Hendra virus disease in horses

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Summary
The author provides an account of the discovery of a previously undescribed disease of horses and a description of the studies involved in determining the aetiology of the disease. The causative virus, now named Hendra virus (HeV), is the reference virus for a proposed new genus within the virus family Paramyxoviridae. The virus is a lethal zoonotic agent able to cause natural disease in humans and horses and experimentally induced disease in cats, guinea-pigs and mice. The virus also naturally infects species of the family Megachiroptera, mainly subclinically, and such animals are the natural host of HeV. The virus appears to transmit readily between species of Megachiroptera, but not readily between horses under natural and experimental conditions, or from horses to humans. The method of transmission from bats to horses is not known. Three incidents of HeV disease in horses have been recorded in Australia — two in 1994 which caused the death of two humans and fifteen horses and one in 1999 which involved the death of a single horse. Hendra virus is related to Nipah virus, the virus that caused disease and mortality in humans, pigs, dogs and cats in Malaysia during 1998 and 1999.

Keywords

Introduction
In August 1994, two horses died suddenly on a property in Mackay, Queensland, Australia. The owners, a veterinarian and her husband, performed post-mortem examinations on the horses, and samples were submitted for laboratory examination. The cause of death was attributed to avocado toxicity and snakebite, respectively, based on histopathological examination, and no further tests into the cause of death were undertaken. Ten days after the death of the second horse, the husband was admitted to hospital with meningitis, from which he made an apparently successful recovery. These incidents would have been consigned to the family history except for a totally unexpected event fourteen months later.

One month after the incident in Mackay, thirteen of twenty thoroughbred horses died or were euthanised at a stable in Hendra, Brisbane, Queensland (approximately 800 km south of Mackay), with the deaths occurring over a period of two weeks. The owner/trainer and a stable worker, both of whom had contact with the affected horses, became ill with an influenza-like disease, from which the trainer died after six days in intensive care. A link between the illness and death in humans and the virulent respiratory disease in the horses was not considered initially because the physician suspected Legionella infection as the likely cause of illness in the trainer. Similarly, the clinical signs and lesions in the horses were suggestive of acute African horse sickness, or perhaps acute equine influenza (diseases exotic to Australia), and investigations were conducted on this basis. However, these potential diagnoses were eliminated rapidly, as were bacterial diseases, plant intoxications and poisoning. A novel paramyxoviral virus was isolated from the affected horses, and from the trainer on post-mortem examination. This virus reproduced the disease syndrome when inoculated into horses, and specific antibodies were detected in the trainer and stable worker, and in all the recovered horses. The gross and microscopic lesions detected at post-mortem in the naturally and experimentally infected horses and in the trainer were similar, and the convalescent human sera reacted strongly in immunofluorescent and immunoperoxidase tests on tissues from affected horses. Furthermore, this virus induced similar clinical signs and lesions in cats inoculated with the virus, and similar microscopic lesions in experimentally infected guinea-pigs. The virus was therefore
considered to be the causative agent of the disease and a new zoonotic pathogen. The name equine morbillivirus was suggested initially because the virus was more closely related to the morbillivirus genus of the virus family Paramyxoviridae than to the other virus groups in the family (12). However, subsequent research demonstrated that the virus was unique and probably best categorised as the first virus of a new genus within the Paramyxoviridae family (16). It has now been named Hendra virus (HeV).

In October 1995, the man who assisted with the post-mortem of the horses in Mackay was again admitted to hospital with clinical signs of a disease of the central nervous system (CNS). He died following an illness which lasted twenty-five days, characterised by seizures and worsening paralysis. Extensive microbiological testing for recognised causes of such disease did not reveal the cause of death. In desperation, tests for HeV infection were requested because of the connection with horses and the earlier death of the horse trainer in Brisbane, although the presenting signs of this disease were different. Hendra virus antigen was demonstrated in the brain using immunofluorescence and immunoelectron microscopy, and typical HeV nucleocapsids were seen in ultra-thin sections of neuronal cells (6, 9). The polymerase chain reaction (PCR) was used to detect HeV in cerebrospinal fluid and brain tissue, and the nucleotide sequence of PCR product was homologous with that of HeV isolated in 1994. A significant rise in specific neutralising antibody titre to HeV was detected during the course of the disease (from 1:16 at admission to 1:5,792 just before death). The virus was not isolated, perhaps because of the virus-antibody complexing. These results incriminated HeV as the cause of the disease, especially as the microscopic lesions (vascular thrombosis and occasional multinucleated giant cells in the endothelium of blood vessels) were also consistent with HeV induced disease. Furthermore, a neutralising antibody titre of 1:4 was detected in a serum sample collected from the patient soon after his recovery from the episode of meningitis in August 1994. This result suggested that the source of infection with HeV may have been the horses that died in 1994, even though these were presumed to have died from avocado poisoning and snake bite. Retrospective testing of stored specimens from both horses, using specific fluorescent antibody and PCR tests, revealed that both horses were infected with HeV and, despite the absence of key tissue samples such as lung, the histopathological lesions were consistent with HeV disease (6).

