, cerebral edema

- **Paroxysmal**
  - Seizures, non-convulsive status epilepticus, post-ictal state

- **Vascular**
  - Ischemic or hemorrhagic stroke, SAH, venous thrombosis, hypoxic-ischemia, hypertensive encephalopathy, cerebral hypoperfusion
Neurological Case Review

Diagnostic Evaluation

- **Blood Work**
  - CMP (includes glucose, electrolytes, renal and liver function)
  - Urine toxicology screen
  - Possible expanded serum tox screen to include acetaminophen

- **Neuroimaging**
  - Urgent non-contrast head CT

- **Lumbar Puncture**
  - Only if cleared from CT and other evaluations negative

- **Neurophysiology**
  - EEG to rule out non-convulsive status epilepticus if other evaluations negative

- **Other**
  - EKG to evaluate for arrhythmias caused by drug overdose (TCA’s prolonging QRS interval)
Always start with the A B C’s.

- Patients with a GCS score of 8 or less need endotracheal intubation for airway protection
- Administer O2 and maintain normocapnea unless increased ICP is suspected
- Administer IV Fluids
- Monitor Cardio/Respiratory status

Unless a specific cause can be immediately identified, consider administering nalaxone, thiamine and glucose (in that order) to look for any clinical response.

If non-convulsive status epilepticus is suspected, order STAT EEG. If not available, consider administering 2-4 mg IV lorazepam.

For ongoing coma, transfer to a medical ICU is warranted after diagnostic studies are obtained.
Neurological Case Review

Results of Evaluation in our patient

CBC:  WBC = 13 (56%P, 40%L, 4%M), H/H = 12/36, Plt = 275K

CMP:  Na+ = 135, Cl- = 112, K+ = 4.5, CO2 = 24, BUN = 15, Cr = 1.2, Glucose = 180
    Anion Gap = 9, AST = 35, ALT = 37, Albumin = 4, T. Pro = 7, Alk Po4 = 110,
    Ca++ = 9.2

CT Brain:

(normal or abnormal?)

LP:  W = 4 (78%L, 4M), R = 120 (tube 1), R = 92 (tube 4), Glc = 92, Pro = 25, G/S = neg,

EEG:  Diffuse background slowing with poor regional differentiation.  **No epileptiform discharges.**
“What is missing?”
Urine toxicology screen + for Barbiturates

The patient’s son found an empty bottle of phenobarbital tablets and a suicide note on the patient’s bathroom counter.
Pearls and Pitfalls (So much yellow!)

Coma without Focality

- **Symmetric** pupils that are equally reactive (whether they are small, mid-sized, or large) usually indicate a **toxic** or **metabolic** cause of the coma, whereas asymmetric or fixed pupils suggest a structural cause.

- **Absent brainstem reflexes** can be caused by sedative/hypnotic overdose, severe hypothermia, neuromuscular blockade, and severe hypoglycemia. As such they **do not always indicate brainstem herniation or infarction**. In this patient, the presence of a normal pupillary light response speaks against brainstem herniation.

- The EEG will be diffusely slow in most cases of coma and is not specific. It can rule out non-convulsive status epilepticus. The presence of overriding beta (fast activity) may indicate drug overdose.

- **Glucose given to malnourished patients without concomitant thiamine** can precipitate Wernicke’s encephalopathy.

- **Hypoglycemia** can present with coma, but also with seizures or **focal neurological deficits**. Check that glucose!
Neurological Case Review

Leg Weakness Case #1
Neurological Case Review

**Leg Weakness Case #1**

A 24 y.o. female had been in her usual state of good health when 2 weeks PTA she c/o URI symptoms associated with a severe holocephalic headache and muscle aches. One day PTA, she noted some tingling in her feet and her legs felt “rubbery”. She also c/o an ache between her shoulder blades that was bothersome but did not require any pain medication.

