

EXOTIC Tioman virus

Fact sheet

Introductory statement

Tioman virus was isolated from fruit bats on Malaysian island of Tioman in 2001 during studies to determine the natural host of Nipah virus following its emergence in pigs and humans in Malaysia 1998-99 (Chua et al 2001). Serological evidence of infection in humans (Yaiw et al 2007 b) and experimental infection of mice (Yaiw et al 2007a) and pigs (Yaiw et al 2008) has subsequently been demonstrated. Although it is not known to naturally cause disease, the closely related paramyxoviruses of bat origin (Hendra virus, Nipah virus, Menangle virus) have caused significant disease in livestock and man and have generated interest in investigating the pathogenic potential of this virus.

The close antigenic relationship between Tioman virus and Menangle virus has strengthened the prediction that Menangle virus is of bat origin despite the failure to date to isolate this virus from bats (seropositive or otherwise) (Philbey et al 2008). It has raised concern that Tioman virus will cause disease if it crosses the species barrier (Chua et al 2001).

Aetiology

Tioman virus, a negative sense single stranded RNA virus.

Family Paramyxoviridae, genus Rubulavirus.

Natural hosts

Island or small flying foxes *Pteropus hypomelanus*

The original virus isolation was made from a sample of 50 pooled urine samples from *P. hypomelanus* and 5 further virus isolates have been made from these bats on Tioman Island (Chua et al 2001). No subsequent work has been published on the prevalence of the virus in this population but a larger study was planned and commenced (Chua et al 2001). This species is not found in Australia. It is native to restricted areas in the Maldives, Andaman and Nicobar Islands (India) and is found on many offshore islands and in coastal lowlands in the Southeast Asian region (including Indonesia; Malaysia; Myanmar; Papua New Guinea; Solomon Islands; Thailand and Viet Nam) and throughout most of the Phillipines. It is extensively hunted for food in the

Phillipines and Melanesia but is regarded as globally stable (IUCN category Least Concern) and is found predominantly in lowland rainforest areas as well as utilising plantations, rural gardens and urban areas (IUCN 2010).

World distribution

Tioman Island, Malaysia.

Occurrences in Australia

Tioman virus has never been reported in Australia.

No positive sample of Tioman Virus are recorded from bats in National Wildlife Health Surveillance Database or the Australian Registry of Wildlife Pathology Database.

Epidemiology

Morbidity

Naturally occurring disease has not been associated with Tioman virus in seropositive humans or fruit bats. In experimental infections, 2/12 subcutaneously infected pigs and 4/4 pigs oro-nasally infected developed pyrexia (up to 40.3°C) between 4 and 9 days post infection (Yaiw et al 2008). No domestic pig farms are found on Tioman Island, in accordance with local religious practices.

Three (2 males, one female, age range 22-60 years) out of 169 Tioman Islanders tested were shown to have neutralizing antibodies against Tioman Virus, indicating probable past infection (Yaiw et al 2007^b). This is an estimated prevalence of 1.8% but note that samples were collected from 6 villages and is equivalent to 6% of the island population).

Mortality

No mortality is associated with this virus.

Incubation period

Incubation period may be as short as 6 days in experimentally infected pigs (Chua et al 2001).

Transmission

Bat-to-human mode of transmission is unknown, although direct transmission via ingestion of fruits by humans has been suggested (Yaiw et al 2007^b). Of the three humans found to be positive for Tioman virus, two had previously consumed fruit partially eaten by bats. However the study examined this further and found that the consumption of fruit partially eaten by bats is quite common: 32 (19%) of the 169 subjects had done so.

Experimental infection of pigs was successful by oronasal (and subcutaneous) inoculation suggesting that this could be a potential route for bat-to-pig transmission, similar to Menangle virus and Nipah virus (Yaiw et al 2008). No evidence of virus was found in the urine of seropositive pigs (using real-time PCR) suggesting that viral transmission via urine is unlikely.

Transmission of virus amongst fruit bats is unknown.

Sources of agent

Limited information is available but initial virus isolation from island fruit bats was from urine (Chua et al 2001).

