

Japanese Encephalitis

For Doctors, Health Workers & Parents

(What, Why, When and How to do approach)

By

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Preface: This handbook answers all the questions asked since
1979 by medical, paramedical personnel, parents, administrators

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and Public representatives from all over India who deal with
cases of Japanese Encephalitis.

Part "A" is meant for use by doctors and paramedical staff
whereas part "B" is for Mass Media for communication to parents.

Dedication

This book is dedicated to all those struggling for a
better tomorrow for the suffering child.

Wednesday, May 03, 2000

DR.P.NAGABHUSHANA RAO

Part "A"

Introduction:

Japanese Encephalitis (JE) is a disease about which
everybody must be aware of, as it is the only virus so far
detected to cause epidemics of encephalitis in India.

In India, JE was first recorded in Vellore & Pondicherry
in mid 1950s. JE has been reported from 24 states/ Union
Territories so far. Frequently affected states include Andhra
Pradesh, Assam, Bihar, Goa, Haryana, Karnataka, Manipur, Tamil
Nadu, Uttar Pradesh & West Bengal. The Directorate of National
Anti Malaria Program (NAMP) is monitoring JE in India since 1978.
An estimated 378 million population is living at the risk of JE in 12
states/ Union Territories that are frequently affected. The spread
of JE to new areas is probably due to agricultural development
and intensive rice cultivation supported by irrigation schemes.

It has high mortality and morbidity rates. Usually
affected age group is 5-10 years though children from 3-14 years
can be affected. In West Bengal, only 36% were children and
64% were adults probably due to fresh introduction of virus. This
trend was seen in Korea also, when pediatric population received
JE vaccine.

Japanese Encephalitis, popularly called "Brain Fever", is
caused by a virus. Since it is carried by mosquito, an arthropod,
it is classified under Arbovirus. Indian strain of Japanese
encephalitis virus (JEV) is GP78, which is phylogenetically closer
to the Chinese SA14 isolate. JE is a zoonotic viral disease. JE
virus has a complex life cycle. In nature, JE virus is maintained in
animals and birds, particularly pigs and Ardiel birds (e.g., Cattle
egrets, pond herons etc.) The virus does not cause any disease
among its natural hosts and the transmission continues
unnoticed through mosquitoes. It is carried by female
mosquitoes from infected pigs or water birds like pond herons
and ducks to susceptible children. The main vector, Culex

Mosquito (Culex tritaeniorhynchus, C. vishnui, C. pseudovishnui and others – totally 8 species) lives in rural rice growing and pig-farming regions. The mosquito breeds in flooded rice fields, marshes, and standing water around planted fields. This is the reason, JE is mostly a rural disease. Culex mosquitoes can fly up to 5 Kms. Venereal transmission of Japanese encephalitis virus occurs in Culex bitaeniorhynchus mosquitoes. This may have epidemiological significance. The virus is transmitted occasionally by Anopheles (3 species) & rarely Mansonia – (1 species).

JE is a seasonal disease. Epidemics coincide with the monsoon and post monsoon period (August to December), & agricultural practices, due to high density of the mosquito vector (because of stagnant water), and presence of reservoir host (pigs). Northern India, including North-eastern India, receives summer monsoons and as such the transmission season begins from May, with incidence reaching peak in August-October depending on the advancement of monsoon. With onset of winter, JE outbreaks subside. However, in endemic areas, sporadic cases may occur throughout the year due to congenial climatic conditions throughout the year (e.g., Southern India).

Pigs are the most important reservoirs. Though they do not manifest the disease, they develop very high titers of virus in circulating blood and infect mosquitoes. Thus pigs are the amplifying hosts. Susceptible children are infected by infected mosquito bites. After mosquito bite disease appears in 5-16 days. The virus then invades the central nervous system and causes disease. Although infection in human is incidental, the virus can cause serious neurologic disease with high morbidity and mortality. Infection during the first six months of pregnancy may result in infection of the fetus and miscarriage.

Frogs, snakes, egrets, bats and most domestic animals like cattle also are infected by the virus.

JE does NOT spread from child to child or from cattle to humans because of the low and transient viremia. This is the reason increase in cattle to pig ratio may reduce the risk of JE (mosquito bites are shared by cattle and pigs).

The incidence of JE disease is never an indication of the risk at which the population is living in JE endemic areas, because of inapparent infections, which tend to outnumber the apparent infections and also due to the life long immunity, which develops despite inapparent infection. The ratio of overt disease to inapparent infection varies from 1:250 to 1:1000. Thus cases of JE represent only the tip of the iceberg compared to the large

number of inapparent infections. Usually the number of cases reported from each village is 1 or 2.

Until few years back, JE diagnosis was the responsibility of PHC doctors and they were expected to be thorough in complicated neurologic examination and its equally tough interpretation leading to both over and under diagnoses. Analysis of our experience has simplified the approach to diagnosis to such an extent that even a nonmedical person can make a confident diagnosis and start the First aid immediately resulting in significant reduction in Morbidity and Mortality all over the country.

Clinical Approach during epidemics

Unconsciousness, **during epidemics**, can be due to encephalopathy or encephalitis.

Encephalopathy and Encephalitis:

Encephalopathy is diffuse dysfunction of the brain and is due to a **systemic metabolic derangement** (*that is, the disease is outside the brain*), which will not present as an epidemic except when there is electrolyte imbalance or severe dehydration due to fluid loss in viral gastroenteritis epidemics. It must be suspected whenever there is reduced urinary output in association with vomiting or loose motions or whenever intractable vomiting (Reye syndrome) follows a viral infection. Management of a case of metabolic encephalopathy is simply management of the metabolic problem like treatment of dehydration, hepatic dysfunction, altered glucose or sodium levels etc. in the blood and the outcome is almost always good and depends mainly on whether the cause for metabolic disturbance is curable or not.

Encephalitis is due to direct invasion and replication of **virus within the Central Nervous System** and can present as an epidemic. There is clinical or pathologic evidence of direct involvement of cerebral hemispheres, brainstem or cerebellum by the infectious process.

Differentiation of Encephalitis and Encephalopathy and making a probable etiological diagnosis on clinical grounds is extremely important to manage the encephalitis case not only as an individual but also for the community since the management **calls for immediate reporting to the Health Authorities for a wider coordinated intervention by many departments to contain the epidemic.**

Epidemics of encephalopathy are infrequent. There have been reports of epidemics of Reye syndrome from India. This syndrome requires proper diagnosis because this also is a treatable condition requiring early diagnosis for management of hepatic dysfunction.

Clinical differentiation of Encephalitis from Encephalopathy: Encephalitis can be differentiated from encephalopathy clinically in the remotest corner of the world with only very simple observations. The differentiating features can be simplified to such an extent that even a paramedical worker will be able to make the diagnosis. No advanced training or sophisticated investigations are necessary to make a distinction.

Differentiation of Encephalitis from Encephalopathy during an epidemic in a *child who behaves abnormally or has lost consciousness suddenly over 1 hour to 4 days but has no dehydration* can be done by *Health Workers and patient's attendants* by using the following table (Table 1) and flow chart (Flow Chart 1).

Table 1

<i>Observation</i>	<i>Encephalitis</i>	<i>Reye encephalopathy</i>	<i>Encephalopathy</i>
Similar cases in the same or adjoining villages / districts [#]	Yes	Usually sporadic. Only rarely present as epidemics. Suspect if viral illness is followed by sudden and intractable vomiting [§] .	No
Fever	Yes	No	No
Focal or Asymmetrical S/S during first few days ^{@,*}	Yes	No	No

[#] The suspicion must be high during the season for JE and careful search for a similar case must be done.

[@] Asymmetrical symptoms / signs mean any newly appeared difference between right and left sides and may be evidenced by sudden appearance on one side of body of paralysis, focal fits, involuntary movements (tremors, ballismus, chorea, athetosis, cycling, pedaling), abnormal posture of limbs (dystonia), squint, or deviation of angle of mouth or tongue {when put out}. If there is no asymmetry on the first day, repeat examinations are necessary during the subsequent 3 days. During later stages, focal or asymmetrical symptoms/signs may not be discernible easily.

