JAPANESE ENCEPHALITIS
(Japanese B encephalitis)

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Definition top

Japanese encephalitis (JE) is an arthropod-borne virus disease affecting the central nervous system (CNS) of human beings and, less frequently, horses. The infection also results in the birth of litters of pigs with a high percentage of stillbirths or pigs affected with encephalitis.

Etiology top

The JE virus is a member of the family Flaviviridae and is in the genus *Flavivirus*. Host range and other characteristics are described in detail in the International Catalogue of Arboviruses (1).

Host Range top

People and horses are victims of the JE virus infection but appear to be dead-end hosts from an epidemiologic standpoint. Viremia levels in infected human beings and equine species are generally too low to provide potential mosquito vectors with an infective blood meal. Under experimental conditions, however, Gould et al. (9) demonstrated horse to horse transmission by *Culex tritaeniorhynchus*. Cattle are frequently infected in enzootic areas (24) but do not develop sickness or viremia (14).

Swine in Japan and Taiwan are both victims of disease as well as amplifiers of infection in nature. This is particularly true when swine are bred to farrow at a time when infected mosquitoes make their first appearance. This type of breeding program is practiced in Japan where, because of immunity or natural seasonal lows in transmission, gilts resist infection during pregnancy, and thus losses due to abnormal litters resulting from JE infection are reduced. However, normal newborn piglets soon lose maternally acquired antibody and are fully susceptible to infection from arthropod vectors.

Although JE infection in shoats is subclinical, viremias are sufficiently high to provide emerging broods of *Cu. tritaeniorhynchus*, which feed readily on swine, with a plentiful source of virus-containing blood. Following a period of extrinsic incubation of virus, the mosquitoes are able to transmit the infection to susceptible vertebrate hosts.

In Japan, herons and egrets play a role in the spread of infection to man and other vertebrates and may be responsible for carrying the virus from rural to urban areas. *Cu. tritaeniorhynchus* feeds readily on herons and egrets and ranges sufficiently high off the ground to feed on the young nesting birds.

Geographic Distribution top

Human encephalitis in Japan was recognized as early as 1871, and Japanese encephalitis in epidemic form has been known since 1924 when 4,000 human deaths were recorded in Japan. The epidemiology of the disease was studied extensively after World War II in Japan by scientists of the U.S. Army's 406th Medical General Laboratory (2). Concurrent with vaccination of people and extensive use of agricultural pesticides in the last three decades, the disease has practically disappeared from Japan.

Japanese encephalitis virus infection is widespread throughout temperate and tropical Asia; increasing numbers of human and equine cases have appeared in India, Nepal, China, Philippines, Sri Lanka, and northern Thailand. The disease in humans is sporadic in Indonesia and northern Australia but is not known in the rest of the world.

Transmission top

The virus is maintained in nature in a cycle involving *Culex mosquitoes* of the genera *tritaeniorhynchus*, *annulus*, *fuscocephala*, *gelidus*, and *vishnui* complex. Mosquitoes transmit the virus to many species of birds and to swine (2,25).

The sequence of events in temperate Asia is initiated by appearance of virus in mosquitoes in late spring followed by the infection and disease in susceptible horses and swine. This is followed by the appearance of disease in man in August and September. In tropical and semitropical areas of Asia, the seasonal nature of the disease is less marked.

Basically, however, it appears the *Culex* mosquitoes and birds are common factors in the epidemiology of JE, regardless of the region of occurrence, and that swine are involved where they are numerous in Asia (15).

The mechanism of maintaining the virus over the winter in temperate areas has not been elucidated. Overwintering in mosquitoes is a possibility either in infected hibernating mosquitoes or by transovarial passage (23). It is also possible that bats may carry the virus for prolonged periods (18,6).

Incubation Period top

In horses, the incubation period is 8 to 10 days. The time between exposure of pregnant swine to an infectious dose of JE virus and delivery of abnormal litters does not seem to be clearly established, although exposure early in gestation appears more likely to result in abnormal litters than later exposure.

Clinical Signs top

In horses, initial signs are fever, impaired locomotion, stupor, and grinding of teeth. Blindness, coma, and death follow in more severe cases. Although the clinical signs resemble those seen in horses with Western equine encephalomyelitis and Eastern equine encephalomyelitis, mortality is relatively low. Inapparent or subclinical infections in horses are far more common than cases of recognizable encephalitis.

The principal manifestation of disease in swine is the expulsion of litters of stillborn or mummified fetuses, usually at term. Viable piglets frequently die shortly after birth and exhibit tremor and convulsions before expiring. Experimental infection of boars leads to diminished sperm count and decreased mobility of sperm. Virus has been transmitted to gilts by way of infected semen (11).

Gross Lesions top

In horses, gross lesions are similar to those observed in animals dying from Eastern equine encephalomyelitis and Western equine encephalomyelitis virus infections and are not specific enough to establish an etiologic diagnosis. Litters from infected pigs contain fetuses that are mummified and dark in appearance (24,4). Hydrocephalus, cerebellar hypoplasia, and spinal hypomyelinogenesis have been noted (20).