In experimental studies with pigs, virus was reisolated only from oral swabs, from three animals (including pigs infected oro-nasally and subcutaneously) all at 6 days post infection (dpi). The main cellular targets of infection are lymphocytes, thymic epithelioreticular cells, and the tonsillar epithelium. This suggests that pigs are capable of being infected and of replicating and shedding virus, mainly at about 6 dpi (possibly 5 to 8 dpi) and that oral secretions might be one potential route of transmission to humans or uninfected pigs (Yaiw et al 2008) from pigs. There is no published evidence for a carrier state existing or being important in the epidemiology of this virus.

Tioman virus is capable of infecting and replicating in mouse neurons (Yaiw et al 2007a) and in human neuroblastoma cells (unpublished data cited by author, Yaiw et al 2008)

Clinical signs

Infection with the virus was not associated with clinical disease in humans or bats (Chua et al 2001, Yaiw et al 2007^b). Pigs developed pyrexia (up to 40.3°C) between 4 and 9 days post infection (Yaiw et al 2008).

Diagnosis

Diagnosis is by laboratory tests only (serum neutralising test, comparative ELISA, real time PCR and virus isolation) as virus is not associated with disease other than in experimentally infected pigs. The following information on pathology comes from work with experimental pigs (Yaiw et al 2008).

Clinical pathology

Experimental studies have reported parameters only related to virus activity. All experimentally infected pigs developed neutralizing antibody titres ranging from 1:40 to 1:640.

Pathology

Gross lesions not described (experimentally infected animals were serially sacrificed).

Histology/ microbiology

In pigs, viral antigens could be seen as early as 2 dpi in the thymus, tonsils, and lymph nodes, using immunohistochemistry (IHC), in situ hybridization (ISH). Electron microscopy revealed paramyxovirus-like budding viruses and viral inclusions in lymph nodes (Yaiw and Hyatt, unpublished, cited in Yaiw et al 2008). All other tissues were negative.

In experimentally infected mice (Yaiw et al 2003) Tioman virus inoculated intracerebrally was neurotropic causing plaque-like necrotic areas, and appeared to preferentially replicate in the neocortex and limbic system. Viral infection of inflammatory cells was also demonstrated. This suggests that neuronal infection was associated with necrosis rather than apoptosis. There was no evidence of central nervous system infection via the intraperitoneal route.

No case reports are available through the Australian Registry of Wildlife Health

Differential diagnosis

Tioman virus could be considered as a possible cause of pyrexia in pigs (especially where they coexist with island flying foxes). Note that Tioman virus is antigenically very similar to Menangle virus.

Laboratory diagnostic specimens

The following information is taken from the standard diagnostic procedures for Menangle virus (Kirkland and Davis 2006):

Blood and serum samples should be chilled during transport to the laboratory and can be stored for about four weeks at 4°C without significant decline in antibody titre. It is important that the serum is aseptically decanted from the blood clot as soon as separation of serum and red cells has taken place. Freezing at -20°C or lower is preferred for longer storage.

Tissue samples When virus isolation is to be conducted, tissues, if not examined within a few days of receipt, should be stored frozen at -70°C or lower

Laboratory procedures

Bats

Virus isolation

Pigs

Serum Neutralisation Test, virus isolation, histopathology, immunohistochemistry (IHC), in situ hybridization (ISH), electron microscopy, real-time PCR (details described or referenced in Yaiw et al 2008)

Humans

Serum Neutralisation Test

Comparative ELISA (details described or referenced in Yaiw 2007^b).

Treatment

No treatment (no disease is associated with infection in humans or bats. No naturally occurring disease is associated with pigs).

Prevention and control

No relevant information available.

The disinfectant susceptibility of Tioman virus has not been published; however, the related Newcastle disease virus is inactivated by formalin, phenol, or acid pH.

Surveillance and management

There are currently no surveillance activities/ programs associated with Tioman virus in Australia. Tioman virus is not considered in AUSVETPLAN nor is there an Import Risk Analysis for this virus.

