

EPIDEMIOLOGICAL SITUATION OF JAPANESE ENCEPHALITIS IN NEPAL

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ABSTRACT

A human Japanese encephalitis (JE) case is considered to have elevated temperature (over 38°C) along with altered consciousness or unconsciousness and is generally confirmed serologically by finding of specific anti-JE IgM in the cerebro spinal fluid. No specific treatment for JE is available. Only supportive treatment like meticulous nursing care, introduction of Ryle's tube if the patient is unconscious, dextrose solution if dehydration is present, manitol injection in case of raised cranial temperature and diazepam in case of convulsion. Intravenous fluids, indwelling catheter in conscious patient and corticosteroids unless indicated should be avoided. Pigs, wading birds and ducks have been incriminated as important vertebrate amplifying hosts for JE virus due to viremia in them. Man along with bovines, ovines and caprines is involved in transmission cycle as accidental hosts and plays no role in perpetuating the virus due to the lack of viremia in them. The species *Cx tritaeniorhynchus* is suspected to be the principal vector of JE in Nepal as the species is abundantly found in the rice-field ecosystem of the endemic areas during the transmission season and JE virus isolates have been obtained from a pool of *Cx tritaeniorhynchus* females. Mosquito vector become infective 14 days after acquiring the JR virus from the viremic host. The disease was first recorded in Nepal in 1978 as an epidemic in Rupandehi district of the Western Development Region (WDR) and Morang of the Eastern Region (EDR). At present the disease is endemic in 24 districts. Although JE as found endemic mainly in tropical climate areas, existence and proliferation of encephalitis causing viruses in temperate and cold climates of hills and valleys are possible. Total of 26,667 cases and 5,381 deaths have been reported with average case fatality rate of 20.2% in an aggregate since 1978. More than 50% of morbidity and 60% mortality occur in the age group below 15 years. Upsurge of cases take place after the rainy season (monsoon). Cases start to appear in the month of April - May and reach its peak during late August to early September and start to decline from October. There are four designated referral laboratories, namely National Public Health Laboratory (Teku), Vector Borne Diseases Research and Training Center (Hetauda), B.P. Koirala Institute of Medical Sciences (Dharan) and JE Laboratory (Nepalgunj), for confirmatory diagnosis of JE. For prevention of JE infection; chemical and biological control of vectors including environmental management at breeding sites are necessary. Segregate pigs from humans habitation. Wear long sleeved clothes and trousers and use repellent and bed net to avoid exposure to mosquitos. For the prevention of the disease in humans, safe and efficacious vaccines are available. Therefore immunize population at risk against JE. Immunize pigs at the surroundings against JE. 225,000 doses of live attenuated SA-14-14.2 JE vaccine were received in donation from Boran Pharmaceuticals, South Korea for the first time in Nepal. Altogether 224,000 children aged between 1 to 15 years were vaccinated in Banke, Bardiya and Kailali districts during 1999. From China also, 2,000,000 doses of inactivated vaccine were received in 2000 and a total of 481,421 children aged between 6m to 10 yrs were protected from JE during 2001/2002. Ministry of Agriculture, Department of Livestock Services has vaccinated around 200,000 pigs against JE in terai zone during February 2001.

Key Words: *Supportive treatment, viremia, amplifying host, vectors, vaccination/immunization.*

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INTRODUCTION

A human Japanese encephalitis (JE) case is considered to have elevated temperature (over 38°C) along with altered consciousness or unconsciousness. For confirmation of a case as JE, it needs to be serologically examined and found positive for specific anti-JE IgM in the cerebro spinal fluid or serum at the time of illness.