On the day of admission, she awoke to find her legs had become weak to the point where she was unable to stand or ambulate and she was unable to get out of bed. She described her legs feeling as though “they were made out of wood” and the interscapular pain had increased in intensity.
Leg Weakness Case #1

General Examination:
PE:  T = 98.7, P = 86, BP = 132/75, R = 18, O2 sat = 96% on RA
HEENT:  No nuchal rigidity. No signs of trauma. Mild pharyngeal erythema.
Lungs:  CTA, no respiratory distress with good air movement.
Abdomen:  Soft, Non-tender. Upon pressing the lower abdomen, the patient is incontinent of a small amount of urine.
Musculoskeletal:  No joint swelling or tenderness. Mild percussion tenderness found over mid-thoracic spine.
G/U:  Flaccid rectal tone
Neurological Case Review  
Leg Weakness Case #1

Neurological Examination:
MS: Alert and Oriented x name, date, location. Speech is fluent and articulate.
CN: PEERLA, EOMI, no papilledema, Face symmetric, Palate/Tongue midline.
Dorsiflexion/Plantarflexion absent. Decreased flaccid tone in legs. DTR’s 2+ bilaterally at biceps and triceps. Absent DTR’s at patella and ankle jerks. Plantar responses unelicitable.
Sensory: Absent pinprick sensation from umbilicus down. Absent vibration/position sense in legs, normal in arms.
Coordination: No dysmetria or tremor in arms (unable to assess legs)
Gait: Unable to assess.
Neurological Case Review
Leg Weakness Case #1

Summarize the Case

A 24 y.o. woman with a 2 day history of progressive weakness and numbness of her legs. On examination, she shows flaccid leg weakness with absent DTR’s, decreased rectal tone, urinary incontinence and a sensory level.
Neurological Case Review

Localization

- Central vs. Peripheral Nervous System?

What features help to localize this patient?

Differential Diagnosis
Diagnostic Evaluation and Management
Neurological Case Review

Localization

- Central vs. Peripheral Nervous System
- Spinal Cord, Brainstem, Cerebellum, Basal Ganglia, Subcortical Structures, Cortex

What level?

Differential Diagnosis
Diagnostic Evaluation and Management
Neurological Case Review

Localization
- **Central** vs. Peripheral Nervous System
  - Spinal Cord, Brainstem, Cerebellum, Basal Ganglia, Subcortical Structures, Cortex
  - T-8 (for T-10 sensory level): Lissauer’s Tract and Substantia Gelatinosa

Why is this presentation inconsistent with Guillan-Barre Syndrome???

Umbilical sensory level: T10
Hip flexion: L1-2
Rectal tone: S2-4
So then why T8? because sensory abnormality was pinprick!
Neurological Case Review

**Why is this presentation inconsistent with Guillan-Barre Syndrome??**

Has ascending paralysis with flaccid weak legs and absent lower extremity DTR’s. However, also has evidence of bowel and bladder dysfunction as well as a T-10 sensory level. All of this put together represents acute myelopathy, **not** Guillain-Barre syndrome!
Why she doesn’t have brisk DTR’s even though has Upper Motor Neuron syndrome?

Brisk DTR’s may take days to weeks to fully evolve.
Neurological Case Review

**Differential Dx Top Considerations**

*** Acute Myelopathy should be considered caused by a compressive lesion to the cord until proven otherwise!!!!!

**Neoplastic:** Epidural Mets

**Structural:** Spondylosis (degenerative arthritis of vertebral joints), Spinal Stenosis, Disc Herniation

**Trauma:** Spondylolisthesis, Epidural Hematoma

**Vascular:** Spinal AVM or Dural AV Fistula

**Infectious:** Pott’s Disease, Epidural Abscess
Neurological Case Review

What is your first step in diagnosis?

- Blood Work
- **Neuroimaging:** Your patient needs an emergent MRI of the Spine (or if not available, an emergent myelogram)
- Lumbar Puncture
- Neurophysiology
- Other
Neurological Case Review

What type of imaging?
Describe the abnormality.

What is the most likely diagnosis?
Answer: Acute Transverse Myelitis
Neurological Case Review

What is your next step in diagnosis?

- Blood Work
- Neuroimaging
- Lumbar Puncture
- Neurophysiology
- Other
Neurological Case Review

What is your next step in diagnosis?

