Peripheral Nervous System Disease

Myelopathy (refer)

Radiculopathy (refer)

Plexopathy
- Brachial Plexopathy aka Parsonage-Turner Syndrome: acute shoulder pain followed by paralysis/atrophy of shoulder muscles, occurs with autoimmune dz, following illness/immunization/stressor (mechanism unknown) or following trauma
- Lumbosacral Plexopathy aka Bruns-Garland Syndrome: similar to brachial plexopathy, occurs with DM, autoimmune dz or following trauma

Polyneuropathy
- General
  - Classically multiple symmetric nerves but if asymmetric multiple nerves then called “Mononeuritis Multiplex” and 2/2 systemic illness esp vasculitis, sarcoidosis, DM, RA, CTD, Lyme
  - Called “peripheral neuropathy” if symmetric peripheral involvement
  - Classification: Axonal Degeneration (painful paresthesias then weakness) vs Demyelinating (just weakness) vs Mixed w/ is determined by NCS/EMG/Nerve-Bx
  - NB in 1/3 of pts a cause is not found!!!
  - Unique autonomic neuropathies w/ impotence, orthostatic hypotension, gastroparesis (DM, Amyloidosis, GBS, Vincristine, Porphyria, HIV, Idiopathic Pandyautonomia)

<table>
<thead>
<tr>
<th>Axonal Degeneration</th>
<th>Demyelination</th>
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<tbody>
<tr>
<td>Acute</td>
<td></td>
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<tr>
<td>Toxins: Thallium, Lead, Organophosphates, Arsenic</td>
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<tr>
<td>Meds: Chemo, Abx</td>
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<tr>
<td>Other: Porphyria, Vasculitis, Critical Illness Polyneuropathy/Myopathy aka CIPN/M (refer)</td>
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<tr>
<td>Demyelination</td>
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<tr>
<td>Infection: Botulism, HIV, Lyme, CMV, West Nile, Rabies</td>
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<tr>
<td>Other: GBS, Porphyria, MG, PM</td>
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<th>Chronic</th>
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<tr>
<td>Metabolic: 1° DM (a unique form called “diabetic lumbosacral polyradiculopathy” aka “diabetic amyotrophy” w/ severe thigh pain followed by LE weakness), uremia, cirrhosis, hypoth, thiamine deficiency (ETOH use), VitB6 deficiency (isoniazid used), folate deficiency (phenytoin use)</td>
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<tr>
<td>Toxins: 1° ETOH, lead, arsenic</td>
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<tr>
<td>Meds: INH, sulfas, metronidazole, vincristine, cisplatin, phenytoin, TCA, infection: HIV, syphilis, leprosy, Lyme, acute hepatitis</td>
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<tr>
<td>Other: sarcoid, malignancy, amyloidosis</td>
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<tr>
<td>Infection:</td>
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<td>Toxins:</td>
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<td>Meds:</td>
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<td>Other:</td>
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Guillain-Barre Syndrome (GBS) aka Acute Inflammatory Demyelinating Polyneuropathy (AIDP)
- History and Epidemiology
  - George Charles Guillain and Jean-Alexandre Barré were co-authors of the classic paper published in 1916
came to public attention when it struck a number of people who received the 1976 Swine Flu vaccine
  - no epidemiologic RFs it can strike anyone but seen slightly more common in men and usually bimodal distribution (20s and 60s)
  - incidence 1/100,000
  - Mechanism: acute rapidly, ascending, symmetric, progressive demyelination of peripheral (not central) motor (not sensory) nerves from ventral root
    - Infection (70% of cases, manifests 2-4wks after infection): Viral (EBV URTI, HIV Seroconversion, HSV-1) vs Bacterial (Campylobacter Dysentery, Mycoplasma LRTI)
    - Immunization (Rabies, Swine Flu, Influenza, Group A Sreptococci)
    - Cancer (Hodgkins)
    - Post-Op
    - SLE
    - Pregnancy
  - Clinical Features
• acute rapidly (days), ascending (legs/arms → trunk esp diaphragm → bulbar esp CN 7), symmetric (R and L) progressive motor deterioration (weakness → paralysis) that is variable (weak vs paralysis) that lasts for wks (good prognosis: 3wks vs bad prognosis: >6wks) with recovery lasting months (100%)
• hypo-/a- reflexia (100%)
• autonomic features including arrhythmias and variations in BP from hypoTN to hyperTN (20%)
• occasional sensory involvement manifesting as painful extremities (20%)
• mentation and sphincter control is spared
• NB a chronic form of GBS exists called Chronic Inflammatory Demyelinating Neuropathy (CIDP)
• Miller Fisher Variant (ophthalmoplegia, ataxia, hyporeflexia)