[§]Reye syndrome is an encephalopathy due to liver dysfunction

Doctors may use the additional criteria mentioned in Table 2

Table 2

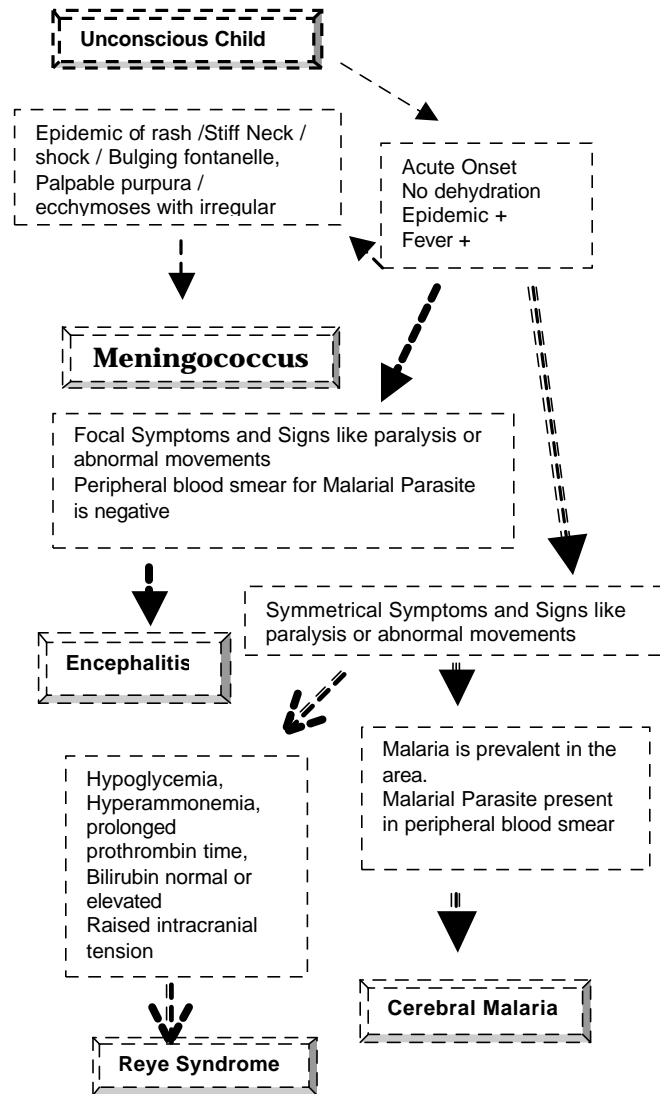
	<i>Encephalitis</i>	<i>Reye Encephalopathy</i>	<i>Encephalopathy</i>
CSF*	Lymphocytosis [#] , Protein elevation, normal glucose	CSF pressure is elevated, but otherwise normal	Normal
JE Serology	JE serology may be positive in 15-20% of cases	Always negative	Always negative

[#] There is pleocytosis. The cell count usually ranges from 6-200 cells/cmm (complete range 6-1000). Neutrophils are seen in early few hours of acute phase and lymphocytes, after the first few hours.

^{*} When there is no epidemic, these changes suggest other viral meningitis or encephalitis / Bacterial meningitis in the resolving or partially treated phase, parameningeal infections (e.g., intracranial abscess, sinusitis, mastoiditis, cortical vein thrombophlebitis), Tuberculous or fungal meningitis in the early phase, parasitic infections (e.g., toxoplasmosis, trichinosis), postinfectious encephalomyelitis, or active demyelinating disease.

In children with dehydration (during epidemic of Viral Gastroenteritis), asymmetric or abnormal pupillary light reflex and / or abnormal Doll's Eye Movement (DEM) confirm the diagnosis of

Flow Chart 1 Diagnosis of Epidemics of Coma (for field use). Source "Epidemiology of JE in AP from 1979 to 1999" by Dr.P.Nagabhushana Rao et al



Encephalitis. (In normal Doll's eye reflex, when the head is rapidly rotated to one side, the eyes deviate to the opposite side, and in abnormal DEM, the eyes do not move or there is asymmetry in the amplitude of movement). Abnormality of spontaneous eye movements (SEM) (asymmetry or absence) also has same significance as abnormal DEM.

Viruses that differ widely in their morphology, chemical composition, and replication can provoke identical clinical presentation and pathologic changes in brain.

Clinical suspicion of encephalitis can be confirmed with CSF analysis. Identification of the specific Virus requires serological tests and viral cultures. Even after extensive investigations in a sophisticated laboratory, about 75 % cases are etiologically undiagnosed. The number of cases in which a viral etiology can be implicated may increase as newer diagnostic techniques, such as Polymerase Chain Reaction (PCR) to detect the viral genome, become widely available and are developed to detect an increasing range of viruses.

Clinical Features:

Arbovirus infections including Japanese Encephalitis virus result in nonspecific symptoms necessitating laboratory studies in an individual case.

The incubation period of JE is 5-16 days. The severity of clinical manifestations depend upon 3 variables, namely

- a. Severity of infection
- b. Susceptibility of the host and
- c. Location of the agent.

The symptoms and signs of encephalitis may be discussed under 4 headings.

- i. **Symptoms and Signs of Infection:** High grade fever, Headache & Malaise.
- ii. **Symptoms and Signs of Brain damage due to infection:** one or more signs may be present. Seizures and/or other abnormal movements, focal neurological deficits like abnormal or asymmetrical spontaneous eye movements (SEM) or Doll's eye movements (DEM), absent corneal reflex, absent pupillary light reflex, deviation of angle of mouth, weakness or abnormal movements or posturing of one or more limbs,

confusion, irritability, loss of consciousness, decorticate or decerebrate rigidity, irregular respiration.

- iii. **Symptoms and Signs of Raised Intracranial Tension:** Headache, vomiting, up going plantars & Abducent nerve palsy (false localizing signs), exaggerated deep tendon reflexes, absent pupillary light reflex on one side (early sign of temporal lobe herniation and compression of III cranial nerve), hemiplegia (late sign of temporal lobe herniation and compression of the brain stem), Bradycardia (due to stimulation of cardioinhibitory area), hypertension (due to stimulation of vasopressor area), irregular breathing (brainstem damage), squint (III or IV or VI cranial nerve palsy).

- iv. **Symptoms and signs of meningeal irritation:** Neck rigidity, Kernig's sign (limitation of knee extension when the hip is flexed to 90°) etc.

Clinical deterioration may be considered in the early stages for the diagnosis of encephalitis, in an epidemic situation even if other signs are absent.

The author has not seen acute flaccid paralysis (reported from Vietnam) due to JE so far among more than 12,500 cases since 1979 in AP.

Diagnosis:

The clinical symptomatology of all Viral Encephalitides is similar and therefore clinical diagnosis at best can only be an educated guess and is made by the association of encephalitis and some symptoms & signs with possible viruses, as mentioned in the accompanying table No 3.

Clinical Assessment: A basic doctor or health worker can make an accurate clinical diagnosis and plan further management immediately so that morbidity and mortality can be significantly brought down. Simple clinical observations help in assessing the depth of coma, planning emergency measures necessary to save the child, disability limitation, and prognostication. This must be followed by neurologic

examination for any localizing signs and to plan for the urgent investigations for a final diagnosis.

Table No. 3 Educated Guess about probable Virus

<u>Symptoms and signs</u>	<u>Probable causative Virus</u>
Summer Colds / Diarrhea / pharyngitis / abdominal pain / rash / Respiratory symptoms / Herpangina / pleurodynia / myocarditis	Enterovirus
Preceding epidemics of Conjunctivitis	Enterovirus 70
Smell / Taste / behavioral abnormalities	Herpes Simplex
Respiratory symptoms / Epidemics of cold	Adenovirus
Rash	Enterovirus, Adenovirus, Measles.
Conjunctivitis	Adenovirus, Enterovirus 70, Measles.
Parotitis	Mumps, Enterovirus, Epstein-Barr virus, HIV
Pharyngitis	Adenovirus, Enterovirus, Epstein-Barr virus, other respiratory viruses
Adenopathy	Epstein-Barr Virus, Cytomegalovirus, HIV
Croup	Measles, Adenovirus, Influenza
Bronchiolitis	Adenovirus, Influenza
Pneumonia	Adenovirus, Measles, Varicella, 6 Cytomegalovirus, Dengue
Enteritis	Enterovirus
Hepatitis	Adenovirus, Cytomegalovirus, Varicella, Epstein-Barr virus

Table 4 shows a simple practical way of rapid assessment of depth of coma by inspection alone.

Table 4: Rapid assessment of depth of coma by inspection:

<i>Depth of Coma</i>	<i>Clinical Observation</i>
<i>Coma is not very deep</i>	Child lies in a natural, comfortable position as in sleep Yawns Sneezes.
<i>Deep coma</i>	Open eyelids and hanging jaw (reduced tone)
<i>No prognostic value</i>	Other automatisms such as coughing, swallowing or hiccupping

There is another simple but crude way (Table 5) of assessing the state of decreased consciousness.

Table 5

Term	Assessment by
<i>Lethargic</i>	Difficulty in maintaining aroused state
<i>Obtunded</i>	Cerebral alerting to stimulation other than pain
<i>Stuporose</i>	Responds only to pain
<i>Comatose</i>	Unresponsive even to pain

Glasgow coma scale (GCS) is a more reliable way of assessing the depth of coma. Though developed for head injury cases, it can be used for other causes of coma like encephalitis also. It is used clinically to assess whether the unconscious child serious or not and whether he is improving or worsening. If the score is worsening, the child may be shifted to a better medical center. This scale assigns points for the best motor and verbal responses, as well as for the presence of eye opening. It has limited usefulness because it minimizes the importance of brain-stem reflexes.