Treatment and Management

- No specific treatment is available. Supportive and symptomatic treatment is indicated.
- Meticulous nursing care is most important.
- If the patient is unconscious, a Ryle's tube needs to be introduced.
- I.V. fluids should be avoided.
- Avoid indwelling catheter in conscious patient.
- Dextrose solution only to be considered if there is dehydration.
- In case of raised cranial pressure, 20% Mannitol injection to be given 8 hourly for 48 hours. (Pediatric dose: 1.5 gm./Kg. can be given 8 hourly).
- Antibiotics to be used only if the patient is having secondary infection.
- Corticosteroids should be avoided unless indicated.
- In case of convulsion, give Diazepam injection or Pheno-barbitone.

Source: "Japanese Encephalitis Case Management and Treatment Protocol" recommended by National Workshop on Vector Borne Diseases, 2002

JE is principally a disease of rural agricultural areas and primarily a zoonotic disease infecting mainly vertebrate animals,

e.g. pigs, birds, horses etc. Pigs, wading birds and ducks have been incriminated as important vertebrate amplifying hosts for JE virus due to viremia in them. Humans and horses may become ill in transmission cycle. Man is involved in transmission cycle as an accidental host and plays no role in perpetuating the virus.

Bovines, ovines and caprines along with humans do not appear to serve as an amplifying and reservoir host. The major vectors of JE feed on bovines and there is serological evidence of bovines being infected with the virus. However, viremia is not found in these animals. They are symptom less and "dead end hosts".

The disease is transmitted by different genera of mosquitoes like *Culex*, *Anopheles*, *Aedes*, *Mansonia* and *Amergeres*. They are mostly zoophilic or feed on animal blood meal. Entomological studies carried out during the outbreaks of 1981-1984, have shown Culicine mosquitoes namely *Cx tritaeniorhyncus*, *Cx gelidus*, *Cx vishnii*, *Cx Pseudovishnii* and *Cx fuscocephala* as suspected vectors of transmitting JE virus both in animals and humans.

The species *Cx tritaeniorhyncus* is suspected to be the principal vector of JE in Nepal as the species is abundantly found in the rice-field ecosystem of the endemic areas during the transmission season and JE virus isolates have been obtained from a pool of *Cx tritaeniorhyncus* females. The mosquito borne mode of JE transmission was elucidated with the isolation of JE virus in 1983 and subsequently in other field studies that also established the role of aquatic birds and pigs in the viral enzootic cycle.