Diagnosis
• CSF Analysis: “Albumino-Cytologic Dissociation” aka high protein – normal cell count
• Nerve Conduction Studies (NCS): decreased motor nerve conduction velocity
• Serum: anti-GM1 and anti-GQ1b

Treatment
• monitor cardiac function w/ ECG and VS → fluids, medications, cardioversion, etc
• monitor pulmonary function w/ FVC/MIP w/ goal <50%/<-60cm → oxygen, mechanical ventilation, etc
• IVIG x5d or Plasmapheresis x7-10d (equivalent but no proven benefit when combined)
• Rehab
• NO steroids

Prognosis
• Good: less acute onset of symptoms, mechanical ventilation not needed, signs of recovery are seen w/in 3wks, young age (most)
  • Pt recovers (75%)
• Poor: more acute onset of symptoms, mechanical ventilation needed, signs of recovery are NOT seen after 6wks, old age (few)
  • Pt remain wheel-chair bound forever (20%)
  • Pt dies arrhythmias while in the past prior to ventilators it was respiratory failure (5%)

Mononeuropathy
• Trauma/Entrapment/Compression (refer to Rheum MS notes)
• DM esp CN 3,4,6
• Bell’s Palsy
  • Etiology: infection (Lyme, HSV, HIV), other (pregnancy, trauma, tumor, GBS, Sarcoid)
  • Mech: swelling on CN 7
  • S/S: acute unilateral CN 7 palsy
  • Dx: clinical
  • Tx: no Tx as most cases resolve in <1mo unless you believe it is 2/2 HSV then give steroids/acyclovir otherwise just supportive Tx by wearing eye patch at night to prevent corneal abrasion but if no improvement then consider surgical decompression

Trigeminal Neuralgia (Tic Douloureux)
• Etiology: idiopathic but 400x more common in MS
• Mech: 2/2 enlarged ecstatic blood vessel compressing nerve
• S/S: brief (seconds to minutes), frequent (?) attacks of very severe lancinating facial pain w/o motor/sensory changes
• Dx: clinical but get MRI to look for MS
• Tx: Acute (IV phenytoin & lidocaine) vs Chronic (1° carbamazepine or oxcarbazepine, 2° phenytoin, gabapentin, baclofen), surgery microvascular decompression, percutaneous radiofrequency rhizotomy, etc
• Prognosis: 85% completely resolve but pts often have other episodes

Post Herpetic Neuralgia (refer)

Junction Disorders
• Myasthenia Gravis (MG)
  • Mech: autoimmune antibodies against Ach receptors at NMJ
  • Epidemiology: 25yo women vs 60yo men
  • S/S
    • weakness worse w/ exertion, fatigue esp end of day, increased body temp, stress, infection, meds (magnesium, aminoglycosides, BB, anti-arrhythmics, morphine) and better w/ rest (NB normal sensation/reflexes/autonomics)
    • Ocular (most common initial Sx): diplopia, ptosis
    • Bulbar: dysarthria, dysphagia, facial weakness, difficulty chewing, aspiration
    • Neck: head drop
    • Limb: proximal>distal
    • Diaphragm: dyspnea to respiratory failure (Myasthenic Crisis)
  • other autoimmune disorder (hyperTH, SLE, DM, RA)
- thymoma (10%) or thymic hyperplasia (70%) (always get a CT-Chest, thymus should not be present in adults so if you find anything it is likely pathologic, it is believed that with thymus dysfxn there is dysfxn of self-tolerance and thus the presence of auto-antibodies)
  - **Dx**
    - Ice Test (ocular S/S improve after placing ice)
    - Acetylcholine Receptor Antibody Test (55(ocular)-75(generalized)% sensitive therefore 20% are false negative therefore check other abs, 80% specific therefore 20% are false positive in the presence of other autoimmune disorders, ALS and post-op, titer does not correlate w/ severity), anti-MuSK aka Muscle Specific Kinase (+ in 70% of pts w/ clinical Sx but negative AchR Ab), anti-Striated Muscle, ANA, RF, etc
    - Tensilon Test (intravenous short acting AChE inhibitor (edrophonium) is given to pt but not anymore)
  - **EMG**
    - After repetitive stimulation there is mild decrement in response
    - Immediately after exercise and then repetitive stimulation there is NO decrement in response aka “early post-exercise facilitation” 2/2 transient increase in release of Ach following maximal contraction
    - Long time after exercise and then repetitive stimulation there is severe decrement in response aka “late post-exercise depression”