Table 6: GLASGOW COMA SCALE:

Activity	Best Response	Score
<i>Eye Opening</i>	1. Spontaneous	4
	2. To Verbal Stimuli	3
	3. To Pain	2
	4. None	1
<i>Verbal</i>	5. Oriented	5
	6. Confused	4
	7. Inappropriate Words	3
	8. Nonspecific Words	2
	9. None	1
<i>Motor</i>	10. Follows Commands	6
	11. Localizes Pain	5
	12. Withdraws in response to Pain	4
	13. Flexion in response to Pain	3
	14. Extension in response to Pain	2
	15. None	1
Note: Signs 1,2,5,7,8,10,11 indicate cerebral cortical response Signs 3,12,13,14 are brainstem responses Sign 6 could be cortical or brainstem response		

Although no single clinical sign reliably predicts the outcome of coma, certain signs are associated with either good or poor likelihood of functional recovery.

Unfavorable signs, on admission include

- i. Lack of pupillary reactions to light,
- ii. Oculocephalic or oculovestibular reflexes,
- iii. Corneal responses, or
- iv. The presence of flaccidity.

Additional unfavorable signs, when persistent for 24 or more hours, include

- i. Lack of eye-opening and
- ii. Absence of spontaneous eye movements,
- iii. Normal oculocephalic or oculovestibular reflexes,
- iv. Normal muscular tone, and
- v. Purposeful motor responses.

Note about interpretation of Glasgow Coma Scale:

- a. Child's developmental level affects the response and GCS score necessitating consideration of age for assessing the status of the child. Though motor response and eye opening are same, verbal response has to be modified in infants and young children with expected or achieved speech milestones. This limits the maximum possible scores to 9 up to 6 months, 11 at 6-12 months, 12 at 1-2 years, 13 at 2-5 years, and reaching adult scores only after the age of 5 years.
- b. Score less than 5 indicates a grave prognosis
- c. Score of 5 - 8 has a better prognosis in the child than in the adult.
- d. Even a dead body will have a Glasgow Coma Scale of 3
- e. Maximum score is 15.

Laboratory Confirmation of diagnosis: CSF lymphocytic pleocytosis with normal glucose level is diagnostic of viral encephalitis. It is extremely important to check Blood glucose also simultaneously with CSF so that tuberculous meningitis can be confidently excluded. Hypoglycemia due to fasting occurs in encephalitis resulting in secondary reduction of CSF glucose and confusing the diagnosis. Serological tests done even by the world's best laboratory can confirm the diagnosis in only about 25% of viral encephalitis cases. The rest 75% cannot be confirmed but can only be clinically suspected.

Serological tests: Serological analysis of all cases is neither possible nor necessary for diagnosis of the epidemic because of the cost involved. A few representative sera samples may be sent for serology.

The diagnosis of JE is by detection of IgM antibodies, which appear after the first week of onset of symptoms and are detectable for one to three months after the acute episode. 5 ml blood is to be drawn, kept at room temperature for 30 minutes (for blood to clot), then kept at 4° C in the refrigerator for 30 minutes (for the clot to retract); serum is separated and sent in a cold chain for serological testing.

New Serological Test: A new commercial enzyme-linked immunosorbent assay (ELISA) for the diagnosis of Japanese encephalitis virus infections showed a sensitivity of 88% with sera and 81% with cerebrospinal fluid and a specificity of 97% with sera from patients with primary and secondary dengue virus infections. Specificity was 100% when samples from nonflavivirus infections were tested.

Demonstration/isolation of virus/antigen from CSF/brain, though ideal, is still not feasible on a large scale.

Neuroimaging: MRI is superior to CT scan of Brain. Cranial MRI reveals either mixed intensity or hypo intense lesion on T₁ and hyper intense or mixed intensity lesion on T₂ in thalami. Thalamic changes may be helpful in the diagnosis of JE especially in endemic area¹.

In Nipah virus encephalitis, multiple small bilateral foci of T2 prolongation within the subcortical and deep white matter are frequent².

Differential Diagnosis:

In an epidemic situation, altered sensorium, acute onset, worsening clinical status, symptoms and signs of infection (fever) and focal or asymmetric brain damage [Asymmetrical symptoms / signs mean any newly appeared difference between right and left sides and may be evidenced by sudden appearance on one side of body of paralysis, focal fits, involuntary movements {tremors, ballismus, chorea, athetosis, cycling, pedaling}, abnormal posture of limbs (dystonia), squint, or deviation of angle of mouth or tongue {when put out}] should lead to the clinical diagnosis of encephalitis in general. If there is no asymmetry on the first day, repeat examinations are necessary during the subsequent 3 days. Asymmetric or abnormal pupillary light reflex or Doll's eye movements, if present, increase the diagnostic accuracy to 100%. CSF changes like normal glucose, elevated proteins and lymphocytosis confirm the diagnosis of encephalitis. The CSF lymphocytic cell count usually ranges from 6-200 cells/cmm (complete range 6-1000). Neutrophils are seen in early few hours of acute phase and lymphocytes after the first few hours.

When there is no epidemic, these changes suggest one of the following:

- a. other viral meningitis or encephalitis
- b. Bacterial meningitis in the resolving or partially treated phase,
- c. parameningeal infections (e.g., intracranial abscess, sinusitis, mastoiditis, cortical vein thrombophlebitis),
- d. Tuberculous or fungal meningitis in the early phase,
- e. parasitic infections (e.g., toxoplasmosis, trichinosis),

- f. postinfectious encephalomyelitis, or
- g. active demyelinating disease.

Serological tests and viral cultures pinpoint the virus responsible for the encephalitis (see above).

Cerebral Malaria: If there are cases of Malaria in the area or if there is a clinical suspicion of Malaria, repeated peripheral blood smear examination (4-6th hourly, if necessary) for Malarial Parasite is important since cerebral malaria can mimic encephalitis, (but symptoms and signs are almost always symmetrical here) and is treatable with antimalarials with good prognosis if diagnosed early.

Reye's Syndrome: A combination of viral illness with 1-3 days of sudden and intractable vomiting should suggest this diagnosis. It is usually not seen as epidemic except when there is an epidemic of Influenza B (it presents in young children with fever, vomiting, diarrhea and abdominal pain and in older children & adults with high fever, headache, severe myalgia, and chills). Measles and varicella zoster emerged as the probable etiologies for the viral prodrome precipitating cases of Reye's syndrome in North India. Aspirin might have had a contributory role and Malathion was another putative cofactor in these reported cases³. (Influenza A or chickenpox infection cause sporadic cases). History of having used aspirin, prodromal Upper Respiratory Tract Infection, altered sensorium, raised intracranial pressure, absence of clinical jaundice / symmetrical symptoms or signs / splenomegaly, presence of hypoglycemia / hyperammonemia, prolonged prothrombin time, normal or slightly elevated Bilirubin, normal cell count in CSF but reduced glucose, are other features of this syndrome. Hepatic microvesicular fatty infiltration is pathognomonic of Reye syndrome.

The treatment is like that of JE but in addition require Vit K₁, 3-5 mg IM or fresh plasma for hypoprothrombinemia, restriction of protein for hyperammonemia, gastric lavage & catharsis for gastrointestinal bleeding. Maintenance fluids using 10% Dextrose should be given at a rate sufficient to produce a urine flow of 1-1.5 mL/kg/h. Particular attention must be paid to normalizing the raised intracranial pressure.

Pyogenic Meningitis: Meningeal irritation symptoms and signs occur early and loss of consciousness occurs later than in JE. CSF

shows reduced glucose with neutrophilia (up to few thousands/cmm).

Tuberculous meningitis: Since there will be CSF lymphocytosis in both JE and TBM, the only simple way of differentiation is by demonstrating reduced CSF glucose in TBM. In our experience, hypoglycemia is frequent in JE resulting in low CSF glucose leading to an erroneous diagnosis of TBM. It is for this reason sending simultaneous samples of CSF and blood for glucose is extremely important.

Presence of Papilledema in a suspected case of JE should suggest Tuberculous meningitis (CSF lymphocytosis [up to 1000 lymphocytes/cmm with reduced glucose]; or ruptured Brain abscess resulting in Pyogenic meningitis (CSF neutrophilia – more than 10,000 neutrophils/cmm and reduced glucose), both of which require additional specific therapy immediately.

Bulbar Poliomyelitis is not seen as epidemics at present. It is suspected by history of having not received polio vaccine, seizures being conspicuously rare and Polio is confirmed by virus isolation from stool.

Management:

There is NO SPECIFIC TREATMENT for JE, meaning that there is only NON-SPECIFIC TREATMENT. Antibiotics are not effective and no effective anti-viral drugs are available. Does this mean that we have to accept a case fatality rate of 35 to 50% ?.

No! It has been the author's experience over the last two decades that **IGNORANCE is killing more children than JE virus per se.**

As per our study, only 1 death out of every 6 deaths is directly due to JE virus and 5 out of 6 are preventable with prompt and early management bringing down the USUALLY REPORTED case fatality rate of JE from 35-50% to less than 10%. Similar degree of lowering of morbidity is also possible.