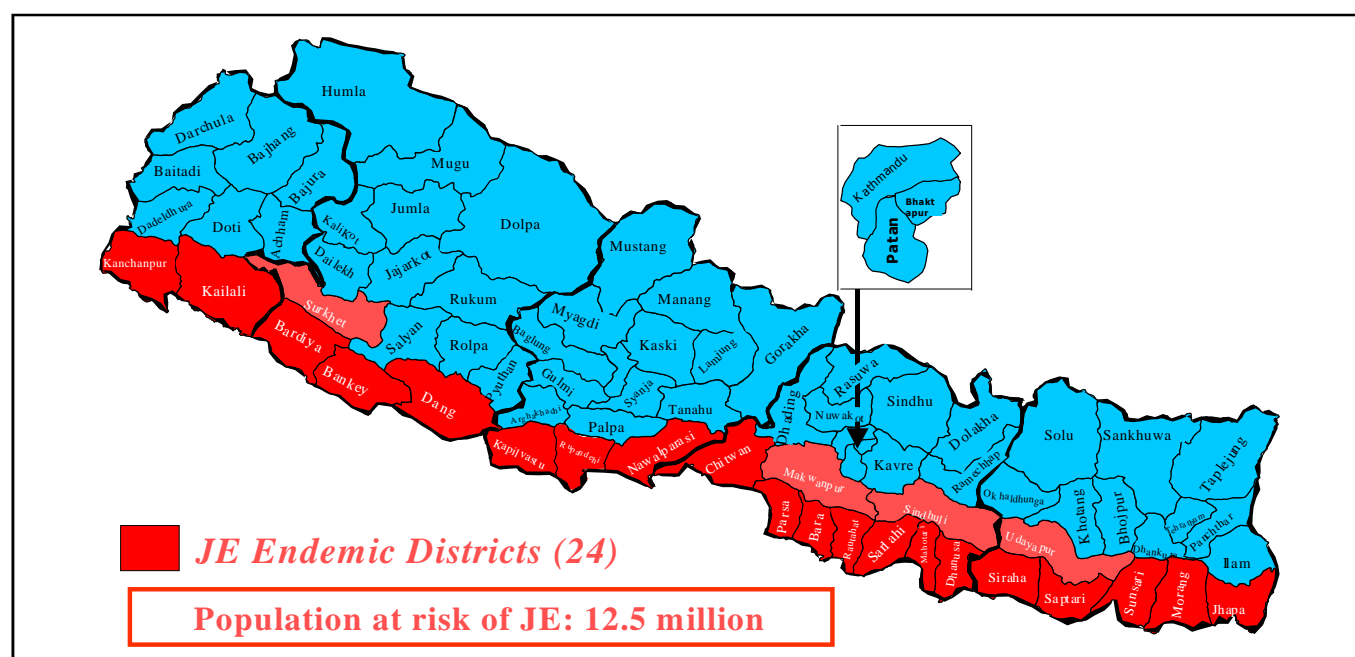


Fig. 1 : Japanese Encephalitis Endemic Districts.

The disease was first recorded in Nepal in 1978 as an epidemic in Rupandehi district of the Western Development Region (WDR) and Morang of the Eastern region (EDR). At present the disease is endemic in 24 districts namely Jhapa, Morang, Sunasari, Saptari, Siraha, Udayapur, Dhanusa, Mahottari, Sarlahi, Sindhuli, Rautahat, Bara, Parsa, Makwanpur, Chitwan, Nawalparasi, Rupandehi, Kapilvastu, Palpa, Dang, Banke, Bardiya, Kailali and Kanchanpur. Among them, 10 districts namely Jhapa, Morang, Sunasari, Parsa, Rupandehi, Dang, Banke, Bardiya, Kailali and Kanchanpur are affected most. (Figure 1)

Distribution of Cases and deaths by Years, Nepal, 1978-2003

Cases of encephalitis are reported throughout the year every year. Upsurge of cases takes place after the rainy season (monsoon). Disease distribution pattern observed during the last 27 years reveals that cases occur in outbreak proportion "epidemic peaks" every 2-5 years. So far, total of 26,667 cases and 5,381 deaths have been reported from 1978 to 2003. More than 50% morbidity and 60% mortality occur in the age group below 15 years. Thus 5.4 millions people aged below 15 years are at high risk. (Figure 2)

JE Case Fatality Rates by Years, Nepal, 1978-2003

The case fatality rates (CFR%) ranged from 9.8% to 46.3% from 1978 to 2003. However, in the recent years, CFR has declined and contained below 20 percent. (Figure 3) The credit goes to intermittent vaccination programme, efforts in raising public awareness, and good nursing care and management at the hospitals. The treatment protocol was formulated through National Workshop in the year 2002.

JE SITUATION IN NEPAL IN 2002 AND 2003

JE case Distribution for 2002 and 2003

Age Distribution: In 2002, the age specific incidence showed that 49.4% (416 cases) of the cases belong to the age group 15 years and below and 50.6% (426 cases) belong to the age group above 15 years. However in 2003, the age specific incidence showed that 55% (512 cases) of the cases belong to the age group 15 years and below and only 45% (419 cases) of the cases belong to the age group above 15 years. Similar pattern have been observed in previous years. On cumulative average for 2002 and 2003, 52% of the total cases belonged to age group 15 years and below, whereas 48% to above 15 years group. (Figures 4 and 5)