- **Blood Work:** NMO antibodies (aquaporin 4 Ab’s), paired serum for MS profile.
- **Neuroimaging:** Brain MRI with and without contrast to assess risk for MS
- **Lumbar Puncture:** Routine studies (Cell Count, Protein Glucose, G/S, Culture), MS Profile (IgG Index, IgG Synthesis Rate, Oligoclonal Bands, Myelin Basic Protein), Infectious Workup as indicated (VDRL, CMV, EBV, HSV, TB, HTLV-1 and 2, etc)
- **Neurophysiology:** Can do evoked potentials (SSEP, BAER, VEP) for baseline as well as to look for subclinical demyelination (lesions separated in space)
- **Other**
Acute Transverse Myelitis

ATM is generally considered to be caused by an autoimmune attack of the spinal cord.

An infectious myelitis may present the same way and should be looked for within the CSF.

Autoimmune ATM may be due to:

1. **Clinically Isolated Syndrome**

2. **Multiple Sclerosis** (tends to affect just part of the cord, often peripherally)

3. **Neuromyelitis Optica** (Longitudinally extensive (>4 spinal segments) and tends to involve the entire cord segmentally, often with central necrosis)
Acute Transverse Myelitis

Since she has mostly myelitis symptoms, NMO antibodies should be looked for in the serum.

Treatment for ATM due to MS generally consists of high dose intravenous Solumedrol followed by the use of Disease Modifying Treatment for MS. Treatment of ATM due to NMO is usually done with Plasmapheresis.

For CIS presenting as ATM, the progression to MS is relatively low if the brain MRI is normal, and relatively high if there are demyelinating lesions.

The predictive value for MS with abnormalities on the MS Profile (elevated IgG Index or synthesis rate, the presence of oligoclonal bands, elevated myelin basic protein) is not as high as with “silent” brain MRI lesions.
Acute Transverse Myelitis

Pearls and Pitfalls / Lots of Yellow!

- Progressive leg weakness, with absent DTR’s and hypotonia may be seen with either GBS or ATM. If you add in a defined sensory level and bowel/bladder dysfunction, ATM is your diagnosis not GBS!!!

- Acute myelopathy should be considered due to a mass lesion compressing the spinal cord requiring emergent neurosurgical laminectomy and cord decompression until proven otherwise (by way of emergent spine MRI).

- Acute myelopathy patients may be insensate and unable to void putting them at risk for hydronephrosis. Bladder catheterization should be performed urgently.

- The sensory level reflects the distal end of a spinal cord lesion two dermatomal levels up due to pain and temperature neurons traveling up or down two segments within Lissauer’s tract before synapsing on dorsal grey matter.

- In lesions involving half the spinal cord, one will see loss of pain and temperature sensation contralateral to the side of the lesion (ascending spinothalamic tract). In addition, motor weakness (descending corticospinal tract) and loss of vibration sense (ascending fasiculus gracilis (legs) and fasiculus cuneatus (arms) occur ipsilateral to the side of the lesion.
Neurological Case Review

Acute Weakness Case #1
A 35 y.o. male presents to the office with a 2 weeks history of difficulty walking and back pain. He complains that he began stumbling a few days ago and his gait has worsened. He is now falling down and having difficulty getting up from the ground. He also complains of numbness of his feet. PMHx. URI two weeks ago. Family history is noncontributory.

PE: T = 98.7, BP = 128/72, P = 80, R = 18

General examination is unremarkable except for bruising on the legs bilaterally.
Neurological Case Review

Neuro Exam:
MS: Speech is fluent
CN: VA = 20/20 OU, Pupils are equal and react from 4mm to 2 mm bilaterally. Full EOMs. Mild facial weakness is present bilaterally, Hearing intact, palate/tongue midline.
Motor: LE: (4/5) with hip flexion, knee flexion and knee extension, tibialis anterior (dorsiflexion) and gastrocnemius (plantarflexion) 4-/5. UE: 4+ deltoid, biceps triceps, 4/5 interossei (finger abduction), APB (thumb abduction). DTR’s absent in all extremities.
Sensory: Vibratory and position sense decreased in all 4 ext’s.
Pinprick: LE: decreased up to mid calf, normal in abdomen and thorax UE: decreased over the hand to the wrist and normal in the forearm and upper arm.
Coordination: No ataxia or tremor.
Gait: Mild Foot drop bilaterally with Trendlenburg gait.
Neurological Case Review

Acute weakness#1

Summarize the Case

A 35 y.o. male with a 2 weeks history of difficulty walking. On examination, the patient has weakness in his face and extremities, distal greater than proximal along with areflexia and decreased distal pain/temp and vibration sensation.
Neurological Case Review

Localization

- Central vs. Peripheral Nervous System?

