Encephalitis

- Inflammation of the brain parenchyma due to a penetration of the BBB or overlying meningitis
    - In meningitis the inflammatory response is limited largely to the meninges – the meninges play a protective role in limiting pathogen spread to the CNS
    - Meningitis is more common than encephalitis
- Encephalitis can be caused by both bacteria and viruses BUTTT viral infections are more of a common cause of encephalitis
    - HSV is the most common cause but its quite rare

Viral spread to the CNS

- Invades the sensory and motor nerves endings causing an infection of the brain microvascular endothelium
- Neurotropic viruses typically cause pathologic injury in distinct regions of the CNS but cant be distinguished only by clinical examination
- They invade the CNS by infecting circulating leukocytes
- Microglial cells:
    - When the infect the CNS it will cause neutrophils to reach the brain parenchyma and activate the microglia cells
        - Microglial cells are NONREDUNDANT (no other cells in the body can perform their role) cells in the CNS that regulate adaptive immune responses after infection
    - The microglia cells that reside in the CNS parenchyma will deploy and innate immune mechanism to control virus spread shortly after CNS infection
    - The microglial cells are involved in the CNS damage following the acute phase of viral encephalitis, which doesn't stop after virus elimination from the CNS

Encephalitis symptoms

- Fever, headache, symptoms of accompanying meningitis (if present; like neck stiffness and +ve kerning's or Brudzinski's sign)
- Parenchymal involvements
    - Altered level of consciousness (hallucinations, agitation, personality changes, behavioral abnormalities)
    - Depressed level of consciousness ranging from mild lethargy to complete coma
    - Evidence of focal or diffuse neurological sing and symptoms (aphasia, ataxia, UMNs or LMNs patterns of weakness, and cerebral nerve palsies)

Commonly encountered pathogens

- Majority of acute encephalitis of suspected viral etiology remain of unknown cause
- Many viruses can cause encephalitis
    - Most commonly identified viruses causing sporadic cases of acute encephalitis in immunocompetent adults are

        - Herpesviruses – HSV,VZV,EBV
    - Epidemics of encephalitis are caused by arboviruses (transmitted by arthropods like mosquitoes and ticks)
        - Since 2002 west Nile virus (WNV) has been the cause of majority of outbreaks
    - Rabies virus are also a cause of encephalitis
        - Rabies is a zoonotic infection that occurs in a variety of mammals, transmitted to humans through bites, most commonly by canines or bats
        - Incubation period ranges from days to less than a year
        - Has encephalitis symptoms it also has episodes of hyperexcitability which are typically followed by periods of complete lucidity that become shorter as the disease progresses
        - Brainstem dysfunction progresses rapidly and coma – followed within days by death – is the rule unless the course is prolongs by supportive measures

Treatment

- The physician must decide whether initiation of post exposure prophylaxis (PEP) is warranted this is on the basis of exposure and local epidemiologic information
    - Prophylaxis involves wound care and passive immunization with rabies immune globulin
- In the initial stages of encephalitis many pts require ICU
- Basic management and supportive therapy should include careful monitoring of vita sings and ICP
- Acyclovir is of benefit of the trx of HSV (and VSV and EBV severe infections) and should be started empirically in pts with suspected viral encephalitis while awaiting viral diagnostic studies
- There is considerable variation in the incidence and severity of sequalae in pts surviving viral encephalitis.
    - Many pts with WNV infection have sequelae including
        - Cognitive impairment
        - Weakness
        - Hyper or hypokinetic movement disorders
            - Tremor
            - Myoclonus
            - parkinsonism

How to diagnose a suspected encephalitis pt

- Lumber puncture
    - CSF profile is indistinguishable form that of viral meningitis and typically consist of
        - Lymphocytic pleocytosis
        - Mildly elevated protein concertation
        - Normal glucose concentration
- CSF PCR

