

Japanese Encephalitis

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Introduction

Japanese encephalitis is a viral disease that infects animals and humans. It is transmitted by mosquitoes and in humans causes inflammation of the membranes around the brain. Intensification and expansion of irrigated rice production systems in South and South-East Asia over the past 20 years have had an important impact on the disease burden caused by Japanese encephalitis. Where irrigation expands into semi-arid areas, the flooding of the fields at the start of each cropping cycle leads to an explosive build-up of the mosquito population. This may cause the circulation of the virus to spill over from their usual hosts (birds and pigs) into the human population.

The disease and how it affects people

Japanese encephalitis (JE) is a disease caused by a flavivirus that affects the membranes around the brain. The Japanese encephalitis virus is related to the St. Louis encephalitis virus, Murray valley virus, and West Nile virus.

In countries where it is endemic, the virus causes SMEDI (stillbirth, mummification, embryonic death, and infertility) in pigs and encephalitis in horses. The Japanese encephalitis virus can infect horses, pigs, humans, cattle, bats, reptiles, and various species of birds. Under experimental conditions, *Culex tritaeniorhynchus* can transmit the virus between horses; under natural conditions, humans and horses appear to be dead-end hosts. Cattle are often infected in endemic regions, but do not become ill or develop viremia. Swine develop clinical signs and also amplify the virus.

Japanese encephalitis is a significant zoonosis: in humans, it can result in a serious and potentially fatal encephalitis. In 1924, an epidemic in Japan was responsible for 4,000 deaths. In Human, Most JE virus infections are mild (fever and headache) or without apparent symptoms, but approximately 1 in 200 infections results in severe disease characterized by rapid onset of high fever, headache, neck stiffness, disorientation, coma, seizures, spastic paralysis and death. The case fatality rate can be as high as 60% among those with disease symptoms; 30% of those who survive suffer from lasting damage to the central nervous system. In areas where the JE virus is common, encephalitis occurs mainly in young children because older children and adults have already been infected and are immune.

Geographic distribution

Japanese encephalitis is a leading cause of viral encephalitis in Asia with 30,000-50,000 clinical cases reported annually. It occurs from the islands of the Western Pacific in the east to the Pakistani border in the west, and from Korea in the north to Papua New Guinea in the south. Because of the critical role of pigs, its presence in Muslim countries is negligible. JE distribution is very significantly linked to irrigated rice production combined with pig rearing.

Japanese encephalitis is a patchy disease and important outbreaks have occurred in a number of places in the past 15 years, including South India (Arkot district in Tamil Nadu) and in Sri Lanka (Mahaweli System H), and also Northern India and Nepal during September 2005.

The cause

The virus causing Japanese encephalitis is transmitted by mosquitoes belonging to the *Culex tritaeniorhynchus*, *C. annulus*, *C. fuscocephala*, *C. gelidus*, and mosquitoes in the *C. vishnui*

complex, which breed particularly in flooded rice fields. The virus circulates in ardeid birds (herons and egrets). Pigs are amplifying hosts, in that the virus reproduces in pigs and infects mosquitoes that take blood meals, but does not cause disease. The virus tends to spill over into human populations when infected mosquito populations build up explosively and the human biting rate increases (these culicines are normally zoophilic, i.e. they prefer to take blood meals from animals).

In temperate regions of Asia, a yearly cycle of infection is seen: mosquitoes appear in late spring, horses and swine become infected in late summer, and human cases peak during August and September. How the virus survives during the winter is unknown. It may be maintained in mosquitoes, either by transovarial passage or during hibernation. Bats might also be able to carry the virus for long periods of time.

Incubation period

The incubation period in horses is 8-10 days. The incubation period in pregnant swine is uncertain; however, exposure early in gestation seems to increase the chance that the litter will be affected.