As there is no specific treatment for JE, the purpose of arresting or minimizing the damage, preventing complications and death is achieved by symptomatic treatment alone and is similar for all viral encephalitides except for Herpes Simplex Encephalitis. **Herpes simplex encephalitis is the only treatable viral encephalitis. Olfactory/gustatory/behavioral problems are characteristic. It presents as sporadic cases and NEVER as epidemics and is treated with Acyclovir 10mg/Kg every 8 hours, infused in 100 ml of standard Intravenous fluid over a 1-hour period for 14-21 days.**

Our study involving 12,506 cases since 1979 in AP revealed that main causes of Mortality and Morbidity are:

1. Pulmonary aspiration of saliva or vomitus
2. Hypoxia
3. Hypoglycemia
4. Uncontrolled Seizures
5. Hyperpyrexia
6. Raised ICT
7. Pulmonary Edema
8. Secondary Infections
9. Brainstem involvement
10. SIADH.

So, the treatment is mainly directed towards preventing and treating complications. By prevention / treatment of complications, 75% of mortality and morbidity can be prevented.

A). If the caes is in a village, it may be referred to an Encephalitis center, but before the case is referred from a Primary Health Center, the doctor or nurse can give the following treatment:

- a) Check breathing and keep the airway patent with an airway.
- b) Check pulse. If pulse is feeble, elevate the legs.
- c) Avoid flexion of neck to ensure patent airway and proper venous return.
- d) Turn the patient to one side to avoid aspiration and suck the throat secretions from the cheek with a mucus sucker. If vigorous suction is done in supine (child on its back) position from the throat, there is a risk of excessive throat stimulation resulting in cardiac arrest due to vagal stimulation.
- e) Turn the child from one side to the other at least hourly to prevent bedsores. Clean with spirit and apply any talcum powder to the dependent parts.
- f) Give 5 ml/kg of 10% Dextrose in warm water as a retention enema. It is prepared by dissolving 2 level teaspoonfuls of glucose powder (or 6 ml of Honey) in 100 ml of warm water. Note: The volume of fluid that may be given rectally (for retention and absorption) is 150 ml for young children and 250 ml for older children.
- g) To treat seizures: Paramedical workers also can give this treatment with one hour's training.

Rectal administration:

- i. Diazepam: Less than 3 years of age – 5 to 7.5 mg; More than 3 years of age – 7.5 to 10 mg. Diazepam rectal

- solution is available. Otherwise, oral syrup may be diluted 1:1 with ordinary water and used.
- ii. Valproate Suspension 30 mg/Kg orally or 60 mg/Kg as retention enema. Oral syrup may be diluted 1:1 with ordinary water and used.
 - iii. Inj. Paraldehyde 4 %, 0.1 - 0.3 ml/Kg, IM or diluted 1:1 with distilled water rectally. It can be repeated after 15 - 30 minutes.
 - h) If there is fever with chills: Give paracetamol 20 mg/Kg diluted in 50 ml saline as a retention enema. Oral syrup may be diluted 1:1 with ordinary water and used.
 - i) If there is fever without chills: Tepid (ordinary) water (not cold water) sponging should be done till the temperature becomes normal.
 - j) If the child is cold, wrap up the child in clothing.
 - k) Raised Intracranial Tension: is indicated by slow heart rate / irregular breathing / squint / one pupil dilated and not constricting to light, headache, vomiting, hemiplegia – one side paralysis (late sign of temporal lobe herniation and compression of the brain stem).
Keep the child in supine position (child on its back) with head end elevated by 30°. Inj Frusemide 1mg/Kg IM 2 times daily. Don't use if there is dehydration. It can be given orally, if there is no doctor or nurse available.
 - l) Oral hygiene by the nurse must be done regularly.
 - m) An extremely hypothermic or febrile child may require vigorous cooling or warming to save life.
 - n) Branding must never be allowed. It does no good and has so many bad effects like secondary bacterial infection & damage to the skin resulting in a scar which becomes bigger & bigger as the child grows.

The danger signals are:

1. Open eyelids
2. Hanging jaw
3. Rapid breathing
4. Accumulation of lung secretions
5. Appearance of excessive sweating
6. Eyes not moving
7. Pupils not constricting to light
8. Persistence of fever, and
9. Absence of response to pain

Technique of Rectal Administration of Drugs

To give drugs rectally, insert a small feeding rubber tube 2.5 cm and then inject the medication (or glucose solution) with a 5ml syringe through it and then tie the outside end of the rubber tube and strap the buttocks with adhesive tape, and keep the patient in lateral position.

Essential equipment at the village level:

1. Air way Sizes "0" and "1",
2. Mucus sucker,
3. Rubber feeding tube size 14,
4. 5 ml Syringe,
5. Thermometer,
6. Adhesive tape
7. Glucose powder
8. Enema set

Essential Drugs at the Village level:

- a. Syrup Paracetamol,
- b. Diazepam rectal solution or Syrup Diazepam,
- c. Suspension Valproate,
- d. Glucose powder
- e. Tab/Inj Frusemide
- f. Inj Paraldehyde

B). Management in small Hospitals where average medical and nursing care can be given, but there is no ventilator facility.

1. Establish an adequate airway. Use an Ambu bag if necessary. Suction throat secretions as and when necessary.
2. Administer oxygen, if possible, even if there is no cyanosis (improvement was faster in our study).
3. Failure of autoregulation of the brain makes the cerebral circulation depend solely on systemic blood pressure. So, insert a large bore IV catheter (for less than 3 years 23G, for more than 3 years 22 G) and stabilize circulation. Fluids, plasma, blood or even a dopamine drip (5-20 µg/kg/min) might be necessary in cases of hypotension.
4. Avoid fluid overload.

5. Hypoglycemia is very frequent. So draw blood for glucose and give 1 ml/kg of 50% Dextrose which supplies 0.85 kcal/ml. IV dextrose suppresses gluconeogenesis and provides a substrate that can be oxidized directly, especially by the brain, RBC & WBC.
6. Seizure management: Avoid Phenobarbitone as it sedates the child and so interferes with the assessment of depth of coma.
 - a) IV Diazepam 0.1 - 0.3 mg/Kg in 1-5 minutes. The dose may be repeated in 5 - 20 minutes.
 - b) Rectal Diazepam: Diazepam for rectal administration: Less than 3 years of age – 5 to 7.5 mg; More than 3 years of age – 7.5 to 10 mg. Diazepam rectal solution is available. Otherwise, oral syrup may be diluted 1:1 with ordinary water and used.
 - c) Inj. Paraldehyde 4%, 0.1 - 0.3 ml/Kg, IM or diluted 1:1 with distilled water rectally. It can be repeated after 15 - 30 minutes.
 - d) Valproate Suspension: Valproate Suspension 30 mg/Kg orally or 60 mg/Kg diluted 1:1 in water as retention enema, May be repeated 3 times daily in a dose of 10-20 mg/kg/dose.
 - e) Phenytoin 10 - 20 mg /Kg over 10 - 20 minutes at a rate of less than 1 mg/Kg/Minute. Repeat dose of 5 - 10 mg /Kg IV may be given after 1 hour, up to a maximum of 1000 mg. Never give IM, Mix only in normal saline (never in dextrose). Then, flush the line with a few ml of normal saline since Phenytoin irritates the veins due to its high pH (pH is 12).
 - f) Give maintenance drug (if only diazepam was enough to stop Status Epilepticus), Phenytoin 5 - 10 mg/Kg may be given through a Nasogastric tube, Valproate if used, may be continued 30-60 mg/kg/day in 3 divided doses.
7. For raised Intracranial Tension:
 - a) Normalize temperature. The increased metabolic demand from Hyperthermia increases cerebral blood flow (CBF), cerebral blood volume (CBV) and intracranial tension/pressure (ICP). Increased CBV & ICP result in increased cerebral edema, reduced CBF and deterioration of the supply to demand ratio. Shivering (can occur during sparging) increases ICP by increasing pleural

- (intrathoracic pressure). This can be prevented by promethazine 1 mg/kg in 3 divided doses in a day.
- b) Mannitol is an osmotic diuretic, draws fluid from the interstitium into the central circulation, causing a reduction in the ICP. It also lowers blood viscosity, alters the microcirculation in the brain and acts as an oxygen radical scavenger to reduce cellular damage and further secondary injury. Mannitol infusion loading dose is 5ml/kg (1g/kg) of 20 % Mannitol IV rapidly over less than 20 minutes, followed by 1.25 ml/kg (0.25 g/kg) every 6-12 hours to treat persistent ICP elevation. Mannitol (& Glycerol) slowly cross the blood brain barrier and on reaching a significant concentration after a few days results in water entering the brain from the vascular compartment due to osmotic pressure gradient. This is called rebound phenomenon. To delay this Mannitol must be used at a dose of only 0.25 g/kg and not higher doses. Urine output must be carefully monitored and replaced to avoid hypovolemia & hypotension. Mannitol is contraindicated in Congestive Cardiac Failure and Pulmonary edema.
 - c) Oral Glycerol 0.5 ml/Kg diluted in twice the volume of water or fruit juice 3 times daily may be used if the child can take orally.
 - d) Give Mannitol for the first three days followed by oral glycerol (either orally or through nasogastric tube) for a few days and then taper it off over the next few days. Osmotic diuretics like mannitol / glycerol must be used in minimum necessary doses for the minimum necessary period only.
 - e) Role of Steroids is controversial.
 - f) In an emergency situation, elevate the head end to reduce the ICP. Hyperventilation with an Ambu bag can be used to reduce the intracranial tension immediately. *Long-term hyperventilation must not be done as it is not useful.*
 - g) If there is pulmonary edema: Inj. Frusemide 1 mg/Kg/dose IM 2 times daily. Don't use if there is dehydration.
8. LP and CSF analysis if possible. CSF shows elevated lymphocytes and Protein but normal glucose levels.