- PRIMARY DIAGNOSTIC TEST for viral CNS infections
- Serology
  - Anti WNV IgM antibodies in the CSF are diagnostic for WNV encephalitis
- Neuroimaging
  - Helps identify or exclude alternative diagnosis and assist in the differentiation between focal as opposes to a diffuse, encephalitic process
- Brain biopsy

Transmissible spongiform Encephalopathies (TSEs)

- Prions
  - Abnormal pathogenic agents
  - Transmissible and are able to induce abnormal folding od specific normal cellular proteins called prion proteins (PRP)
  - They're found most abundantly in the brain
  - So prions are composed of prion proteins (PrP) are hypothesizes as the cause of TSEs
- TSEs
  - Group of diseases that affect the brain and nervous system of humans and animals
  - Characterized by : degeneration of cerebral cortex and cerebellum tissue giving spongelike appearance (hence the spongiform)
- TSEs in humans include
  - Creutzfeldt-Jacob disease – MOST COMMON & HAS 4 FORMS
    - Sporadic - sCJD
      - Infectious prions are believed to be made by an error of the cell machinery that makes proteins and control their quality
      - These error are more likely to occur with aging which explain the general advanced age at onset of CJD and other prion disease
    - Hereditary/familiar -fCJD
      - If the prion protein gene is altered in a persons sperm or egg cells , the mutation can be transmitted to the persons offspring
      - The particular mutation found one ach family affects how frequently the disease appears and what symptoms are most noticeable
    - Iatrogenic – iCJD
      - Accidental transmission of CJD to humans appear to have occurred with corneal transplantation , contaminated electrode implantation (EEG) and surgical procedures
    - Variant - vCJD

        - Acquired by eating meat from cattle affected by BSE ''mad cow disease''
    - Kuru – NOT COMMON
    - Fatal familial insomnia (FFI)
- TSEs in animals include
    - Scrapie in sheep and goats
    - Bovine spongiform encephalopathy (BSE) in cows – MAD COWS DISEASE
- Signs and symptoms of CJD
    - Rapidly progressive dementia
    - Rigidity
    - Agitation, apathy and mood swings
    - Myoclonus
        - Definition
            - Brief involuntary twitching of a muscle or group of muscles caused by sudden contractions (positive myoclonus) or brief lapses of contraction (negative myoclonus)
        - Characteristics
            - Most pts (90%) with CJD exhibit myoclonus that appears throughout the illness
        - It persists during sleep UNLIKE other involuntary movements
    - As the condition worsens physical manifestations such as
        - Ataxia
        - Speech impairment
        - Changes in gait
- Diagnosis of CJD
    - EEG (electroencephalography)
        - can be particularly valuable because it shows a specific type of abnormality in major but not all types of CJD.
    - MRI
        - Recently been found to be accurate in about 90% of cases
    - ONLY WAY TO CONFIRM DAIGNOSIS OF CJD IS BY BRAIN BIOPSY OR AUTOPSY
        - in a brain biopsy, a neurosurgeon removes a small piece of tissue from the person's brain so that it can be examined by a neuropathologist.
- Treatment of CJD
    - NO KNOWN CURE OR EFFECTIVE TREATMENT FOR CJD
    - But medication can be used to treat some of the mental changes and personality abnormalities that occur
    - Treatment is usually focused on making pts comfortable and to help them function safely in their environment – Palliative
    - OPIOTE DRUGS
        - Help relieve the pain if it occurs
    - Clonazepam + sodium valproate

        - Helps relieve myoclonus

Spinal cord can be involved in infections as well – INFECTIOUS MYELOPATHIES

- Myelitis
    - Arises from intrinsic infection and inflammation of the spinal cord
    - Clinical manifestation
        - Depends on the exact level and location within the cord
        - Herpesvirus and enterovirus are ubiquitous, accounting or a substantial number of viral myelitis cases
- Pyogenic epidural abscess
    - Cause of extrinsic cord compression, requires immediate recognition, because permanent neurologic deficits may develop within 36 hrs of symptoms onset
- Treponema pallidum
    - Causative agent of syphilis
    - Rare etiology of myelopathy in the 21st century