Clinical signs

In horses, most infections are subclinical. Horses with clinical signs resemble animals with Western equine encephalomyelitis or Eastern equine encephalomyelitis, but the mortality rate is relatively low. The symptoms may include a fever, impaired locomotion, stupor, and teeth

grinding. Blindness, coma, and death are possible. In some cases, the only symptoms may be a fever and short period of lethargy. The most common symptom of Japanese encephalitis in pigs is the birth of stillborn or mummified fetuses, usually at term. Piglets born alive often have tremors and convulsions and die soon after birth.

Post mortem lesions

Only nonspecific post-mortem lesions are seen in horses, similar to the signs in animals that die from Eastern or Western equine encephalomyelitis. The fetuses from infected pigs are mummified and dark. Hydrocephalus, cerebellar hypoplasia, and spinal hypomyelination may be seen.

Morbidity and Mortality

Inapparent infections are common in horses; mortality in this species is approximately 5% or less. The mortality rate is high in piglets born to infected sows, but close to zero in adult pigs. Vaccines are available for swine in Japan and Taiwan and are expected to provide good immunity.

Diagnosis

Clinical

Japanese encephalitis should be suspected in horses with fever and the symptoms of a central nervous system (CNS) disease. The principal sign in pigs is the birth of a litter with a large number of stillborn or weak piglets. In temperate regions, the disease is most common in the late summer and early autumn.

Differential Diagnosis

Laboratory Tests

Japanese encephalitis can be diagnosed by virus isolation. The virus is isolated from blood, spinal cord samples, or portions of the corpus striatum, cortex, or thalamus of the brain. Samples are inoculated into 2-4 day old mice and the virus is identified by hemagglutination inhibition. Japanese encephalitis virus may also be identified by infection of cell cultures (chicken embryo or hamster kidney cells, or the mosquito cell line C3/36). Virus isolation from sick or dead horses is often unsuccessful. Serology may also aid in diagnosis. A significant rise in titer should be seen

with paired samples from the acute and convalescent stages. Serologic tests include the plaque reduction virus neutralization test, hemagglutination inhibition, and complement fixation. In horses, specific IgM and IgG antibodies can also be detected in the cerebrospinal fluid with enzyme immunoassays and are good evidence of infection.

Samples to collect

Before collecting or sending any samples from animals with a suspected foreign animal disease, the proper authorities should be contacted. Samples should only be sent under secure conditions and to authorized laboratories to prevent the spread of the disease. Biocontainment conditions are required for all potentially infectious material from a Japanese encephalitis case. Human encephalitis has been seen after infection through a scratch. Brains should be submitted from animals with encephalitis; half should be fixed in 10 percent formalin and the other half unfixed. Paired serum samples should be taken at least 14 days apart for serology. In horses, cerebrospinal fluid should be submitted for virus-specific IgM and IgG. All samples must be kept cool. Samples to be saved for later virus isolation should be frozen to -80°C .

Interventions

An effective killed vaccine is available for Japanese encephalitis, but it is expensive and requires one primary vaccination followed by two boosters. This is an adequate intervention for travellers, but has limited public health value in areas where health services have limited resources. An inexpensive live-attenuated vaccine is used in China, but is not available elsewhere.

Chemical vector control is not a solution, as the breeding sites (irrigated rice fields) are extensive. In some rice production systems faced with water shortages, however, certain water management measures (alternate wetting and drying) may be applied that reduce vector populations. Personal protection (using repellents and/or mosquito nets) will be effective under certain conditions.

Biosafety level 3 practices are recommended for investigators working with this virus. Japanese encephalitis virus is inactivated by 70% ethanol, 2% glutaraldehyde, 3-8% formaldehyde, 1% sodium hypochlorite, iodine, phenol iodophors, and organic solvents/detergents. It is also sensitive to heat, ultraviolet light, and gamma irradiation.

Eliminating the pig population is often a measure taken in the wake of outbreaks. Certainly, the introduction of pig rearing as a secondary source of income for rice-growing farmers in receptive areas must never be encouraged.

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