Differential Diagnosis

Diagnostic Evaluation and Management
Neurological Case Review

Localization

- Central vs. Peripheral Nervous System

Differential Diagnosis
Diagnostic Evaluation and Management
Neurological Case Review

Localization
- Central vs. Peripheral Nervous System
- Anterior horn cell, peripheral nerves, NMJ, muscle?

Differential Diagnosis
Diagnostic Evaluation and Management
Neurological Case Review

Localization

- Central vs. **Peripheral Nervous System**
- Anterior horn cell, *peripheral nerves*, NMJ, muscle

Why is the lesion not in the spinal cord???
Localization

- Central vs. Peripheral Nervous System
  - Anterior horn cell, peripheral nerves, NMJ, muscle

Why is the lesion not in the spinal cord???

No sensory level is apparent on examination. Sensory examination is suggestive of a neuropathic pattern with distal > proximal involvement (stocking-glove distribution).

No bladder and bowel involvement. Although bladder and bowel involvement can at times be present in GBS, it is highly unusual and cord involvement must be ruled out.
Localization

- Central vs. Peripheral Nervous System
  - Anterior horn cell, peripheral nerves, NMJ, muscle

**Why is the lesion not in the NMJ, anterior horn cell or muscle?**

Sensory involvement! Diseases in the NMJ, muscle and anterior horn cell do **not** have sensory involvement.

Another clue are the reflexes. In the classic NMJ disease of autoimmune myasthenia gravis, the reflexes are typically **preserved**. With muscle involvement, the reflexes are typically **decreased** with increased muscle pathology.
Neurological Case Review

Differential Diagnosis Top Considerations

Toxic/Metabolic: Acute Arsensic poisoning, B1 deficiency, N-hexane toxicity, Tick paralysis

Infectious/Post-Infectious/Autoimmune: GBS, CIDP, Myasthenia Gravis, Miller Fisher Variant of GBS, Critical Illness polyneuropathy

Neoplastic/Paraneoplastic: Acute Polymyositis.
Further Consideration of our Differential

Toxic/Metabolic:
- **Acute Arsenic poisoning** - Suicidal, Homicidal, Occupational, Environmental including mining, ground water contamination, copper and lead smelting also with GI symptoms
- **B1 deficiency** - burning feet, alcoholic or malabsorption
- **N-Hexane toxicity** - glue or gasoline sniffing to get high - usually in young males

Neoplastic/Paraneoplastic:
- **Acute Polymyositis** - no sensory involvement and CK should be very elevated.

Infectious/Post-Infectious/Autoimmune:
- **GBS** - looks promising - should be at the top of our list
- **CIDP** - not chronic enough (over 8 weeks to reach nadir of weakness)
- **Tick paralysis** – wooded area few days prior to symptoms, look for tics in hair
- **Myasthenia Gravis** – would have exertional related course and abnormal EOMs and no sensory involvement
- **Miller Fisher Variant of GBS** – would have abnormal EOMs and ataxia and areflexia
Lumbar Puncture - typical finding in LP in patients with GBS is an elevated cerebrospinal fluid (CSF) protein with a normal white blood cell count. This finding is called *albuminocytologic dissociation*, and is present in up to 66 percent of patients with GBS at one week after onset of symptoms.
Neurological Case Review

Diagnostic Evaluation

- **Neurophysiology** - electromyography and nerve conduction studies show evidence of an acute polyneuropathy with predominantly demyelinating features (slowed nerve conduction velocities and conduction block) in acute inflammatory demyelinating polyradiculoneuropathy (AIDP) (most common variant of GBS in North America).
Clinical features of Guillain-Barré syndrome

- Progressive, fairly symmetric muscle weakness
- Accompanied by absent or depressed deep tendon reflexes
- Weakness can vary from mild difficulty with walking to nearly complete paralysis of all extremity, facial, respiratory, and bulbar muscles requiring ventilation
- Severe respiratory muscle weakness necessitating ventilatory support develops in 10 to 30 percent!
Clinical features of Guillain-Barré syndrome

- GBS usually progresses over a period of about two weeks.
- By four weeks after the initial symptoms, 90 percent of GBS patients have reached the nadir of the disease.
- Disease progression for more than eight weeks is consistent with the diagnosis of chronic inflammatory demyelinating polyradiculoneuropathy (CIDP).
Up 30 percent of patients develop neuromuscular respiratory failure requiring mechanical ventilation.

