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 Pandysautonomia)

	Axonal Degeneration	Demyelination
Acute	• **Toxins**: Thallium, Lead, Organophosphates, Arsenic • Meds: **Chemo**, Abx • Other: **Porphyria, Vasculitis, Critical Illness Polyneuropathy/Myopathy aka CIPN/M** (refer)	• Infection: **Botulism**, **HIV, Lyme, CMV, West Nile, Rabies** • Other: **GBS, Porphyria, MG, PM**
Chronic	• 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) • Toxins: 1° **EtOH**, lead, arsenic • **Meds**: INH, sulfas, metronidazole, vincristine, cisplatin, phenytoin, TCA • Infection: HIV, syphilis, leprosy, lyme, acute hepatitis • Other: **sarcoid**, malignancy, amyloidosis	• Genetic: Hereditary Motor Sensory Neuropathy (HMSN) aka **Charcot-Marie-Tooth Disease** (pes cavus aka high arches, clawed/hammer toes, distal foot muscle atrophy, foot drop, manifests during 1st decade) • Acquired: Chronic Inflammatory Demyelinating Poly Neuropathy aka **CIDP** (chronic form of GBS, Tx w/ steroids and immunosuppressants), **Paraprotein** (anti-myelin-associated-glycoprotein MAG), **Paraneoplastic** (+anti-Hu)

- **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
        - rare ocular findings (10%)
        - NB a chronic form of GBS exists called Chronic Inflammatory Demyelinating Neuropathy (CIPD)
        - Miller Fishser Variant (ophthalmoplegia, ataxia, hyporeflexia)
    - Diagnosis
        - CSF Analysis: "Albumino-Cytologic Dissociation" aka high protein – normal cell count
        - Nerve Conduction Studies (NCVs): 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%)

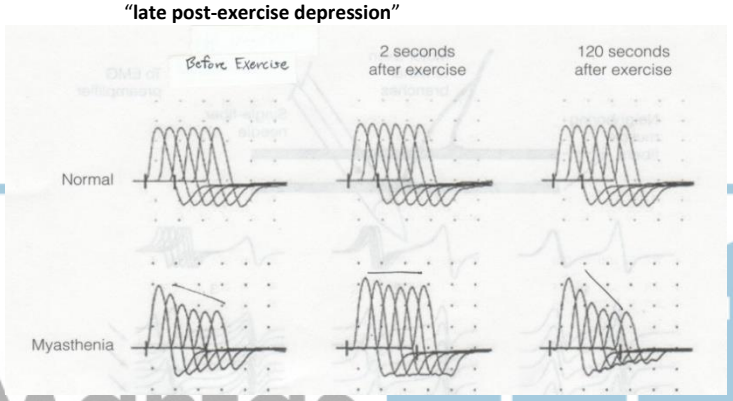
<u>Mononeuropathy</u>

- **Trauma/Entrapment/Compression** (refer to RheumMS 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/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)

<u>Junction Disorders</u>

- **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 the 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**"



    - Tx
        - General: AChE Inhibitors (pyridostigmine (Mestinon) and neostigmine (Prostigmine), NB pts often get anticholinergic SEs) AND Immunosuppression (Prednisone, Cyclosporine, Azathioprine, Mycophenolate Mofetil), Thymectomy (can help w/ Sx, consider not taking out in the elderly)
        - Crisis: IVIG, plasmapharesis, prednisone, supportive
- **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)
        - Weakness (more commonly limb weakness)
        - 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 exhaustive 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 + Hypoparasympathetic Activity (symptoms begin ~12hrs after ingestion) → 5 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 calve psuedohypertrophy 2/2 fatty/fibrous infiltration into degenerating muscle, elevated CPK, mild MR, Tx is supportive w/ most dyeing 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, Adddison's/Cushing's)
    - Viral (Influenza, coxsackie, HIV)
    - Bacterial (pyomyositis, Lyme)
    - Fungal (trichinosis, toxo)