- **Lambert Eaton Myasthenic Syndrome (LEMS)**
  - **Mech:** autoimmune antibodies against pre-synaptic voltage gated calcium channels (VGCC) preventing calcium influx and thus Ach release
  - **Epidemiology:** 50% 2/2 cancer (1° SCLC (seen in 2% of pts, 2° non-SCLC, thyroid cancer, thymoma, cervical cancer, germinoma, leukemia) vs 50% idiopathic
  - **S/S (similar to MG except below, often precedes Dx of cancer by up to 2yrs)**
    - Occasionally paresthesias
    - Occasionally hyporeflexia
    - Occasionally autonomic dysfxn
    - Other paraneoplastic syndromes and autoimmune disorders
  - **Dx (similar to MG except below)**
    - Antibody
    - EMG (facilitation)
  - **Tx:** NM meds (AChE inhibitors, 3,4-diaminopyridine, guanidine) and tumor resection or if tumor is not found then aggressive search for a tumor and only after an exhaustve search can you say that LEMS is idiopathic and thus you treat w/ immunosuppressive drugs (prednisone, azathioprine, etc) but only until you absolutely ruled out cancer, you can also do plasmapharesis/IVIG to remove the auto-ab

- **Botulism**
  - **Mech:** *Clostridium botulinum* pre-formed toxin in improperly canned food (Adult) or spore in honey (Infant) but in most cases is just found in soil → Enters Parasympathetic and Neuromuscular Neurons → Cleaves SNAP, Syntaxin, and vAMP and thus No Release of Ach → Muscle Flaccid Paralysis + Hypoparasym pathetic Activity (symptoms begin ~12hrs after ingestion) → S D’s: diplopia 2/2 ophthalmoplegia, dysphonia, dysarthria, dysphagia, descending symmetric flaccid paralysis w/ areflexia and constipation, death from respiratory failure (infant S/S include hypotonia, weak suck, poor feeding, weak cry, etc)
  - **Dx:** history, as opposed to GBS there is no elevation of CSF protein, stool toxin, EMG/NCS similar to LEMS
  - **Tx:** resp support in ICU, gastric lavage / enemas only in first few hours, toxoid to neutralize unbound toxin but controversial, penicillin, EMG w/ High Hz (20-50Hz) reverses presynaptic blockade, AChE inhibitors, inform CDC
Myopathy

- S/S: proximal weakness
- Dx: elevated creatine kinase, EMG, muscle Bx, genetic testing, occasionally myoglobinuria, other enzymes like aldolase/AST/ALT/LDH are less helpful
- DDx
  - Rheumatic Myalgias (Polymyalgia Rheumatica, Fibromyalgia, Somatization Pain Syndrome)
  - Rheumatic Myositis (Polymyositis/Dermatomyositis/Inclusion Body Myositis, Sarcoidosis)
  - Muscular Dystrophies
    - **Duchenne Dystrophy** (X-linked mutation of dystrophin, presents ~5yo, muscle weakness w/ Gower sign and calf pseudohypertrophy 2/2 fatty/fibrous infiltration into degenerating muscle, elevated CPK, mild MR, Tx is supportive w/ most dying by 20yo)
    - **Becker Dystrophy** (same just slightly different mutation resulting in milder Sx, presents ~10yo)
    - Myotonic
    - Limb-Girdle Dystrophy
  - Mitochondrial Myopathies
    - **Mitochondrial Myopathy** (mitochondrial mutation therefore passing from mother to offspring, Bx: “ragged red fibers”, Sx: ophthalmoplegia)
    - **Myotonic Myopathy** (AD, presents ~25yo, Sx: inability to relax muscles esp grip along with MR, baldness, gonad atrophy)
  - Inborn Errors of Carb/Lipid Metabolism
  - Trauma (contusion, EMG, acute compartment syndrome, chronic compartment syndrome aka "shin splints", pull/tear, spasm, acute exercise = increase lactic acid vs subacute exercise = microtears)
  - ICU (Critical Illness Myopathy)
  - Drugs (steroids, statins/fibrates/niacin, AZT, cyclosporine, colchicines, hydroxychloroquine)
  - Excessive Movement (seizure, exercise)
  - Electrolytes (hyperNa, hypok, hypoca, hypoPO4, hypoMg) w/ Periodic Paralysis
  - Toxins (alcohol, amphetamines, cocaine, heroin)
  - Endo (hypo/hyperTH, Addison’s/Cushing’s)
  - Viral (Influenza, coxsackie, HIV)
  - Bacterial (pseudomysitis, Lyme)
  - Fungal (trichonosis, toxo)