Vigilance is essential when caring for a patient with GBS, since deterioration due to progression of muscle weakness can occur rapidly.

Frequent measurement of vital capacity and negative inspiratory force (NIF) should be instituted initially in all patients.

Bulbar dysfunction with swallowing problems and inability to clear secretions may add to the need for ventilator support.

Succinylcholine should be avoided when invasive airway management becomes necessary.
Autonomic dysfunction is a well-recognized feature of GBS and is a significant source of mortality.

Dysautonomia occurs in 70 percent of patients and manifests as symptoms that include tachycardia (the most common), urinary retention, hypertension alternating with hypotension, orthostatic hypotension, bradycardia, other arrhythmias, ileus, and loss of sweating.

Severe autonomic disturbances occur in about 20 percent of patients, mostly (but not always) in patients who develop severe weakness and respiratory failure.

Close monitoring of blood pressure, fluid status, and cardiac rhythm is essential to the management of patients with GBS.
Two main modalities of therapy include:

- Plasma exchange
- Administration of intravenous immune globulin (IVIg)

(Both have been shown to have equal efficacy in large randomized trial)
Guillain-Barré syndrome
Pain Control

- **Neuropathic pain** occurs in about 40 to 50 percent of patients during the course of **GBS** and often requires treatment.

- **Gabapentin** or carbamazepine may be used for intensive care unit pain control during the acute phase of **GBS**

- For the **long-term** management of neuropathic pain, **tricyclic antidepressants**, tramadol, gabapentin, carbamazepine, or pregabalin may be useful.
Guillain-Barré syndrome
Pearls and Pitfalls

- Perform a detailed sensory examination to decide what type of distribution the sensory loss is occurring. Is there a sensory level? If so, this is a spinal cord process and not a peripheral neuropathy.
- Is there bladder and bowel involvement? If so, must make sure that a spinal process has been ruled out.
- If patient has significant weakness, check NIF, ABG and pulse ox to make sure patient is not in need of respiratory support.
- A sensory level, marked persistent asymmetry of weakness, severe and persistent bowel and bladder dysfunction, or more than 50 WBC’s in the CSF make the diagnosis of GBS doubtful.
Neurological Case Review

Diplopia Case #1
Neurological Case Review
Diplopia Case #1

A 28 y.o. woman presents to the office with a 6 week history of intermittent double vision. The double vision is predominantly horizontal and varies throughout the day, generally being more noticeable in the evening. She also reports episodes of slurred speech and occasional drooping of her eyelids over this time. PMHx is significant for thyroid surgery 6 months previously for “an overactive thyroid” and she is currently taking levothyroxine 150mcg/day. Family history is noncontributory.

PE: T = 98.7, BP = 128/72, P = 80, R = 18

General examination is notable only for a healed surgical scar over her thyroid gland without underlying thyroid enlargement.
Neurological Case Review
Diplopia Case #1

Neuro Exam: MS: Speech is slightly nasal but otherwise fluent
CN: VA = 20/20 OU, Pupils are equal and react from 4mm to 2 mm bilaterally. Ptosis is present bilaterally. Horizontal eye movements are limited to a few mm’s in the right eye, the left eye can adduct fully but has a 50% reduction in abduction. Both eyes have full vertical gaze but there is fatigue on sustained upgaze after 30 seconds. Facial strength, jaw opening, neck flexion/extension are full. Hearing intact, palate/tongue midline.

Motor: Slight proximal weakness (4+/5) with arm abduction and hip flexion that worsens with repetitive sequential testing to 4-/5. Normal strength distally all 4 ext. DTR’s 2+ and symmetric.

Sensory: Normal light touch, vibratory and position sense all 4 ext’s.