Thus, in 1994, two outbreaks of HeV disease occurred in Queensland, on properties approximately 800 km apart and between which no apparent direct or indirect contact existed (3). A ‘think-tank’ of scientists within the Queensland Department of Primary Industries conjectured that birds or bats may have been the source of the virus and the link between the two affected properties. Serological testing of birds and bats known to inhabit both Brisbane and Mackay was therefore undertaken. Specific serum neutralising antibody was soon detected and HeV isolated in bats of the four species of the genus Pteropus found in Australia. Specific antibody was not detected in other fauna tested, or in horses, following an intensive structured serological survey in Queensland and elsewhere in Australia. This data pointed to fruit bats of the genus Pteropus as being the natural reservoir host of HeV (21), and these animals were the probable source of infection for the horses, although the mode of infection is unknown.

A further case of HeV disease in a horse occurred in north Queensland in 1999. This was the first recorded case since 1994, despite intensive on-going surveillance by government animal health agencies and private veterinary practitioners. This history suggests that transmission of virus from the natural host to horses is a sporadic and occasional event, a concept supported by a failure to detect HeV infection during retrospective examination of stored lung samples collected from horses with pneumonic lesions.

Nipah virus, a virus closely related to HeV, caused a dramatic outbreak of disease in humans and pigs, and some other animal species, in Malaysia in 1998 and 1999. Affected humans exhibited clinical signs of neurological disease following exposure to pigs with respiratory and/or CNS disease caused by the virus (1). Nipah virus transmits naturally and easily between pigs on a farm and between pig farms (by movement of pigs). Transmission from pigs, and perhaps other animals, to humans requires close contact (e.g. as during obstetrical interventions), and transmission between humans does not occur readily, if at all. Serum neutralising antibody to Nipah virus has been detected in bats and, as with HeV, these are suspected to be the natural host of the virus. Nipah virus is related morphologically, antigenically and genetically to HeV, and is probably the second member of the putative megamixovirus genus of the family Paramyxoviridae. Nipah virus is distinguishable from HeV using serological and molecular tests (1). The finding that bats of the genus Pteropus, family Megachirotrema, may be the natural host of these viruses, as well as the possible host of other new viruses such as Menangle virus (14) and new strains of lyssavirus (4), points to a need for a better understanding of the microbiological status of these creatures.

**Importance for animal and public health**

Hendra and Nipah viruses are previously unrecognised viruses which can cause fatal disease in humans and animals. Hendra virus emerged in 1994, and Nipah virus in 1998, although there are now indications that Nipah virus may have been present in pigs in Malaysia before that time. Each has caused variable clinical manifestations in animals, ranging
from severe to mild disease in the respiratory tract, in addition to disease in the CNS. The same symptoms have also been observed in humans, sometimes with relapses following a primary CNS disease episode, in one instance (with HeV), fourteen months after the first occurrence (13). Humans become infected as a result of handling infected animals. No instances of human-to-human transmission of HeV or Nipah virus have been recorded to date. Infected animals may include the natural host, thought to be fruit bats of the Megachiroptera family, and unusual hosts, such as horses for HeV, or pigs, dogs and cats for Nipah virus. The mechanism of transfer of the virus from the usual to the unusual animal host is not understood, nor is the mode of transmission to humans, although close contact with the infected animal seems to be necessary. No vaccines are currently available to control these diseases in animals or humans and, at the time of writing, no documented information exists regarding the effectiveness of antivirals, although these have been tested in Malaysia. The relative lack of information about the viruses and the epidemiology of the diseases they cause, together with the unavailability of vaccines and antivirals with assessed effectiveness as therapeutic compounds in humans, have caused regulatory agencies to require work with these viruses to be performed at the highest possible level of microbiological security, i.e. biosecurity level 4 (BL4). Thus, extreme care is required in defining procedures for field staff working with infected animals and on contaminated premises, and laboratory staff working both in vitro and in vivo, within the confines of BL4.