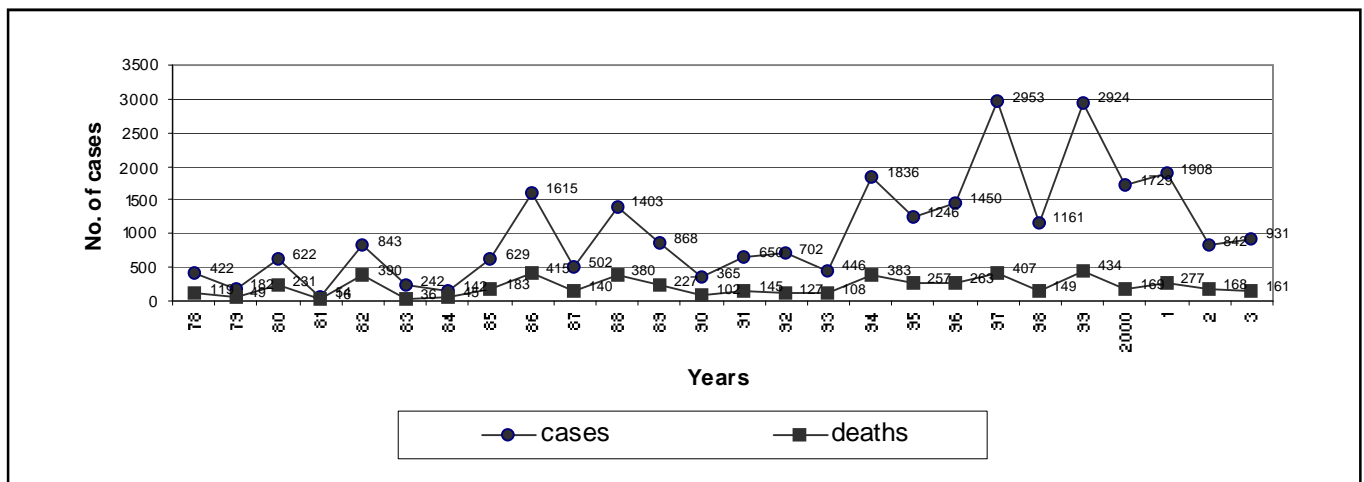


Fig. 2 : Distribution of JE Cases & Deaths During Period 1978-2003, Nepal.

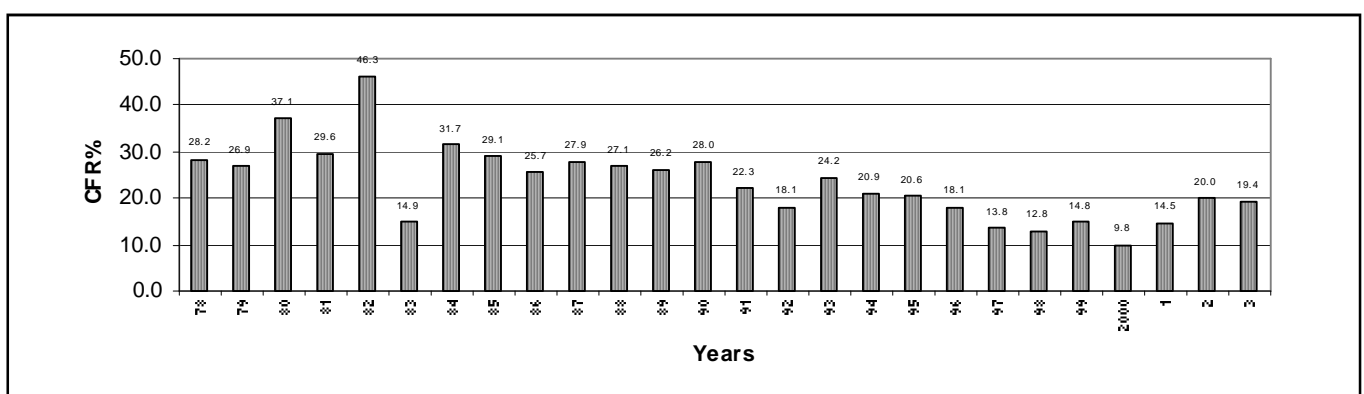


Fig. 3 : Case Fatality Rate Due to JE During Period 1978 - 2003, Nepal.