Coordination: No ataxia or tremor.

Gait: Normal except for some mild difficulty arising with repetitive sequential squatting.
Neurological Case Review
Diplopia Case #1
Summarize the Case
A 28 y.o. woman with a 6 week history of horizontal diplopia who, on examination, shows bilateral ptosis, restricted eye movements and proximal mild fatigable weakness.
Neurological Case Review

Localization

- Central vs. Peripheral Nervous System?
Neurological Case Review

Localization

- Central vs. Peripheral Nervous System

Differential Diagnosis

Diagnostic Evaluation and Management
Neurological Case Review

Localization
 Central vs. Peripheral Nervous System
 Anterior horn cell, peripheral nerves, NMJ, muscle?

Differential Diagnosis
Diagnostic Evaluation and Management
Neurological Case Review

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Why is the lesion not in the brainstem???
Localization

- Central vs. Peripheral Nervous System
- Anterior horn cell, peripheral nerves, NMJ, muscle

Why is the lesion not in the brainstem???

Ptosis can be localized to disorders of the Oculomotor nerve (CN III), the sympathetic nervous system innervation of the face and head (as part of Horner’s syndrome), or due to weakness of the facial muscles [not Facial nerve (CN VII) dysfunction however as this results in widened palpebral fissures due to weakness of the orbicularis oculi muscle].

Restricted movements of the EOM’s can be due to dysfunction of the Oculomotor nerve (CN III), the Trochlear nerve (CN IV), or the Abducent nerve (CN VI). Abnormal EOM’s can also be due to weakness of the extraocular muscles themselves or due to masses impinging on the muscles within the orbit itself.
Neurological Case Review

Localization

- Central vs. Peripheral Nervous System
  - Anterior horn cell, peripheral nerves, NMJ, muscle

**Why is the lesion not in the brainstem???

This patient had normal pupil function making CN III palsy less likely and ruling out Horner’s syndrome. One could argue that the right eye has a “one and a half syndrome” (impaired abduction due to right PPRF (lateral gaze center) or right Abducens nucleus/nerve dysfunction and a Medial Longitudinal Fasciculus lesion. You would then need to give the left eye a separate PPRF or Abducens nucleus/nerve lesion though the left eye can still adduct fully which is inconsistent with the MLF being affected!

Neuromuscular junction disease processes frequently affect the extraocular muscles and cause ptosis sparing the pupillary function (so-called “external ophthalmoplegia”). NMJ disorders may also affect bulbar muscles and respiratory muscles when severe.
Neurological Case Review

Right Eye
One and a half syndrome
Neurological Case Review

Differential Diagnosis Top Considerations

Toxic/Metabolic: Wernicke’s Encephalopathy, Botulism

Infectious/Post-Infectious/Autoimmune: Myasthenia Gravis, Miller Fischer Variant GBS, Graves Disease, Multiple Sclerosis (MLF)

Neoplastic/Paraneoplastic: Lambert-Eaton syndrome

Structural: Horner’s Syndrome, Oculomotor Nerve Palsy, Cavernous Sinus thrombosis

Vascular: Brainstem stroke

Degenerative/Neurogenetic: Kearns-Sayer Syndrome (CPEO, Mitochondrial Disease)

Why is brainstem stroke unlikely?
Neurological Case Review

Diagnostic Evaluation

**Blood Work:** Acetylcholine Receptor Antibodies (binding, blocking, modulating), T4, TSH, anti-TPO and anti-thyroglobulin antibodies, ANA, Rh Factor as patients with MG are at higher risk for other autoimmune disorders. Muscle-Specific Tyrosine Kinase (MuSK-MG) antibodies may be found in 50% or seronegative patients. It predicts ocular and bulbar involvement, frequent attacks and the need for plasmapharesis for crisis.

- Neuroimaging: No
- Lumbar Puncture: No

**Neurophysiology:** Repetitive Stimulation Nerve Conduction (look for >15% decrement of CMAP amplitude at 3 HZ). Also Single Fibre EMG (look for jitter when stimulating two nearby muscles from the same motor unit).
Neurological Case Review
Diagnostic Evaluation

Other:

Edrophonium Challenge Test
- 2mg Edrophonium given as a test dose then saline placebo or 8mg intravenous Edrophonium given and patient is observed for transient improvement in weak muscles

Ice Pack Test
- If the patient has ptosis, apply an ice pack over the affected eye(s) for 10 minutes and look for transient improvement of ptosis.