The virus

Hendra virus was originally isolated from horse tissues using Vero (African green monkey kidney) monolayer cell cultures in which the virus induced a focal syncytial cytopathogenic effect (CPE) after approximately three days. The human virus was isolated in LLC-MK2 and MRC5 cell monolayers in which it induced focal CPE after approximately twelve days. However, the horse trainer had detectable levels of serum neutralising antibody at the time of death, and thus the amount of virus present in the tissues may have been quite small. The virus was isolated from the kidney only. Hendra virus will grow on a remarkably wide range of cell culture systems, although Vero cells are most commonly used. Morphological characteristics place HeV within the family Paramyxoviridae, but it cannot, on defining morphological, biological and genomic grounds, be easily categorised into the existing genera of the family (i.e., rubulavirus, morbillivirus, respirovirus, pneumovirus and metapneumovirus). Wang et al. have suggested that HeV is the first virus of a new genus within the family (16). This suggestion is currently being considered by the International Committee for the Taxonomy of Viruses. Nipah virus is probably the second member of this proposed new genus within the family.

Hendra virus has unique morphological characteristics that are useful for diagnostic purposes. Electron micrographs of negatively stained virus reveal pleomorphic enveloped particles containing characteristic paramyxovirus nucleocapsids. The envelope is very characteristically covered with surface projections of 10 nm and 18 nm in length, giving the particle a unique 'double-fringed' appearance. Such a double-fringed arrangement is not a feature of previously described members of the Paramyxoviridae family. Free-lying herringbone-shaped nucleocapsids, which were 18 nm wide and had a periodicity of 5 nm, were frequently seen in negatively stained preparations (9).

The virus is enveloped and consequently, inactivation is possible using compounds that disrupt this envelope. In the laboratory, one of the following is normally used: 3% lysol for 3 min at 20°C; 2% sodium dodecyl sulphate (SDS) for 2 min at 100°C; 1% glutaraldehyde for 10 min at 20°C; 100% acetone for 15 min at 20°C; pure methanol for 10 min at 0°C; or gamma-ray irradiation for diverse virus inactivation requirements, in addition to formaldehyde fumigation of HeV contaminated animal rooms.

The disease

The clinical course in both naturally and experimentally infected horses is short, with horses usually dying within 36 hours of the onset of clinical signs. Affected horses are febrile (>40°C), depressed and have an increased respiratory and heart rate. An increase in the heart rate, in particular, is an indicator of imminent death. Ataxia, head pressing and recumbency, together with a frothy nasal discharge, occur as the disease progresses. The incubation period in experimentally infected horses is six to twelve days. Only one of eight experimentally infected horses has recovered following the onset of clinical disease. Seven horses recovered or were subclinically infected during the field outbreak at Hendra (all developed detectable specific serum antibody to the virus). Two of these horses subsequently developed tonic spasms of the muscles of the neck and hind limbs (15).

The most significant gross lesions are found in the lungs which are congested, firm and fluid filled with dilated lymphatics, particularly in the ventral portions. Some lungs have fibrin tags on the pleura. Some naturally occurring cases have a thick, foamy haemorrhagic exudate in the airways, and some also have approximately 100 ml of serous fluid in the pericardial sac.

Interstitial pneumonia with proteinaceous alveolar oedema associated with haemorrhage, dilated lymphatics, alveolar thrombosis and necrosis of the wall of small blood vessels are the main microscopic lesions. However, perhaps the most remarkable microscopic lesion is the presence of syncytial
giant cells in blood vessel walls, especially in the endothelium. These are common in lung capillaries and arterioles, though they are also present in blood vessels in lymph nodes, spleen, brain, stomach, heart and kidney. These syncytial giant cells react strongly in indirect fluorescent and immunoperoxidase tests using specific HeV antiserum. Cytoplasmic inclusion bodies containing nucleocapsid structures can be seen in these syncytial giant cells when examined under the electron microscope.

Epidemiology

The index case in the Brisbane outbreak was a pregnant mare kept at a spelling paddock approximately six kilometres from the stable. The trainer noted that the mare was ill, and moved the animal, together with another healthy horse, to the stable where treatment was commenced. The mare died within two days, showing typical clinical signs. The horse transported with the mare never became ill or detectably infected. A further twelve horses died within a period of seventeen days (ten horses in the stable, one in the neighbouring stable, and another that was transported from the main stable to a paddock 150 km away). Seven other horses were infected, some sub-clinically (four in the main stable and three others, all connected in some way with the main stable or the neighbouring stable). These seven horses were euthanised by order of veterinary authorities as uncertainty existed about whether the horses were persistently infected with the virus and, if so, whether they might periodically excrete the virus. Fourteen other horses, considered by animal health professionals as likely to have been exposed to infected horses, did not become detectably infected with the virus (2).