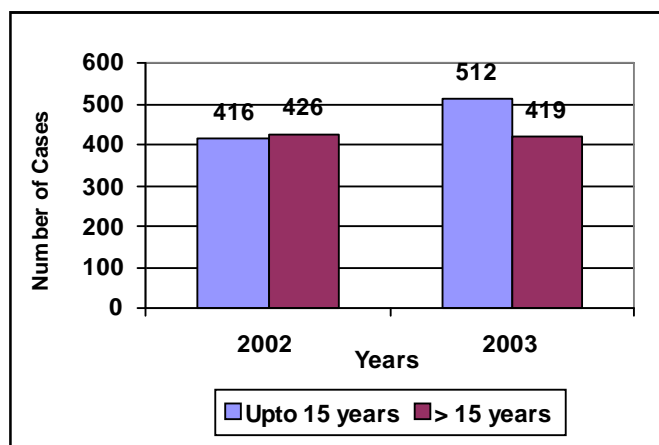


Fig. 4 : JE Cases: Age Distribution, 2002 and 2003

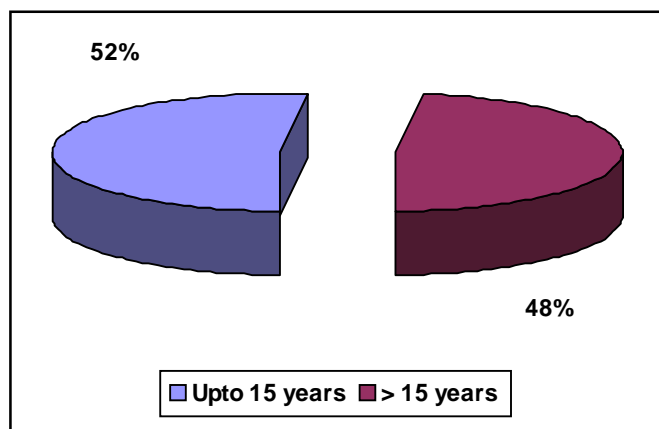


Fig. 5 : JE Cases: Cumulative Age Distribution, 2002 and 2003

Gender Distribution: In 2002, the gender specific incidence showed that 55.7% (469 cases) of the total cases belong to the male group and 44.3% (373 cases) the female group. Similarly in 2003, 53.8% (501 cases) of the total cases belong to the male group and 46.2% (430 cases) to the female group. On cumulative average for 2002 and 2003, 55% of the total cases belonged to male group, whereas 45% for female group. Hence, male and female ratio is 1.22:1 which is slightly below that was observed during the last 5 years (1.3:1). (Figures 6 and 7)