9. Urinary catheterization in all unconscious children is a must. If not done, bladder distension makes the child restless. This restlessness will not respond to sedatives. Intermittent clamping of Catheter must be done to maintain bladder tone. Catheter may be removed when the child regains consciousness.
10. Prevent aspiration. Suck the throat secretions as and when necessary. Pass a Nasogastric tube and suction from the stomach if necessary. If excess throat secretions are a problem, keep the child on its side with the head slightly lowered.
11. *Method of suctioning Throat Secretions:* Turn the patient to one side to avoid aspiration and suck the throat secretions from the cheek with a mucus sucker. If vigorous suction is done in supine position from the throat, there is a risk of excessive throat stimulation resulting in cardiac arrest due to vagal stimulation.
12. Turn the child from one side to the other at least hourly to prevent bedsores. Clean with spirit and apply any talcum powder to the dependent parts.
13. If raised intracranial tension is the problem, place the child in supine position with head end elevated by 30°. Prevent flexion of neck and any possible obstruction to neck veins (caused by turning of the head to a side).
14. Minimize external stimulation since it will increase brain metabolism and so increase brain damage in the face of limited oxygen & nutrient supplies. Bright lights and loud noises and vigorous tactile stimulation are to be avoided as far as possible. Crying or conversation, even by parents, near the child must be avoided.
15. Restlessness and agitation during recovery may require diazepam (0.04 to 0.2 mg/kg or chloral hydrate 4-40 mg/Kg/dose orally or rectally every 8 hours or Haloperidol (0.05 to 0.15 mg/Kg/day {maximum 6 mg/day} in 2 or 3 divided doses) may be used. Sudden withdrawal of chloral hydrate results in delirium or seizures.
16. An extremely hypothermic or febrile child may require vigorous cooling or warming to save life. Ref to 6.a.
17. Give a sponge bath daily.
18. Oral Hygiene. Cleaning the mouth regularly with plain water reduces oral sepsis.
19. Prevent and treat pain.

20. Any correction of serum sodium abnormalities must be done slowly in order to prevent central pontine myelinolysis.
21. Nutrition & fluids are given by Ryle's tube if there is no risk of aspiration. Routes of oral feeding may be nasogastric or orogastric.

Enteral nutrition is better than total parenteral nutrition in the critically ill patient because of its beneficial effects directly on the gastrointestinal integrity and indirectly on hormones and immune function. Gastric emptying and colonic motility are decreased in critically ill patients but small intestinal motility, digestion & absorption remain adequately functional. Bowel sounds are not reliable indicators of small intestine function. Early enteral feeding blunts the hypermetabolic or hypercatabolic response (breakdown of skeletal muscle, gastrointestinal mucosa, and other tissues (to provide nutrients to vital organs) to critical illness by the neuroendocrine system. Therefore the dictum is **"if the gut is available, use it"**. Luminal nutrients directly, and by releasing gut trophic hormones (enteroglucagon etc) indirectly, increase gut blood flow, prevent Intestinal mucosal atrophy, maintain the gut barrier, prevent gut bacterial invasion by supplying adequate nutrients to maintain the high metabolic rate and constant turnover of enteric mucosal cells, maintain gut-associated lymphoid tissue & secretory IgA, and maintain adequate hepatic function. Glutamine & ketones are the nutrients for the small bowel and, short-chain fatty acids derived from dietary fiber (fiber is present in adequate quantities in Fruits & Vegetables) by bacterial fermentation, for the Colon. Parenteral feeding alone reduces bacterial counts in the colon and compromises fuel supply to colonocytes. Mucosal atrophy is hastened by the deficiency of glutamine (not available in most of the parenteral fluids).

Nutrient administration should be initiated as soon as possible.

The standard tube feeding formula should contain 1kcal/ml. Protein requirement is calculated as 1 g/kg/day. Calorie and fluid requirements are met with by using fortified milk. See Table 7.

When gastric or nasogastric tube feeding is initiated or increased, residual gastric volumes should be checked every 4 hours to determine that residual volumes do not exceed 50% of the volume delivered. If it exceeds, the quantity of milk for the subsequent feed may be reduced. See table 4. Once this dose is tolerated, additional increments of milk may be given or calorie

concentration may be increased by adding additional sugar/oil/any flour etc.

Table 7. Formula of Fortified milk to be fed through Ryle's tube

Nutrient	Quantity	Energy in kcal	Protein in g
Sugar	2 g [#]	8	
Oil (coconut or any vegetable oil)	3 ml [*]	27	3
Milk to make	100 ml	100	3
Total	100 ml	100 kcals	3

[#] 2 Gms is slightly less than ½ teaspoon

^{*} 3 ml is slightly more than ½ teaspoon

After the first two days, raw egg white, fruit juices, buttermilk, vegetable soups, any flour mixed in milk, and medications may be added to enriched milk and can be given through the Ryle's tube.

Technical complications of enteral nutrition are quite common and are due to misplacement of feeding tube. Malpositioned feeding tubes are most often associated with blind bedside methods of tube placement. Critically ill children are at increased risk for misplacement into the endobronchial tree or pleural space, secondary to alterations of mental status induced by brain damage, absence of the gag reflex, inability to cough, or dysphagia. To avoid pulmonary damage and pneumothorax, the tube position in the gastrointestinal tract must be confirmed by aspiration of gastric contents (pH 2 to 4 – check with litmus paper), aspiration of bile (green in colour) or radiography. Alternatively direct laryngoscopy can visualize the tube passing into the esophagus. Auscultation can be misleading. A feeding tube placed into the base of the left lung can produce sounds similar to those heard in tubes placed into the stomach.

Pulmonary aspiration is one of the most serious complications of enteral feeding. Large gastric volume, patient's position (supine) predisposes to gastric reflux and aspiration. Elevating the head of the bed to 30°, keeping the child in prone position, advancing the nasogastric tube to a transpyloric position, treating gastroparesis with promotility agents (i.e., erythromycin, domperidone, or cisapride) may be useful in decreasing gastric volume and the risk of aspiration.

Diarrhea, erosions at insertion sites, sinusitis, and otitis media are other possible complications of enteral feeds.

Once the child is able to eat, semisolids & solids may be given.

22. IV Fluids: If there is risk of aspiration, IV maintenance fluids are given. Avoid fluid overload. Avoid 5 % Dextrose solution for maintenance. Always Use ½ Normal saline in 5 % Dextrose (if it is not available, mix 500 ml of 10 % Dextrose with 500 ml of Normal Saline and use this solution) in a dose of 70 ml/Kg/24 hours at the age of 1 year and 35 ml/Kg/24 hours at the age of 15 years. Ringer's lactate may also be used. Any losses as Vomiting or Loose motions have to be compensated in addition.

Body Weight in Kgs	Quantity of fortified milk per feed	Body Weight in Kgs	Quantity of fortified milk per feed
10	165	25	270
11	175	26	270
12	185	27	270
13	190	28	280
14	200	29	280
15	210	30	280
16	220	31	285
17	225	32	290
18	235	33	295
19	240	34	295
20	250	36	300
22	260	38	310
23	260	40	315
24	260	50	350

Table 8 showing the approximate quantity of milk per each of 6 feeds per day. Such milk feeds are given 6 times daily. Small quantities of water are given in between feeds.

22. Supplement therapeutic doses of vitamins like B Complex, C, D, E & K and other micronutrients (iron, zinc, copper, chromium) must be given.

23. Bowel care: Prevent and treat impaction.

24. Prevent corneal injury by taping the eyelids closed or by methylcellulose eye drops.

25. The treating doctor can use

antibiotics depending on necessity as urinary tract infection or/and pulmonary infections/nosocomial infections (Hospital acquired infections from other inpatients) can occur. We found

third generation cephalosporins, ampicillin & aminoglycosides to be useful.

26. Stress ulcers occur occasionally and are often multiple and associated with hemorrhagic gastritis and erosions, and may be terminal events. Cimetidine (20-40 mg/kg/day in 4 doses or Ranitidine (4-6 mg/kg/day in 2 doses) may be used orally or Inj Ranitidine may be used.

Poor prognostic signs are:

- Open eyelids,
- Hanging jaw,
- Dilated nonreacting pupils,
- Rapid breathing,
- Accumulation of bronchial secretions,
- Appearance of excessive sweating,
- Abnormal spontaneous eye movements or Dolls eye movements, Pupils not constricting to light,
- Persistence of fever,
- Refractory seizures,
- Decerebrate posture,
- Decorticate posture.

If the child with these problems is being shifted to a better hospital, a medical attendant must accompany the patient.