Two horses died during the Mackay incident (15). The affected horses were held in adjoining paddocks, but only for a period of less than 24 hours after onset of clinical signs in the first horse. Clinical signs in this horse, a pregnant mare, were reported to be severe respiratory disease, ataxia and marked swelling of the head, particularly the infra-orbital fossa and cheeks. The second horse, a stallion, reportedly showed aimless pacing, muscle trembling and haemorrhagic nasal discharge, and the lungs were full of blood at post-mortem. In both instances, death occurred within 24 hours of the onset of clinical signs. The second horse had brief contact with the carcass of the first horse, which was lying slightly inside the dividing fence between the adjoining paddocks. The eleven day interval between the deaths is consistent with the incubation period of between six and twelve days, seen in experimental HeV disease and during the outbreak in Brisbane. No other horses on the property, or in Queensland, were found to be infected following epidemiological investigations and serological testing (17), nor were other animal species found to have detectable levels of specific antibody (15).

The case in Cairns involved a single nine-year-old thoroughbred horse which shared a paddock with another horse. The affected horse succumbed quickly with clinical signs of depression, oedema of the face, lips and neck and an elevated heart rate. Rectal temperature and respiratory rate were not recorded. The disease was diagnosed on the basis of microscopic pathology, immunostaining, molecular virological tests and electron microscopy. The second horse was not detectably infected, based on clinical examination and serological testing, although the animal shared a feed bin with the affected horse.

The disease is not highly contagious under natural or experimental conditions. A five-kilometre radius around the infected premises in the Brisbane outbreak encompassed many other training stables, as the area lies between two major thoroughbred racing and training tracks. Therefore, many horses could have become infected if the virus was readily transmissible. However, no spread occurred to other stables contiguous with the infected premises, and not all horses on the premises became infected. Similarly, horses in the infected premises placed in uncleaned stalls that previously contained horses that succumbed to the disease, did not become infected. In addition, other horses on the infected premises at Mackay and Cairns were not infected.

Williamson et al. were unable to demonstrate transmission of the virus between infected and in-contact horses under experimental conditions, although the infected horses developed the expected disease (albeit without the frothy nasal discharge seen in the Brisbane outbreak) (20). However, one horse did apparently become infected following exposure to experimentally infected cats kept in close contact with the horses. Similarly, Westbury et al. found transmission of the virus and disease to only one of two cats cohabiting with affected cats, but not to cats in contiguous cages (19). Therefore, natural transmission does occur but seems to require very close contact. The low transmissibility of HeV between horses and cats contrasts vividly with that of Nipah virus where the virus spreads readily and rapidly between infected and in-contact pigs under experimental conditions (H.A. Westbury and D. Middleton, unpublished data). Nipah virus is not only excreted in the urine of infected pigs, but is also undoubtedly present in aerosols generated during coughing (a common clinical sign of the disease), as the virus multiplies in cells lining the upper and lower respiratory tracts and has been detected in exudate present in the airways of affected pigs.

Virological and serological testing suggests that bats of the Megachiroptera family are the natural reservoirs of HeV (21, 22) although the method of transmission from bats to horses is not known at this time. Similarly, little is known about the biology of the virus in bats.
Pathogenesis

Horses can be experimentally infected with HeV following parenteral challenge, and by the oronasal route (12, 20). Virus has been isolated from the buccal cavity, blood, brain, spleen, lungs, bronchial and prescapular lymph nodes, kidneys of experimentally infected horses, and perhaps most significantly, from urine (20). The virus has also been isolated from a variety of tissues of experimentally infected bats, including animals that were pregnant. During these studies, the virus was isolated from the urine of experimentally infected pregnant bats, and specific immunostaining was observed in the placenta of experimentally infected pregnant bats (18). These results indicate that HeV does not induce congenital disease following transplacental transmission. Indeed, Halpin et al. describe the isolation of HeV from uterine discharges of a bat that had miscarried twin foetuses, and from three other bats (3).

Detailed sequential studies into the pathogenesis of HeV disease in horses have not been undertaken because such work is expensive and must be performed under current Australian standards, at BL4 (i.e. staff working in fully encapsulating suits: a requirement that makes working with horses difficult). Infected animals provide an excellent model for the study of the natural disease process in experimentally infected cats (H.A. Westbury and D. Middleton, unpublished data) and, in contrast to HeV, Nipah virus has also been found to be infective to cats. Therefore, sound reasons exist for using cats in the study of these new zoonotic diseases. Compression cages and rapidly acting anaesthetics make the handling of cats under BL4 conditions practical and safe, and so these animals offer the opportunity to discover more about the pathogenesis of Hendra and Nipah viruses.