Morbidity and Mortality top

The equine mortality caused by JE has been reported at about 5 percent in Japan and may actually be less than this in Southeast Asia. Mortality in adult pigs is close to zero. Litters of pigs from infected sows may be dead at delivery or, if living, may be quite weak and apt to succumb to encephalitis shortly after birth.

Diagnosis top

Field Diagnosis top

Presumptive diagnosis can be made in horses that manifest CNS disease accompanied by fever, particularly in an epizootic period. It has been observed that illness in horses at race tracks in Malaysia is frequently due to JE infection. The infection is manifested only by fever and a short period of lethargy (16,12,22). In temperate zones, the disease appears during late summer and early fall.

A presumptive diagnosis in swine is based on the birth of litters with a high percentage of stillborn or weak piglets.

Specimens for the Laboratory top

One half of a brain from animals having signs of encephalitis should be submitted unfixed and the other half fixed in 10 percent formalin. Paired serum samples collected at least 14 days apart should be submitted from animals that survive. Cerebrospinal fluid from horses with CNS signs should be submitted for detection of JE-specific IgM.

Laboratory Diagnosis top

Confirmation of JE can be accomplished by demonstrating seroconversion in animals that survive long enough to yield properly spaced blood samples. Neutralization, complement fixation, hemagglutination inhibition, immunofluorescence, and enzyme-linked immonosorbent assay tests are used to show a rise in titer from the acute stage to death or recovery. Reliance on seroconversion or IgM as a means of diagnosis in horses is not definitive because seroconversion may have resulted from exposure to another nonpathogenic *Flavivirus*.

Demonstration of JE-specific IgM in serum of an encephalitic equine is presumptive evidence of the diagnosis.

Further confirmation of JE in horses can be obtained by examination of the cerebrospinal fluid and the brain. Specific IgM in the spinal fluid is excellent evidence of CNS infection. Although microscopic lesions of the brain are of value, definitive confirmation is based on isolation and identification of the virus from the brain. Virus isolations are more likely to be successful from brains of animals that died after a short course of the disease.

Confirmation of JE in diseased litters of pigs is accomplished by isolation of the virus from fetal brains or brains of piglets that die after manifesting signs of encephalitis. Demonstration of antibody increase in dams bearing affected litters is probably not a reliable measure because seroconversion in such animals would probably have occurred earlier in infection.

Differential Diagnosis top

The disease in horses must be differentiated from other viral encephalitides. In Asia, JE is the only recognized arboviral infection causing encephalitis in horses. Because there are many mild or subclinical infections, laboratory confirmation is essential.

Various forms of toxic encephalitis must be considered in differential diagnosis. In temperate-zone Asia, the midsummer seasonal occurrence of JE in horses aids in differential diagnosis.

Japanese encephalitis in pigs must be differentiated from a hemagglutinating DNA virus infection that appears to be as commonplace in Japan as JE (21) and causes the same pattern of disease. There is evidence that the DNA virus infection is established in gilts in the middle or last trimester of pregnancy. Seasonal patterns of DNA virus infection need more complete study, but the disease does appear concurrently with Japanese encephalitis and therefore requires laboratory tests for differentiation.

Another hemagglutinating virus, myxovirus parainfluenza 1 (Sendai), has been shown capable of producing stillbirth in swine under experimental conditions (20). Encephalitis in neonatal pigs is also associated with a coronavirus infection. This agent is known to cause encephalitis in piglets in at least North America and Europe (19).

Vaccination top

A live attenuated vaccine produced in hamster kidney tissue culture is in widespread use in horses in China (13). This vaccine reduced disease by about 85 percent. An inactivated vaccine prepared in mouse brain is licensed in Japan, Korea, Taiwan, India, and Thailand for use in humans. A similar inactivated product made in hamster kidney tissue culture has been used to immunize children annually in China since 1965. Live attenuated vaccines are used to immunize pigs in Japan and Taiwan (8) and humans in China (13A).

Control and Eradication top

Options for control include elimination of the vectors, prevention of amplification of the infection cycle in birds and pigs, or immunization of horses, pigs, and people. Although some success in vector control was achieved by modification of irrigation methods to minimize breeding of *Cu. tritaeniorhynchus* in Southeast Asia and coincidentally by the use of agricultural pesticides, vector control has never been more than marginally successful. Reduction of the avian reservoir hosts does not appear feasible.

The most promising approach to reducing livestock losses and at the same time reducing the totality of infection in nature is widespread immunization of swine. Live attenuated vaccines are in use in Japan and Taiwan (8). Immunization of shoats prevents infection in vaccinees and neutralizes their role as amplifiers of infection in nature. It is anticipated that those animals retained for breeding will remain immune, and, because of immunity or natural seasonal lows in transmission resist infection during pregnancy and therefore bear normal litters. Although controlling the disease in swine dampens the spread of infection in nature, there is a continued threat to horses and human beings from other sources.

The introduction of JE virus into the United States is always a possibility, but whether the infection, once introduced, would become established in nature is difficult to assess. Animal health authorities must continue to be alert to detecting and identifying agents associated with encephalitis in horses and with abnormal litters of pigs. The means for rapid diagnosis and identification of JE are available, although it is doubtful that control of the disease in Asia will be achieved in the near future.

Public Health top

Japanese encephalitis can cause an explosive, highly fatal form of human encephalitis.

GUIDE TO THE LITERATURE top

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