- In general, patients with PNS dysfunction complain of;
  1. sensory disturbance, e.g.
     - Negative disturbance (-) like: numbness, loss of sensation.
     - Positive disturbance (+) like: tingling, burning or both.
  2. Or motor weakness, e.g. A loss of muscle mass, paralysis (muscle weakness), painful cramps, spastic paralysis, or fasciculations.
  3. Or Autonomic disturbance e.g loss of bladder control
  4. Or Both (Motor , sensory, and autonomic)
- Infectious causes for PNS diseases is very rare and are underrecognized but potentially treatable if caught early
- Different causes of PNS diseases
  - Metabolic - diabetes
  - Vascular – ischemia, atherosclerosis
  - Inflammatory -
  - Infections (rare causes)
  - Traumatic
    - Most common causes are vascular and inflammatory
- Pathogens with clinical implications in the PNS
  - HIV
    - Retrovirus that affects BOTH the CNS AND PNS
    - Transmission
      - Sexual contact
      - Contaminated blood
    - Causes
      - Distal symmetric polyneuropathy (DSP)
        - Occurs DISTALLY at BOTH SIDES and similar symptoms affecting multiple nerves
        - Distributed like stocking and glove distribution
        - MOST COMMON FORM in HIV pts with advanced stages
        - MOST PREVALENT INFECTIOUS CAUSE OF PNS dysfunction
        - Caused by NEUROTOXCITY of the HIV itself or neurotoxicity of cART
      - Mononeuropathy multiplex
      - Ascending demyelinated polyneuropathy
        - Causes ascending weakness early in disease
        - Happened in Guillain-Barre Syndrome
      - Polyradiculopathies
        - The nerve roots emerge dysfunction and the area it supplies are affected

- Virus – Herpes Virus I,II and Varcilla Zoster Virus
    - All share that theyre relatively large, double stranded linear DNA genomes
    - Latent recurring infections are typical of this group
    - Pathogenesis
        - The herpes virus will infect the nervous ystem and typically initiate at the peripheral sites such as mucosal epithelia
        - Then the virus will enter the termina of the sensory neurons of the PNS in which they will go in a retrograde direction towards the cell bodies and they will deposit theyre genomes in the nucleus to establish lifelong latency
        - Reactivation from latency will normally cause the infection to spread in the anterograde direction back out towards the periphery
            - This latency is normally asymptomatic but the reactivation is whaat caused the lesions to occur
        - HOWEVER, sometimes they will go towards the CNS and cause lethal encephalitis
    - VZV
        - Causes varicella and herpes zoster
        - Pathogenesis:
            - It starts as chicken pox which normally happens in childhood
            - After a while the varicella caves and disappears to sit latent in the sensory ganglia
            - Sometimes it comes back as zoster (shingles) which is a rash that is distributed according to dermatomal distribution
        - Symptoms – usually self limiting
            - Constant deep, aching, or burning pain
            - Paroxysmal lancinating pain
            - Hyperalgesia – painful stimuli are more painful than expected – the slight touch would be painful
            - Allodynia – pain associated with typical non-painful stimuli
            - Most problematic symptoms is the pain that accompanies the rash called post-herpetic neuralgia
                - This is also the most commonly reported PNS complication
                - Its persists for 3 months or more following an outbreak of shingles
        - Reactivation normally occurs in elderly and immunocompromised pts
        - Imp to ask the pt if the pain is preceded by a rash since that almost a characteristic sign of post-herpetic neuralgia which can also affect cranial nerves
        - Pharmacological treatment
            - Acyclovir – for post herpetic neuralgia

        - Early trx of VZV infection is recommended with these antiviral agents like acyclovir, valacyclovir and famciclovir for 7 days
    - Topical analgesia + opioids - for pain
    - Alpha 2 delta ligands – gabapentin + pregabalin
    - Tricyclics antidepressants is pt was prone to depression
        - Like amitriptyline , nortriptyline and dozepin
- Poliovirus
    - Member of the enterovirus
        - Enterovirus since it enters fecal orally
    - Rare since there is a vaccine
    - Causes polio or infantile paralysis
    - Asymptomatic – some have flaccid paralysis
    - Pathogenesis
        - Enters fecal-orally
        - Invades the small intestine
        - Enters the blood stream
        - Causes primary viremia – if you have been vaccinated before you already have antibodies or you will form antibodies very quickly
        - If not vaccinates- dissemination occurs
        - It will cross the BBB into the CNS damaging both the PNS and the CNS
        - This will cause flaccid paralysis – irreversible damage even if you give anti-virals
    - Diagnosis
        - Very rare
        - Look in stool
        - Look through rising antibody titer in blood
- Borrelia Burgdorferi – Lyme Disease
    - Its tick borne – one of the spirochetes – gram negative – seen using darkfield microscopy
    - Symptoms
        - Skin rash – called ERYTHEMA MIGRANA
        - Myalgias
        - Arthralgia
        - General fatigue
        - Fever
    - Causes
        - Cranial neuropathies
        - Painful radiculopathies
        - Diffuse polyneuropathies
    - Diagnosis
        - Clinical presentation , history and serology are important in diagnosis

