JAPANESE B ENCEPHALITIS
HISTORY

• Epidemics of encephalitis - Japan from the late 1800s.

• First isolated in Japan during an epidemic in 1935.

• In India first recognized in 1955 in Vellore.

• JE is a positive sense single stranded RNA virus.

• Family of Flaviviridae.
EPIDEMIOLOGY

- Annual incidence in endemic areas 1-10/10,000 population.
- Children <15 yr of age are principally affected.
- Highly endemic areas - A P, T N, Karnataka & UP.
- Peak starts after rains- July to December.
TRANSMISSION

• Transmitted as zoonotic cycle
  – Mosquito
  – Culex tritaeniorhynchus
  – Culex vishnui

Vertebrates like-
  Pigs & wading birds
  Pigeon, Sparrow,
  Duck, Horses, Swine,
  Cattle & Buffalo

• Humans are dead end host.

• Pigs serve as amplifying host.
PATHOLOGY

• Areas of brain most commonly thalamus, substantia nigra, anterior horns of spinal cord, Cerebral cortex and cerebellum

• Other organs affected are: Lymph nodes, spleen, myocardium, lungs and kidney

• After transmission virus multiplies locally and in regional nodes- transient viremia- invasion of CNS- in the neurons virus multiplies in the neuronal secretary system
• Affect endoplasmic reticulum & Golgi apparatus and destroy them.
• After primary infection IgM response in serum and CSF usually within 7 days.
• Immunization with inactivated JE vaccine induces T cell activation in vivo.
CLINICAL FEATURES

• Incubation period 1 to 14 days.

• Onset is abrupt, acute, sub-acute or gradual.

• Typically progress through 4 stages
  Prodromal stage: 2 to 3 days
  Acute stage (3-4 days)
  Sub acute stage (-10 days)
  Convalescence (4- 7 wk)
PRODROMAL STAGE

Abrupt onset of high grade fever

Head ache

Malaise

Abdominal pain

Nausea & vomiting

Sensory changes and psychotic episodes.
ACUTE STAGE

- Neurological symptoms 3 to 5 days
- Altered sensorium, Convulsions
- Neck stiffness, muscular rigidity
- Mask like facies, ICT
- Characteristic are rapidly changing central nervous system signs.
- Gastric hemorrhage, pulmonary edema
CONVALESCENCE STAGE

- Stage of recovery
- Slowly regain neurological function over several weeks
- Speech defects
- Paresis
- Intellectual deficit
DIAGNOSIS

• CSF: pleocytosis (100-1000 leukocytes/mm³)
  Increased protein
  Normal glucose

• CT: involvement of thalamus, basal ganglia, mid brain, pons & medulla

• EEG: diffuse theta & delta waves
ETIOLOGICAL DIAGNOSIS

• Four fold rise or greater in serum antibody.
• Isolation of virus/ demonstration of viral antigen or genomic sequences.
• IgM capture Elisa
STANDARD CASE DEFINITION

- Suspect case of JE- clinical description
- Probable JE- presumptive lab results
- Confirmed JE- confirmatory lab results
- Antigen or genome in tissues or blood by immune chemistry or immune fluorescence or by PCR
- JE virus specific IgM in CSF
- 4 fold or greater rise in JE virus specific antibody in paired sera
PRESumptive lab diagnosis

• Detection of acute phase antiviral antibody response by any one of the following
  – Increased and stable serum antibody titres of JEV by ELISA.
  – Hemagglutination or virus neutralization assay
    IgM antibody to the virus in serum.
DIFFERENTIAL DIAGNOSIS

• West Nile virus
• Entero virus
• Herpes virus
• CNS tumors
• SLE
• Enteric encephalopathy
TREATMENT

• No specific treatment.

• Symptomatic & supportive aimed at prevention of

  Pulmonary aspiration, hypoxia

  Hypoglycemia, hyper pyrexia

  Uncontrolled seizures, raised ICT

  Pulmonary edema, SIADH

  Secondary infection, brainstem involvement
TREATMENT CONT..

- Airway, breathing & circulation
- Seizures: Diazepam, Valproate
- Fluid, electrolyte & blood sugar maintained
- Raised ICT: Hyperosmolar therapy
- Coma - prevent aspiration, bedsores, nosocomial infection, malnutrition & contractures
- Extra pyramidal symptoms: Haloperidol, Diazepam, chloral hydrate
SPECIFIC THERAPY

• Monoclonal antibodies

• Recombinant Interferon alpha
PROGNOSIS

• Patient fatality rates are 24-42%.

• Frequency of sequelae is 5-70% and is directly related to the age of the patient and severity of the disease.

• Most common sequelae are mental retardation, severe emotional instability, personality changes, motor abnormalities and speech disturbances.
PROGNOSIS

• Poor prognostic signs are:
  Younger age
  Hyponatremia
  Shock
  Low GCS
  Presence of immune complexes in CSF
  Increased levels of tumor necrosis factor

• Good prognostic sign: high levels of neutralizing antibodies (IgG) in CSF
PREVENTION

• Control of mosquito: insecticide, fogging, larvicidal measures & pyrethrum.
• Prevention of bites: Avoid out door activities, clothing, mosquito repellants, bed nets or house screening.
• Control/ protection of reservoirs, piggeries, vaccination in pigs- decrease viral amplification.
• Vaccination in high risk areas, susceptible population
VACCINATION

• Travelers to endemic countries who plan to be in rural areas of the endemic region during the expected period of seasonal transmission.

• Travelers in rural areas experiencing endemic transmission should receive JE vaccine.

• In humans, prior dengue virus infection provides partial protection from clinical JE.
VACCINATION

• Inactivated mouse brain vaccine- Nakayama strain- dose: 0.5-1 ml SC – 1 to 3 years- 3 doses- 0-7-10 days, booster every 3 years- till 10-15 years

• Inactivated primary hamster kidney cells- China- SC 0.5ml- 1to2 years- booster 6 yrs -cheap

• Live attenuated primary hamster kidney cells- cheap- single dose- not approved by WHO
VACCINATION CONT.

• Vaccination of travelers- 0-7-30

• The final dose should be completed at least 1 wk prior to the patient's expected arrival in a JE endemic area.

Newer vaccines:-

• Recombinant JE vaccine
• DNA multivalent vaccine
• Chimeric vaccine