Imaging of the Thymus
- Malignant thymoma is found in up to 15% of patients with MG. 66% show evidence of thymic hyperplasia on pathology.
Myasthenia Gravis
Pearls and Pitfalls (Lots of Yellow!)

- Treatment of **MG** is with a long-acting oral **Cholinesterase inhibitor** (Mestinon) and immune suppression (usually glucocorticosteroids, with or without other immunospressive agents).
- **Glucocorticosteroids** can hamper neuromuscular transmission and one may see worsening of weakness until the immune system suppression kicks in.
- **Ocular-only MG** is often seronegative for AChR antibodies.
- **Myasthenic crisis** can be provoked by infection, stress, or a variety of medications (including macrolide and tetracycline antibiotics, steroids, beta blockers, penicillamine, depolarizing muscle relaxants, etc).
- Cholinergic crisis can also present with worsening of strength by amplifying neuromuscular blockade. As such, Cholinesterase inhibitors should **never** be used to try and get somebody out of a myasthenic crisis.
- **Myasthenic crisis** can be treated with pulse **Solumedrol, IVIg, or Plasma Exchange**.
Neurological Case Review

Movement Disorder Case #1
Neurological Case Review
Movement Disorder Case #1

A 62yo right-handed man with 3 years of gradually worsening tremor. His family first noticed that he didn’t swing his left arm when he walked and his left hand would occasionally shake. About 6 months later, he started to notice his right hand starting to shake. His writing has become smaller. His wife often asks him to repeat himself. He has noticed some difficulties with cutting food, fastening buttons, and dragging his left leg when he walks. His smell is not as sharp as years past. He will occasionally scream out or thrash about in his sleep. He has experienced nausea in the past and took a medication for it, the name of which he does not recall.
MSE: Awake, alert, attentive, and Oriented x name, date, location, and events. Speech is fluent with normal naming, repetition, and comprehension, though somewhat hypophonic. No neglect noted. Recent and remote memory are intact. Affect is constricted but appropriate. No evidence of responding to internal stimuli.

CN: PEERLA, EOMI, Face symmetric, Palate/Tongue midline.

Motor: Mildly increased rigid tone, L>R. Normal strength. Intermittent moderate tremor noted with the hands at rest, L>R. Mild difficulty with finger taps and toe taps, L>R. Decreased facial expression and blink rate.

Reflexes: DTRs 2+ and symmetrical. Plantar responses flexor.

Sensory: Normal.

Coordination: No dysmetria with FTN, FNF, HTS. Slow RAM but no DDK.

Gait: Able to get up on his own. Mildly forward flexed posture. Narrowed stance. Stride length is shortened. Decreased armswing bilaterally, L>R. Tremor noted in the hands with walking. Took 3-4 steps when pulled backwards.
Neurological Case Review

Movement Disorder Case

Summarize Case

A 62yo man with 3 years of slowly worsening tremor and walking changes who displays resting tremor, rigidity, difficulties with fine motor movements and gait changes on exam.

Localization?

Basal Ganglia
Localization

- Central vs. Peripheral Nervous System
  - Spinal Cord, Brainstem, Cerebellum, Basal Ganglia, Subcortical Structures, Cortex

Differential Diagnosis Top Considerations

Toxic/Metabolic:
- Hyperthyroidism, Renal or liver failure, Heavy metal toxicity, Medications (antipsychotics/antiemetics, lithium)

Vascular:
- Lacunar subcortical infarcts

Structural:
- Acute stroke, tumor

Degenerative/Neurogenetic:
- Essential tremor, Parkinson’s disease
- Parkinson plus syndromes
  - Multiple system atrophy, Progressive supranuclear palsy, Dementia with Lewy Bodies, Corticobasal degeneration
Diagnostic Evaluation: **Parkinson’s disease**

- **Blood Work**
  - CMP (rule out renal and liver failure as causes of tremor), thyroid studies, heavy metal screen (especially manganese intoxication can affect the basal ganglia and cause parkinsonism)