        - Treatment
            - Doxycycline
                - Given to adults with suspected Lyme disease
    - Clostridium tetani
        - Spore forming, anaerobic G+ve rod
        - Causes tetanus
        - Produces tetanospasmin
        - Causes
            - Dirty wounds like stepping on a rusty nail that has spores of C.tetani
        - Pathogenesis
            - Tetanospasmin inactivates proteins that regulate release of the inhibitory neurotransmitters glycine and GABA
            - This leads to unregulated excitatory synaptic activity in the motor neurons, resulting in spastic paralysis
        - Symptoms
            - Locked jaw – sardonic smile
                - The spasm of respiratory muscles can make the tetanus fatal
        - Diagnosis
            - Based on physical exam , immunization history and clinical presentation
            - Admission to ICU is highly recommended
        - Treatment
            - Human tetanus immune globulin should be given as soon as tetanus is suspected
            - Antimicrobial therapy is typically metronidazole as the preferred trx for tetanus with penicillin G as an option for second line therapy for 1 week to 10 days
                - antimicrobial therapy plays a relatively minor role in the management of tetanus and of primary importance is wound debridement and toxin mitigation.
            - So most important thing is to monitor the vital signs and give IVIG
        - This disease is relatively rare because of the high incidence of vaccine-induced immunity
    - Clostridium botulinum
        - Spore forming
        - Anaerobic
        - G+ve rod that causes tetanus
        - Causes
            - Pts with foodborne botulism from consumption of home-canned foods
            - Infant botulism is associated with consumption of foods like honey and infant milk powder
        - Pathogenesis

        - Infant botulisms is caused by the neurotoxin produced in vivo colonizing the GI tracts of infants
        - The toxin remaisn at the neuromuscular junction and the botulinm endopeptidase then inactivates the ptoeins that regulate the release of Ach blocking neurotransmission at peripheral cholinergic synapses resulting in flaccid paralysis
    - Symptoms
        - Bilateral descending weakness of the peripheral muscles – flaccid paralysis
        - Death is the most commonly attributed to respiratory paralysis
    - Diagnosis
        - Initially its based on clinical symptoms
        - Labortatory confirmations is done by demonstrating the presence of botulinum toxin in serum, stool or food
    - Treatment
        - Supportive care and the use of antitoxins have been effective in the treatment of botulism form food borne
            - The effectiveness of antitoxin in the treatment of inhaled C.botulinum has not been proven
- Campylobacter jejuni
    - Common cause of bacterial gastroenteritis
    - Infections are zoonotic
    - Microaerophilic
    - Curved
    - G-ve rods
    - Major triggering agent of Guillain-Barre syndrome – GBS
        - Immune-mediated demyelinated polyneuropathy of PNS characterized by acute or subacute symmetrical ascending motor weakness, areflexia and mild-moderate sensory abnormalities
    - Pathogenesis
        - Molecular mimicry between sialylated lipooligosaccharide structures on the cell envelope of these bacteria and ganglioside epitopes on the human nerves that generates cross-reactive immune response results in autoimmune-driven nerve damage.
    - Treatment
        - Most are self limiting, occasionally a more invasive illness can occur that requires effective antimicrobial therapy
        - Plasma exchange
        - IVIG

- Mycobacterium leprae
  - Leprosy (Hanses disease) One fo the most common causes of nontraumatic peripheral neuropathy in the developing world
  - Morphologically indistinguishable form M.tubercolosis
  - Pathogenesis
    - The agent has a prediclation for schwan cells where it it multiplies unimpeded by organism specific host immunity, resulting in destruction of myelin, secondary inflammatorhy chanes and destruction of the nerve architecture
  - Symptoms
    - Mainly affects the
      - Skin
      - Peripheral nerves
      - Mucosal surfaces of the upper respiratyr tract and the eye
      - Causes hypopigmented or hyperpigmented skin macules that exhibit loss of sensation (anesthesia) due to infection the peripheral nerves supplying the region
  - Diagnosis
    - Skin or nerve biopsy and acid fast staining
  - Treatment
    - Hansens disease is treated with multidrug therpay (MDT) using a combination of antibiotics depending on the form of the disease