Essential equipment at the Secondary level Hospital:

- Air way Sizes "0" and "1",
- Mucus Sucker,
- Rubber feeding tube size 14,
- 5 ml Syringe,
- Thermometer,
- Adhesive tape,
- IV cannula, 22, 24,
- Burette sets,
- Ambu Bag,
- Foley's Catheters of various sizes
- Lumbar Puncture sets
- Provision for Cerebrospinal fluid analysis
- Ryle's tube
- Enema set

Essential Drugs at the Secondary level Hospital:

1. Syrup Paracetamol,
2. Rectal solution or Syrup Diazepam,
3. Suspension Valproate,
4. Syrup Chloral hydrate,
5. Inj Diazepam,
6. Inj Phenytoin,
7. IV fluids N/2, N/5 with 5 % Dextrose, Hypertonic saline, 50% Dextrose
8. Normal saline,
9. Inj Dexamethasone,
10. Inj Mannitol 20 %,
11. Inj Frusemide,
12. Oral Glycerol
13. Inj Dopamine
14. Vitamins
15. Ringer's Lactate
16. Syrup / Tab Haloperidol
17. Syrup Chloral Hydrate
18. Inj Paraldehyde

Referral :Patient may be referred to Tertiary care Hospital after providing medical & Nursing supervision during transport if there is

- i. Brainstem involvement
- ii. Cardiac arrest require resuscitation measures.
- iii. Uncontrolled Seizure activity
- iv. SIADH

Care in Tertiary Level Hospitals:**Additional Complications requiring management:****Critical care units:**

- i. Brainstem involvement may necessitate intubation & mechanical ventilation may be required.
- ii. Cardiac arrest require resuscitation measures.
- iii. Uncontrolled Seizures require a general anesthetic.
- iv. SIADH (Syndrome of Inappropriate Anti Diuretic Hormone) Water retention with volume expansion and sodium wasting are responsible for hyponatremia. SIADH is diagnosed by

- a. Hyponatremia with corresponding serum hypoosmolality
- b. Urine osmolality greater than appropriate for concomitant serum osmolality (i.e., less than maximal dilute)
- c. Continued urine sodium excretion that is excessive for the degree of hyponatremia, with elevated urine sodium concentrations
- d. Normal renal, adrenal & thyroid function
- e. Absence of volume depletion

Give only maintenance plus replacement fluids.

Very slow hypertonic saline infusion must be done if hyponatremia is associated with concentrated urine (osmolality >300 mosmol/kg), in the absence of edema, hypotension or dehydration. Concomitant use of Frusemide can increase free water excretion relative to sodium excretion and diminish volume expansion induced by hypertonic saline.

Method of sodium repletion is important to prevent Central Pontine Myelinolysis. Hypertonic saline (3%) is given only if hyponatremia has induced seizures (clinical hint: metabolic seizures are always generalized or multifocal, JE induced seizures are focal) or other brain dysfunction. In cases of severe hyponatremia (Serum Sodium <120 meq/L, IV 3% Na Cl is given over 1 hour to raise the sodium to 120 meq/L. In general, 6 ml/Kg of 3% Na Cl will raise the serum sodium by 5 meq/L if 3% Na Cl is given, estimated sodium & fluid deficits should be adjusted accordingly. Further correction should be done very slowly by using the formula:

Sodium deficit=

$$(\text{Sodium desired}-\text{Sodium Observed})\times \text{body Wt (Kg)} \times 0.6$$

One half the deficits are given in the first eight hours and the remainder over the next 16 hours. The rise in serum Sodium should not exceed 2 meq/L/h. Maintenance & replacement fluids also must be administered using 5% dextrose with 0.45% saline.

What if this treatment is given to other cases presenting with Coma?

Any other coma case also will improve with these measures. However, other causes of coma might require additional specific measures.

Long Term Therapeutic Measures:

Physiotherapy and rehabilitation measures may be instituted in survivors with residual neurological deficits.

Referral of Complicated cases:

The case may be referred to Pediatric Neurology Department available at Niloufer Hospital, Hyderabad; Institute of Child Health, Chennai, or SAT Hospital, Trivandrum, for management of complications and sequelae. Seizures, movement disorders, spasticity and rigidity are treatable and various training programs are available for the mentally handicapped children.

Drug therapy of sequelae

1. **Spasticity:** Benzodiazepines, Baclofen, Dantrolene, Tizanidine, Clonidine, Phenytoin + Chlorpromazine, Vigabatrin
2. **Hemiballismus** – chlorpromazine
3. **Choreoathetosis** – Haloperidol (blocks dopamine receptors), Tetrabenazine (depletes central monoamines), Pimozide, Phenothiazines
4. **Dystonia** –Diazepam, Baclofen, CMZ, amantadine, trihexyphenidyl, Levodopa, and for focal dystonia - Botulinum A toxin
5. **Myoclonus** – VPA, CNZ, 5 OH Tryptophane
6. **Tremor**
 - a. Rest – trihexyphenidyl
 - b. Action – Propranolol
 - c. Intention – Buspirone (Serotonin agonist)

Long Term Preventive Measures:

Measures to control mosquitoes, pig reservoirs, environmental sanitation, mosquito nets, and vaccination of the susceptible population will go long way in prevention of JE; Environmental Sanitation, Protected Food and Water supply for Enteroviruses.

Prognosis:

Sequelae include seizures, paralysis, psychiatric problems, movement disorders etc.

Earlier statistics indicate that for JE the rule of thirds applies. 33.3% recover well. 33.3% suffer significant morbidity and 33.3% die. With implementation of above management guidelines, (which can be implemented even in a poorly equipped dispensary in a village), the mortality and morbidity can be brought down significantly (mortality <10%, morbidity <20% and normal 70%) as has been done in our Department of Pediatric Neurology, Niloufer Hospital, Hyderabad, India.

Preventive Measures:

1. **Vector Control:** In spite of the fact that the principal vector of JE, *Culex tritaeniorhynchus*, is an outdoor biter and outdoor rester, when indoor residual spray (IRS) was undertaken for control of malaria, JE incidence was reduced significantly. Therefore in hyperendemic areas, whenever vector density increases, IRS (including animal sheds) with appropriate insecticide is necessary. Anti-larval measures may not be practical in view of the large breeding points (thousands of hectares of land) in rural areas.
2. **Agricultural practices** : Water management practice of Paddy cultivation- At least one dry day every week will conserve water, reduce larval population increase rice grain yield, and reduce the emission of methane into the environment thereby reducing the Global warming effect. Using neem products as fertilizers will also reduce the mosquito population.
3. **Animal Reservoir:** JE was controlled in Japan by vaccinating the pig population. But this is unlikely to be possible in India since there is no centralized pig rearing. So all pig rearing practices should be undertaken at least 5 Kms away from human habitations and all measures to promote pig husbandry (Bank Loans) should be subject to this condition.
4. **Vaccine:** JEV envelope protein represents the most critical antigen in providing protective immunity.

A killed JE vaccine is produced at the Central Research Institute (CRI), Kasauli from the brain of Suckling mice inoculated with the Nakayama JE strain. JE live vaccine is safe for children and effective for prevention from JE disease in JE endemic areas. At present JE vaccine is available only on a very limited scale and at a high cost only for Govt. Institutions and is not available for

sale for private doctor's use. Two doses of 1 ml each (0.5 ml for children under the age of 3 years) should be administered subcutaneously at an interval of 7-14 days. A booster injection of 1 ml should be given after 4 weeks to 1 year in order to develop full protection. Revaccination may be given after 3 years. Desirable age group for vaccination in our experience is 2-15 years. Since the risk of JE is not universal and is limited to focal areas, JE immunization is not included in the National Immunization Program in India, because the disease is restricted to agricultural regions of India. But, the feasibility of providing the vaccine to population at high risk is being examined.

As there is no Man-to-Man transmission and man is a dead end for the virus, vaccination protects only the vaccinated individual and not the community.

In epidemic situation, vaccination program should take into consideration, the one-month gap (after the second dose) before actual protection starts, the necessity of two doses and a third one for longer protection. This is the reason JE vaccine is not useful for control of epidemics and so must be used during inter-epidemic periods.

Unless 80-90% of children less than 15 years are vaccinated, there will not be any obvious effect on morbidity and mortality.

In endemic areas, where sporadic cases occur, throughout the year, the cost effectiveness of vaccination is very low to be considered as the method of choice.

Reactions to Vaccine:

- i. Redness, swelling, tenderness,
- ii. Malaise, headache, Fever,
- iii. Rash, chills, dizziness,
- iv. Nausea, vomiting, abdominal pain

Most of these side effects are transient.

As is the case with any other vaccine, anaphylaxis can occur immediately or as late as nine days. Laryngeal edema is a medical emergency. The allergic reaction may be rashes, urticaria, or bronchospasm.

Anaphylaxis is a MEDICAL EMERGENCY and requires admission & treatment in a hospital. Fever can be treated with paracetamol (acetaminophen).

Risk factors for allergic reactions: are young age, female gender and previous allergic skin reactions or hay fever. Cases more often react to nickel and more often had severe edema

after mosquito or other insect bites. Hormone intake was more often spontaneously reported by females in the case group⁴.