Statistics

Wildlife disease surveillance in Australia is coordinated by Wildlife Health Australia. The National Wildlife Health Information System (eWHIS) captures information from a variety of sources including Australian government agencies, zoo and wildlife parks, wildlife carers, universities and members of the public. Coordinators in each of Australia's States and Territories report monthly on significant wildlife cases identified in their jurisdictions. NOTE: access to information contained within the National Wildlife Health Information System dataset is by application. Please contact admin@wildlifehealthaustralia.com.au.

No records are maintained in the National Wildlife Health Surveillance Database relating to serological evidence of Tioman virus in fruit bats. It is not offered as a differential diagnosis in the search directory. No clinical disease is associated with Tioman virus in bats.

Research

Whilst the importance of Tioman virus is unknown experimental studies have demonstrated that there is potential for the virus to affect pigs. The island fruit bat is distributed widely in coastal and lowland regions in South East Asia including areas where pigs are kept traditionally and intensively so passive surveillance may be prudent in those areas. In some parts of its range (e.g. Philippines and Melanesia) the island flying fox is extensively hunted and eaten which would increase opportunities for bat - human spill-over.

The concentration of zoonotic viruses isolated from bats in Malaysia and their related counterparts in Australia is also interesting (i.e. Tioman and Menangle viruses, Nipah and Hendra viruses). A third syncytia-forming virus, Pulau virus, was isolated in 1999 from island fruit bats on Tioman Island during the same early investigations for a natural virus for Nipah virus (Pritchard et al 2006). Pulau is closely related to other reoviruses Nelson Bay Virus, previously described in the grey headed flying fox *Pteropus poliocephalus* in Australia in 1968 (Gard and Compans 1970), and Melaka virus, isolated from a (human) family group with respiratory disease on the other side of the Malaysian Peninsula in 2006 (Chua et al 2007). Screening of sera collected from human volunteers on the island revealed that 14 of 109 (13%) were positive for both Pulau and Melaka viruses (Chua et al 2007). Whilst direct evidence of a bat origin for Melaka virus was not obtained at the time, the affected family had a known exposure to a bat in the week before the index case. Kampar virus represents yet another reovirus isolated in Malaysia from a human with respiratory disease in Malaysia and fruit bats-specific antibodies have been demonstrated in at least two different bat species, *Pteropus vampyrus* and *Pteropus hypomelaunus* (Chua et al 2008). It is important to note that smaller fruit bats (i.e. not of genus *Pteropus*) such as *Eonycteris spelaeae* and *Cynopterus brachyotis*, are more commonly found in the areas where Kampar virus and Melaka virus were discovered. Clearly much research is needed to understand the spillover of viruses from bats in Malaysia and elsewhere, and of the significance of these viruses. Further field study is required to elucidate the bat species mainly responsible for the spill-over of these viruses into human population and the significance of potential amplification hosts.

Human health implications

Tioman virus is not known to exist in Australia and is not discussed on the Australian Government Department of Health and Ageing website (see <http://www.health.gov.au>). There is limited reference by the World Health Organisation.

Conclusions

It is clear that a number of viruses can spill over to humans and livestock from fruit bats in the Australasian, South, East and South East Asian regions. Whilst Tioman virus itself may be of limited importance to Australia, and possibly to S. E. Asia, the expertise and collaborative relationships developed in Australia and Malaysia are very significant and have resulted in further identification of bat related viruses and respiratory infections of (previously) unknown origin.

The wildlife health implication of Tioman virus, as with other identified zoonotic viruses from fruit bats is an indirect one as these diseases appear to be apathogenic to bats. Land use that increases human – bat interactions including the replacement of natural habitat with plantations, and including the placement of livestock (particularly pig) rearing operations will increase opportunities for viral spillover; affect fruit bat population dynamics; feeding, seed and pollen dispersal patterns; species composition and may result in persecution of bats.

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A good source of additional information

The Hendra, Nipah, Menangle, Tioman Resource list (2007) contains an extensive list of references and media at <http://www.csiro.au/files/p7wp.pdf>

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To provide feedback on this fact sheet

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or call +61 2 9960 6333