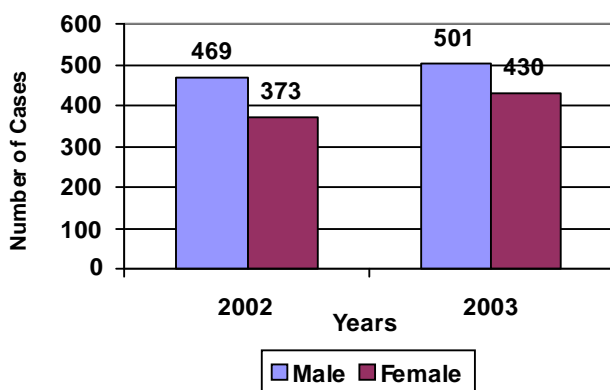


Fig. 6 : JE Cases: Gender Distribution, 2002 and 2003

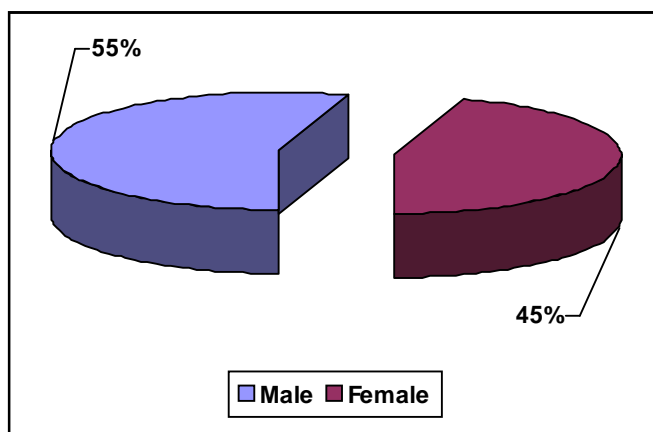


Fig. 7 : JE Cases: Cumulative Gender Distribution, 2002 and 2003

Deaths due to JE in 2002 and 2003

Age Groups: In 2002, the age specific deaths showed that 51.8% (87 deaths) of the total deaths occurred in the age group 15 years and below, and 48.2% (81 deaths) in the age group above 15 years. However in 2003, 44.7% (72 deaths) of the total deaths occurred in the age group 15 years and below, and 55.3% (89 deaths) in the age group above 15 years. On cumulative average for 2002 and 2003, 52% of the total deaths occurred in the age group 15 years and below, whereas 48% in the age group above 15 years. (Figures 8 and 9)

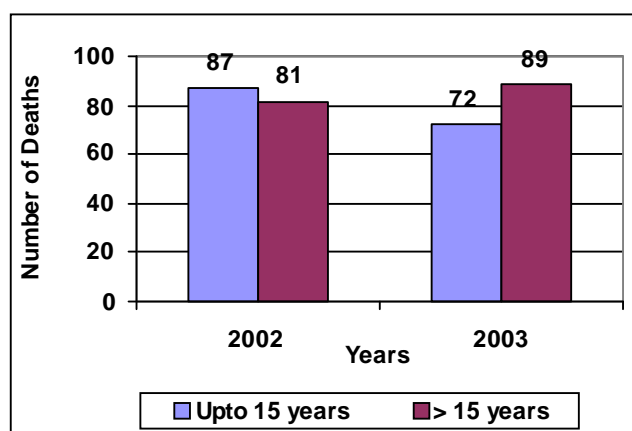


Fig. 8 : JE Deaths: Age Group, 2002 - 2003

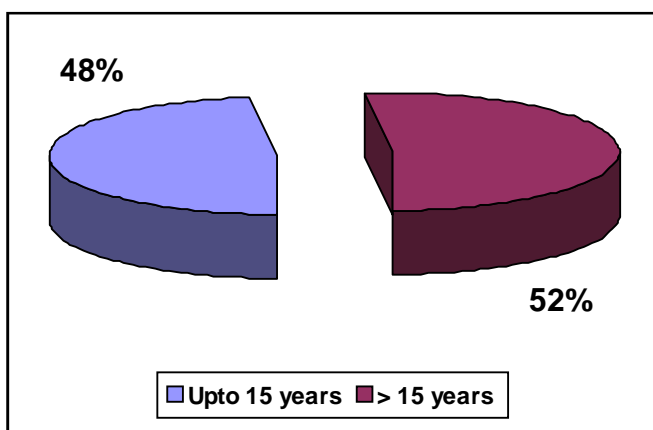


Fig. 9 : JE Deaths: Age Group Cumulative, 2002 and 2003

Gender distribution: In 2002, the gender specific deaths showed that 56.5% (95 deaths) of the total deaths occurred in female group. Similarly in 2003, 55.9% (90 deaths) of the total deaths occurred in the male group and 44.1% (71 deaths) in the female group. On cumulative average for 2002 and 2003, 56% of the total deaths occurred in the male and 44% in the female group. (Figures 10 and 11)