As there is no man-to-man transmission and man is a dead end for the virus, vaccination (Unlike polio) protects only the vaccinated and does not protect the community at large.

Feasibility of JE vaccine in India: China, Korea, Japan, Taiwan and Thailand faced major epidemics of JE in the past but controlled it primarily with vaccination. Can JE vaccine be given to all susceptible children in India? It is desirable, but is going to be very expensive. It may cost the country more than Rs. 600,00,00,000. Shall we restrict vaccination only to at risk children? An estimated 378 million population is living at the risk of JE in 12 states/ Union Territories.

Even if the country allots the amount, we are not in a position to have adequate supplies for all susceptible states from Kasauli. We have to see whether we can import the vaccine. When we do not have adequate supplies of vaccine, we can supply only about 0.1% of the vaccine requirement. When there is short supply of the vaccine, the medical profession will have difficulty in deciding which child must get the vaccine and why? The problem can be unmanageable in the face of pressures from various circles. When we cannot vaccinate our children, can we afford to vaccinate pigs?

When Government cannot allot such huge amounts for the recurring problem of JE epidemics, can we make it available in open market? If so can we subsidize the cost? Alternatively can we remove all taxes and subsidize mosquito nets and sell them at minimum price.

Limitations of vaccination:

- a. Limited production & high cost
- b. Protects only those who are vaccinated
- c. Require 80-90% coverage for perceptible impact
- d. Requires cold chain
- e. Adverse reactions to vaccination
- f. Require booster doses

Before we start JE vaccination on a large scale we have to answer 3 questions:

- i. Whom and when to vaccinate?
- ii. How to delimit areas for vaccination?
- iii. Since a large population is at risk, will it be cost effective?

The other aspect we have to think is whether we will be justified in spending such colossal amounts for a recurring expenditure on JE vaccine. Spending the same amount for improvement of environmental sanitation and drainage system, we can eradicate polio, and reduce the incidence and prevalence of other diseases like Malaria, Gastroenteritis, typhoid, Filariasis etc.

Newer Vaccines (not yet available in India):

JE live vaccine is safe for children and effective for prevention from JE disease in JE endemic areas⁵. A freeze dried vaccine also has been developed and proved to be stable⁶.

Co administration of JE vaccine & MMR vaccine:

It can be done. Simultaneous and nonsimultaneous vaccination with MMR and JE vaccines were similar in immunogenicity.

Role of Belladonna:

Qualified Homeopathic Physicians assure that Belladonna, a homeopathic drug, does prevent JE. We must undertake a prospective study on its efficacy. If it is proved with double blind studies, it will definitely be a cheaper and practical answer to our recurrent and regular epidemics of JE.

Vector surveillance is being monitored by 72 entomological Zones of NAMP and Regional Health and Family Organization in high risk areas. The questions requiring an answer are

- a. Feasibility of vector monitoring
- b. Usefulness of sentinel villages
- c. Critical density of vector that prompts for vector control
- d. Efficacy of IRS to prevent an outbreak
- e. How to target areas for Indoor residual spraying
- f. Role of ant larval & BE measures
- g. Agricultural practices that can prove effective when implemented on a large scale

Serosurveillance: The following institutions are identified for Serosurveillance.

1. National Institute of Virology, Pune

2. NICD (National Institute of Infectious Diseases), Delhi
3. School of Tropical Medicine, Calcutta.
4. Centre for Research in Medical Entomology, Madurai.
5. KG Medical College, Lucknow.
6. Gorakhpur Medical College, Gorakhpur.
7. Kings Institute of Preventive Medicine, Chennai
8. Burdwan Medical College, Burdwan.
9. Assam Medical College, Dibrugarh.
10. VBRI (Veterinary Biological Research Institute), Shanthinagar, Hyderabad, Andhra Pradesh.
11. Kyasanoor Forest Disease Laboratory, Shimoga, Karnataka.
12. Institute of Vector control and Zoonosis, Hosur, Tamil Nadu.
13. Central Research Institute, Kasauli.
14. Goa Medical College, Panaji.

Inter Epidemic Campaigns:

Control of JE in India requires coordinated efforts of Panchayat Raj, Municipal Administration & Urban Development for environmental sanitation; Agricultural department for convincing the farmers to follow alternate wet and dry methods of paddy fields; Medical & Health department for prevention of the disease and care of the patient; Information Department and mass media like Newspapers, TV channels for health education. Unless every individual feels his responsibility to keep the environment clean and takes personal care, JE continues to be a national problem.

Outbreak Management:

1. Vector control: In outbreak areas, IRS may not have any significant role. Fogging with technical Malathion should be carried out outdoors to bring down the vector density immediately. Anti-larval measures may not be practical in view of the large breeding points in rural areas and in addition will be ineffective.
2. Early diagnosis, First Aid & referral
3. Health Education:

Control of JE

JE Control is now the responsibility of NAMP. It is a difficult task due to

1. Limited knowledge of the transmission dynamics of JE
2. Outdoor habits of vectors
3. Sporadic nature of occurrence
4. Spread over relatively large areas
5. Relative role of different zoonotic reservoir hosts.
6. Specific vectors for different geographical and ecological areas.
7. Immune status of various population groups is not known resulting in difficulty in delineating high risk population groups, and in forecasting outbreaks.

The current strategy is as follows:

- a. Surveillance & Epidemic forecasting systems:
 - i. Sero-surveillance to delineate high-risk population groups and to monitor JE specific antibodies in sentinel animals or birds as an indication of increasing viral activity
 - ii. Vector surveillance in JE prone areas for vector behaviour and population build up for timely intervention.
 - iii. Clinical surveillance for early diagnosis, First aid and timely referral.
 - iv. Epidemiological monitoring.
- b. Interruption of Transmission: Prevention of transmission is possible through vector control. For effective control of vectors, residual insecticidal spraying has been suggested in all animal dwellings with appropriate insecticide before the onset of transmission season. During outbreaks, interruption of transmission can be achieved only by elimination of adult mosquito population, and therefore Ultra Low Volume (ULV) fogging of malathion or fenitrothion has been suggested. Because of the exophilic nature of the vector, residual spraying of insecticides and fogging operation may have only a limited role in JE epidemics.

Adult *Culex tritaeniorhynchus* mosquito, in Delhi, India, was resistant to various insecticides (DDT, malathion,

fenitrothion and propoxur) used under public health programs in India. However they were highly susceptible to synthetic pyrethroids, viz., deltamethrin - 0.025%, permethrin - 0.25%, and lambda-cyhalothrin - 0.1%. Larvae were resistant to many larvicides (DDT- 0.008, temephos- 0.02, fenthion- 0.008, fenitrothion- 0.125, and malathion- 0.005 mg/l)⁷.

Alternatively control may be attempted by Inter epidemic campaigns for Personal protection, environmental sanitation and segregation of reservoir host etc.

- c. Early diagnosis and case management.
- d. Health Education and Community involvement.

Outbreak Management:

- a. Vector Control
- b. Shifting pigs
- c. Early diagnosis of JE cases & management/referral.

Part "B"

What the parents should know about Prevention, Diagnosis and management of Japanese Encephalitis till medical assistance is available.

Introduction:

It has been the author's experience over the last decade that IGNORANCE is killing more children than JE virus per se.

Japanese Encephalitis is caused by a virus, which is carried by mosquitoes from infected pigs or water birds like pond herons and ducks to susceptible children. Susceptible children are infected by infected mosquito bites. After mosquito bite disease appears in 5-16 days.

1. Prevention & Control

The virus multiplies in pigs and water birds like pond herons & Ducks. JE Virus can spread to subsequent generations of mosquitoes by transovarial transmission. Infected pigs do not suffer from encephalitis. Presence of cattle reduces the risk of JE.

Japanese Encephalitis does not spread from man to man. So there is no danger of spread from patients of Japanese

encephalitis to attendants. It is always from pig/pond herons/ducks to man.

The virus is transmitted by 12 species of mosquitoes (8 species of Culex, 3 species of Anopheles and 1 species of Mansonia), some of which bite mainly in the evening and some during the nights. Precautions should always be taken to avoid being bitten by any mosquito both in the daytime and at night.

- a) Take necessary precautions to prevent mosquito bites, such as
 - i. Use full-sleeved clothes,
 - ii. Use mosquito nets (small mesh, preferably pyrethroid impregnated) at night tucked under mattress,
 - iii. Door & window curtains impregnated with pyrethroid, and
 - iv. Mosquito repellants.
 - v. Burn mosquito/insect coils during the evening.
 - vi. Use insecticidal spray indoors in the evening.
 - vii. While going out, use insect repellent on all exposed skin (one containing at least 30% concentration of DEET). Instructions on the package insert must be followed carefully.
- b) Scented products attract mosquitoes. So use nonperfumed cosmetics and toiletries.
- c) Avoid sleeping in or near pigsties.
- d) All the stagnant water areas around human habitation should be filled up and the surroundings of each house and the habitation kept clean and dry
- e) Air coolers, if used regularly, will not breed mosquitoes. But in winter, when they are not in use, will breed mosquitoes if there is any water inside. So remove water, dry up and cover the air cooler after summer.
- f) Open drains should be kept clean and stagnation should not be allowed.
- g) Rank vegetation in and around habitations should be cleared.
- h) Smoke generated by burning neem leaves repels mosquitoes from the vicinity of houses.
- i) Isolation of pigs is essential. The minimum distance for pigsties is 5 kms from human habitations.