- **Neuroimaging**
  - MRI Brain to look for structural changes (strokes or tumor) in the basal ganglia (acute strokes and tumors in the basal ganglia or midbrain can produce parkinsonism – tumors tend to be subacute)
Diagnostic Evaluation: **Parkinson’s disease**

- **Neuroimaging**
  - Also look for brainstem (PSP), cerebellar (possible MSA), or cortical atrophy (DLB or CBD)
  
  - MRI tends to be normal in Parkinson’s disease

- **Other**
  - Better history of medications taken in the past (antiemetics such as metoclopramide, promethazine, and prochlorperazine block dopamine)

  - **Antipsychotics** are a common cause of medication-induced parkinsonism
Management of Parkinson’s disease

Parkinson’s disease involves degeneration of dopaminergic neurons in the substantia nigra.

**Levodopa-Carbidopa (Sinemet)**

- **Levodopa can cross blood brain barrier; Dopamine cannot**

- **DOPA-decarboxylase** breaks down levodopa into dopamine in the gut and at the blood brain barrier.

- **Carbidopa inhibits DOPA-decarboxylase** peripherally, which allows more non-metabolized levodopa to cross BBB. Carbidopa itself does not cross BBB so centrally acting DOPA-decarboxylase is able to convert levodopa into Dopamine for the neurons within the substantia nigra.
Management of Parkinson’s disease

Levodopa-Carbidopa (Sinemet)

- Levodopa improves all clinical features of Parkinson’s disease, especially the bradykinesia.

- Controversy exists about when to start medication because the effects become less predictable over time.

- Treatment may be deferred and then used in conjunction with dopamine agonists.
Dopamine Agonists

- Pramipexole and Ropinirole

- Slightly less effective than levodopa in relieving the symptoms of parkinsonism but less likely to cause dyskinesias

- First drug of choice in young or less severe cases of Parkinson’s to leave the therapeutic response of levodopa for later in the disease
Management of Parkinson’s disease

Catechol-O-Methyltransferase (COMT) Inhibitors

• Tolcapone, Entacapone, Stalevo

• Adjunctive therapy to Levodopa

• Decreases peripheral conversion of L-Dopa into 3-O-methyldopa (by Catechol-O-Methyltransferase) thus reducing dose requirements of Levodopa/Carbidopa

• Leads to more sustained plasma levels of levodopa

• Stalevo: combination of Levodopa/Carbidopa/Entacapone
Management of Parkinson’s disease

- **Rasagiline, Selegiline (MAO-B Inhibitors)**
  - Inhibits breakdown of dopamine (MAO-B Inhibitor)
  - Enhances antiparkinsonian effects of Levodopa
  - May delay appearance of motor signs and disability

- **Amantadine**
  - Mild parkinsonism
  - Mode of action unclear
  - Improves all clinical features
  - Benefits short-lived, most patients fail to respond
  - Useful in reducing dyskinesias caused by levodopa
Management of Parkinson’s disease

Anticholinergics

• **Trihexyphenidyl** (Artane)

• Reduce reuptake of Dopamine by striatal neurons

• Helps to restore the balance of acetylcholine and dopamine within the basal ganglia

• **Avoid in elderly** due to confusion and urinary retention.
Neurological Case Review

Parkinson’s disease

Clinical Pearls/Pitfalls

- Parkinson’s disease is a clinical diagnosis – symmetry, early dementia, profound autonomic symptoms, cortical signs, poor response to levodopa are red flags
  - If dementia comes at the same time as motor symptoms or soon after, consider DLB
  - If prominent autonomic symptoms at onset, consider MSA
  - If early falls, decreased upgaze, and midline rigidity, consider PSP
  - If highly asymmetric with myoclonus, apraxia, alien limb, consider CBD
- Decreased sense of smell and REM sleep behavior disorder (acting out dreams) are often associated with α-synuclein diseases (PD, MSA, DLB)
  - May precede motor symptoms by up to a decade
- Resting tremor is most often seen in PD but not all PD patients have tremor.
- Patients on dopamine agonists must be monitored for impulse control disorders (gambling, eating, increased libido, etc.)
End of Week 1