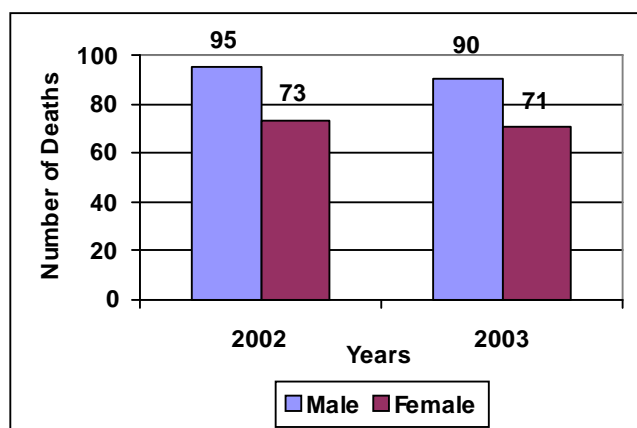


Fig. 10 : JE Death: Gender, 2002 - 2003

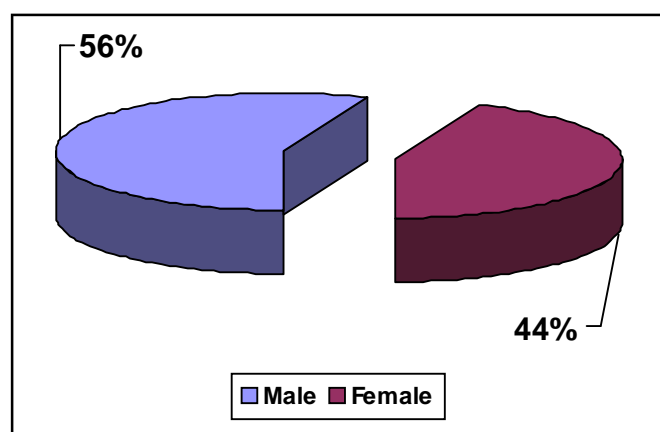


Fig. 11 : JE Deaths: Gender Cumulative, 2002 and 2003

LABORATORY CONFIRMATION OF JE

There are four designated referral laboratories, namely National Public Health Laboratory (Teku), Vector Borne Diseases Research and Training Center (Hetauda), B.P. Koirala Institute of Medical Sciences (Dharan) and JE Laboratory

(Nepalgunj), for confirmatory diagnosis of JE. (Table I) Generally paired serum or CSF samples are collected for the confirmatory diagnosis using anti-JE-IgM capture ELISA.

Internal quality control is done at National Public Health Laboratory (Teku), whereas external quality assurance is performed at Armed Force Research Institute of Medical Sciences, Thailand. From 1999 to 2003, with the support of the USAID funded EHP-Project in Nepal on infectious diseases, the laboratory capacities of above-mentioned laboratories were upgraded. It established a JE diagnostic laboratory at Bheri zonal hospital premises. The project also helped in transporting the samples to referral laboratories from the periphery. Now, this responsibility has been taken over by World Health Organization (Polio Eradication Nepal).

CONTROL MEASURES

Control measures during inter epidemic period of JE

- Vector Control: Chemical and biological control of vectors including environmental management at breeding sites.
- Personal Protective Measures: Segregate pigs from humans, wear long sleeved clothes and trousers, use repellent and bed net to avoid exposure to mosquitos.
- Community awareness on Japanese Encephalitis.
- Information from animal health and facilitating integrated farming.
- Prophylaxis: Immunize population at risk against JE.

Control measures during epidemic period of JE

- Active case detection and appropriate case management.
- Strictly following personal protective measures to avoid mosquito bite: bed net, mosquito coil, spray and repellent cream can be used. All windows of the house should be fixed with wire net. Whenever outside, wear long sleeved clothes / trousers.
- Eliminating Culex species breeding places by proper drainage system, filling all pools and ditches. Keep piggeries clean by periodic fogging and fumigation.
- Segregation and vaccination of pig population. Vaccinate workers in the pig farms, young children of endemic districts and travelers staying more than 4 weeks in endemic areas.