- j) Water management practice of Paddy cultivation: At least one dry day every week and using neem products as fertilizers will reduce the mosquito population.
- k) Report any suspected case of Japanese Encephalitis to the Health Authorities so that immediate vector control measures like spraying of insecticides & fogging can be undertaken.
- l) Inform & Cooperate with the Health staff to effectively utilize the meager resources for antimosquito measures in the best possible way.

2. **Diagnosis can be made by parents**

JE can be recognized /diagnosed and First aid treatment must be given by parents till the child is taken to a hospital.

Diagnosis is by the presence of all of the following symptoms:

- a. The presence of similar cases in the same or neighboring district,
- b. Fever,
- c. Loss of consciousness or altered behavior appearing over 1 hour to 4 days,
- d. New development of any difference between right and left sides (like paralysis on one side, fits on one side, abnormal movements on one side or abnormal postures on one side, mouth deviating to one side, or squint).

3. **First aid Management by parents till child is taken to the doctor / hospital:**

Child must be taken to the doctor at the earliest. However, till medical assistance is available, the parents must follow the following guidelines.

- I. Keep the nose and mouth clean.
- II. Patient must be kept on the side with head in a little lower position than the body to prevent saliva from blocking the airway till the patient is reached to the doctor.
- III. Saliva must be cleared from the mouth for the same reason.
- IV. Avoid flexion of head and neck.
- V. Patient must be turned from one side to the other at least every hourly.

- VI. If the patient is very cold he must be wrapped up in clothing.
 - VII. If the child has fever, sponge the entire body with ordinary water.
 - VIII. Avoid Bright lights, loud noises and touching the patient,
 - IX. Keep the eyes closed and cover with a cloth.
 - X. Do not force the doctor to give glucose intravenously. Let the Doctor decide what is necessary for the child to survive and recover.
- Once the first-aid measures are started, take the child to the nearest encephalitis ward at the earliest.

In Conclusion

In our experience JE continues to be a National problem, not because of poverty but because of lack of Health Education.

There are regular epidemics of JE in India. Every year we try to control the problem after it reaches gigantic proportion.

The vicious cycle we see is epidemic of JE → Isolate pigs → Supply Belladonna → Natural end of epidemic → Rains → Vector increase → JE epidemic → Isolate pigs → Supply Belladonna → Natural end of epidemic. See Fig. 1.

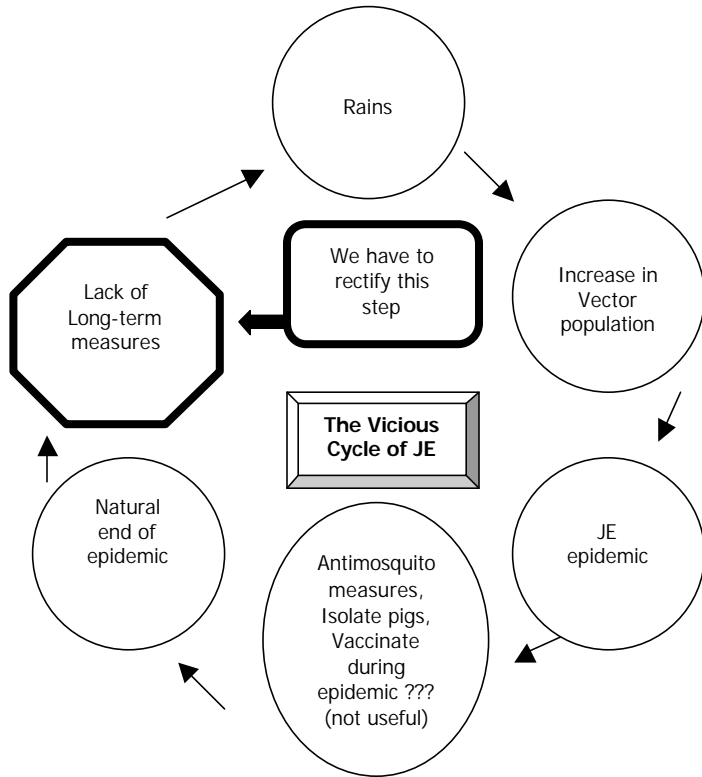
How long are we to observe this with crossed fingers? Japanese encephalitis (JE), once a major public health problem in South Korea, has declined since the 1980s, as a result of improved living conditions, a mosquito eradication program, and a national JE vaccination program, which includes annual booster vaccine for all children less than or equal to 15 years of age. Increased immunity has greatly reduced illness and death; however, vaccine adverse effects are increasing, and a National Compensation Program for Vaccine Injury was begun in 1995 in South Korea.

Control of JE in India requires coordinated efforts of Panchayat Raj, Municipal Administration & Urban Development for environmental sanitation; Medical & Health department for prevention of the disease and care of the patient; Information Department and mass media like Newspapers, TV channels for health education. Unless every individual feels his responsibility to keep the environment clean and takes personal care, JE continues to be a national problem.

JE must be made a NOTIFIABLE disease immediately. It is a high time that we all do react urgently to prevent this

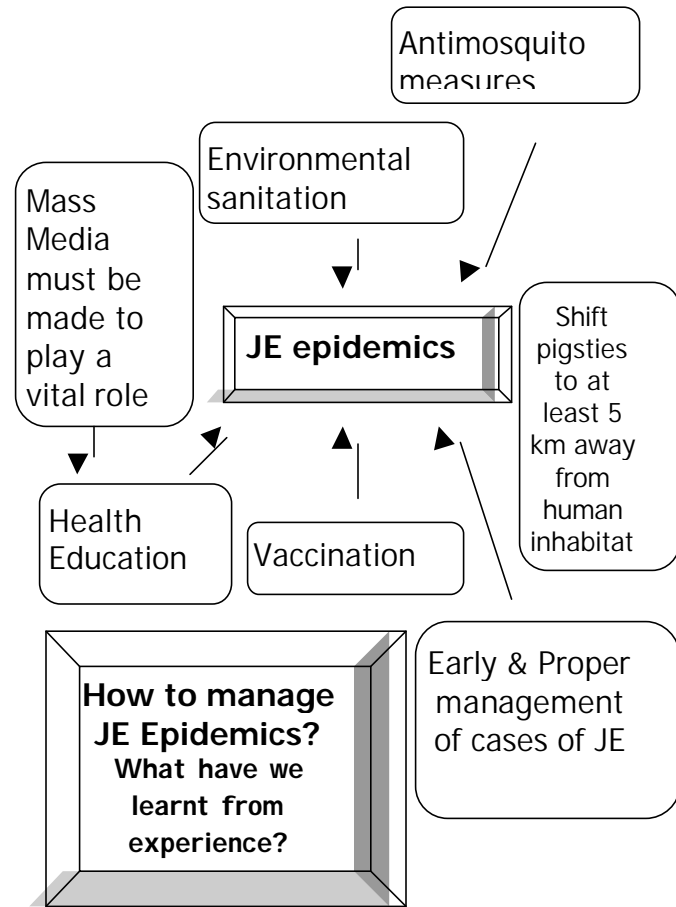
recurring national problem, mass panic, loss of precious lives and morbidity among survivors. We have to be wise at least after four decades of recurrent JE.

The Vicious Cycle of JE we have to break.



Recurrent seasonal encephalitis has been a problem in India. In spite of all our dedicated efforts, only about 15% are serologically positive for JE. Though it is true that even in the sophisticated serological laboratories, only less than 25% samples from clinically diagnosed encephalitis yield positive results, the question I personally have in the mind is whether we are missing an as yet unidentified virus?. Recapitulating the experience of suspected Japanese encephalitis among pig farmers in Malaysia & pig slaughterhouse workers in Singapore in 1998-1999 and subsequent isolation of Hendra-like paramyxovirus named Nipah virus this does seem to be a possibility². The efforts of NICD & Virological institutes of India have not been able to isolate any

other virus in spite of their devoted efforts over the past few decades. Our search for the truth continues, because what we know is less and what we do not know is more! Since the treatment of JE is not different from any other Viral encephalitis, we are justified in implementing these guidelines. But for epidemiological purpose we must have an etiologic diagnosis by better methods of serological evaluation, so that we can prevent or contain the epidemics².



There are other aspects to be considered:

1. Effectiveness of mosquito proofing of pigsties
 2. Legislation/condition for pig rearing practices
- There is an urgent need for frequent reorientation of paramedics & professionals by using videoconferencing or Television for countrywide coverage.

Is it not the right of every child to be alive and the responsibility of every medical worker to struggle to achieve this goal?

This is not the end, not even the beginning of the end. We can't even say it is the end of the beginning. Probably it is the beginning of the beginning. What we have done is little. What we have to do may be beyond our capacity both financially and physically. But if everybody joins hands there will be a brighter tomorrow for our future citizens.

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