Table I : Laboratory Diagnosis (QA), 2000-2003

Referral Laboratories: NPHL (Teku), VBDRCT (Hetauda), BPKIHS (Dharan), BHZH (Nepalgunj)

Year	Referral Labs			NPHL			AFRIMS, Thailand		
	Tested	Positive	Positive %	Tested	Positive	Positive %	Tested	Positive	Positive %
2000	399	45	11.3				399	50	13.0
2001	880	374	43.0				858	381	44.0
2002	516	197	38.1	372	93	25.0	384	98	25.5
2002	277	249	89.9				277	153	55.2

Source: EHP/USAID, VBDRCT (Hetauda), NPHL (Teku), BPKIHS (Dharan) and JE lab (Bheri Zonal Hospital, NPG)

- Strengthening epidemiological surveillance: Case detection and appropriate case management.
- Study of socioeconomic factors associated with JE transmission.
- Strengthening laboratory facilities.
- Co-ordination between livestock services (veterinary), Irrigation and education services will be more effective for the consideration and implementation of other possible control measures.

Vaccination for JE prevention and control

Intermittent vaccination against JE in selected districts

225,000 doses of live attenuated SA-14-14-2 JE vaccine (Table II) were received in donation form Boran pharmaceuticals, South Korea for the first time in Nepal. Altogether 224,000 children aged between 1 to 15 years were vaccinated in Banke, Bardiya and Kailali districts during 1999. From China, 2,000,000 doses of inactivated vaccine (Table III) were received in 2000 and total of 481,421 children aged between 6m to 10 yrs are protected from JE during 2001/2002.

Table II : Live attenuated SA-14-14-2 JE vaccine

Age group (1–15 yrs.): single dose		
Bardiya	Banke	Kailali
121,000	57,000	46,000

Note: There is 40% drop in the recipients of the vaccines in case of successive doses of inactivated JE vaccine administration.

Table III : Inactivated cell culture JE vaccine

Districts	1 st Dose (Day 0)	2 nd Dose (Day 7)	3 rd Dose (Day 180)
Rupandehi	151,450 (75%)	149,237 (74%)	89,923 (45%)
Dang	33,369 (67%)	33,369 (67%)	33,369 (67%)
Banke	41,786 (72%)	40,986 (71%)	37,080 (64%)
Kailali	156,812 (89%)	152,799 (84%)	130,185 (74%)
Kanchanpur	98,004 (95%)	91,062 (88%)	87,555 (85%)

Types of human vaccines

- **Mouse brain inactivated vaccine:** It is Nagayama strain (Beijing–1 strain) vaccine. Two doses of this vaccine are given subcutaneously 4 weeks apart. Booster dose is given after 1 year and subsequent booster doses are given at every 3 years. Dose is 0.5 ml. for 1-3 year's age group and 1 ml. for above 3 years age group.
- **Cell culture inactivated vaccine:** It is Beijing P-3 strain vaccine and propagated in primary hamster kidney cells. Two doses of this vaccine are given subcutaneously 1 week apart. Booster doses are given after 6 months to 1 year and 3 years later. Dose is 0.5 ml. for all age groups.

Types of animal vaccines:

WHO does not recommend vaccination of swine population as

the prevention strategy for JE states that swines are reared for 8 to 12 months only. In Nepal, most of the pig farmers are not commercialized. Hence, vaccinating the pigs in JE endemic areas are being suggested as it prevents the disease in amplifying host.

- **Formalized mouse brain vaccine:** It is used in horses and pigs.

Live attenuated vaccine (SPF chicken embryo fibroblast): It is used in pigs to prevent stillbirth. Dose is 1 ml. and given intramuscularly. For sows, the booster dose is given in the following year. For piglets and gilts, 2 doses of vaccines are applied 3 to 4 weeks apart and booster dose is given at the age of 1 year.

- Ministry of Agriculture, Department of livestock services has vaccinated around 200,000 pigs against JE in terai zone during February 2001.
- **Cell culture live attenuated vaccine:** It is SA-14-14-2 strain vaccine and propagated in primary hamster kidney cells. Single dose of vaccine is given subcutaneously. Booster dose is given after 2 years. Dose is 0.5 ml. for all age groups.

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