Hendra virus and bats

Six of eight susceptible bats inoculated with a dose of HeV known to infect and induce disease in horses, cats and guinea-pigs, developed detectable levels of specific antibody to the virus, without exhibiting obvious clinical signs of disease (20). Only two of these animals had microscopic vascular lesions suggestive of HeV infection when examined twenty-one days after challenge. The vascular lesions observed were similar to those seen in experimentally infected guinea-pigs and could be specifically stained using immunohistochemical techniques. No virus was isolated from samples collected at post-mortem which is perhaps not surprising as the bats had developed specific antibody at the time of virus sampling. Additional experimental studies also induced sub-clinical infection in bats, including animals that were pregnant. During these studies, the virus was isolated from the foetuses of experimentally infected pregnant bats and specific immunostaining was observed in the placenta (M.M. Williamson, personal communication). Studied in combination, these results indicate that HeV does not induce disease in bats, at least under the conditions of the experiments, but is responsible for a sub-clinical infection, except perhaps in pregnant animals where the virus might induce congenital disease following transplacental transmission. Indeed, Halpin et al. describe the isolation of HeV from uterine discharges of a bat that had miscarried twin foetuses, and from three other bats (3).

A range of issues concerning HeV infection of bats requires further study. Little is known of the biology of the virus in bats including the mode of transmission between bats, when transmission occurs and, perhaps most importantly, how the virus is transmitted to its unusual host, the horse. The virus infects the four species of priapulid bats (flying foxes) present in Australia and has been found across the geographic range of these bats. Serological data also suggests infection of bats in Papua New Guinea and New Britain (11). This, together with the fact that infection seems to be subclinical in bats, suggests that the virus is part of the natural microbiological experience of bats. Why infection has only apparently emerged recently is a frequently asked question and opinions and answers are diverse.

Diagnosis and surveillance

Experience indicates that HeV disease in horses in Australia is uncommon and sporadic, although this provides no grounds for complacency as there is widespread appreciation of the importance of the disease from both an animal and human health perspective. The possibility of HeV disease in horses should be considered in cases of sudden death, particularly if there is premonitory respiratory disease, and if the case occurs in an area or region where fruit bats are common. Clinical signs of the onset of disease are a rise in rectal temperature, increased respiratory and heart rates and, occasionally, signs of CNS involvement. Field veterinarians need to take stringent microbiological security precautions when handling potentially infected horses and during autopsy of such horses. These include, as a minimum, effective eye, nose and mouth protection from fomites and aerosols, complete covering of the body with overalls, and double gloving with gloves tied by adhesive tape to the cuffs of the overalls/shirt. In the Australian Animal Health Laboratory of the Commonwealth Scientific and Industrial Research Organisation (CSIRO), all in vivo and in vitro work with live virus and infected animals is performed at BL4. The possibility of bone-stick injuries and injuries from other sharp equipment used during autopsy needs to be in the forefront of planning for such work.

The gross pathology in the lungs of affected horses is highly suggestive, but is not pathognomonic. Not all naturally and experimentally infected horses have exhibited the typical lesions of pulmonary oedema and dilation of the ventral lymphatic of the lung, together with haemorrhage and froth in...
the trachea, bronchi and bronchioles. Histologically, syncytial giant cells in blood vessel walls, particularly in the endothelium of lung capillaries and arterioles are very characteristic of the disease. These syncytial cells can also be seen in lymph nodes, spleen, brain, stomach, heart and kidney (7, 8). The syncytial cells can be immunostained with specific antibody using fluorescent or immunoperoxidase staining techniques. The virus grows well in a range of cell culture systems, though Vero cells are commonly used. It induces CPE of the syncytial type after approximately three days in Vero cells in the first passage, rarely requiring blind passaging. Electron microscopy (EM) can be used to visualise the virus by negative staining in ultrathin sections of infected cell culture material. The virus can be similarly seen in tissue sections from infected animals (9). The unique ‘double fringe’ of the virus can be seen in this way, and the identity of the virus can be further confirmed by immune EM using gold labelled probes. Detection using PCR, and nucleotide sequence characterisation has been performed using cell culture propagated virus and fresh and formalin-fixed tissues from affected animals (6). Specific antibody is detected using an enzyme-linked immunosorbent assay (ELISA) or virus neutralisation tests (12, 15).

Epidemiological investigations and structured serological surveys were conducted in Queensland and other parts of Australia, following the detection of HeV infected horses in Brisbane and Mackay (2, 15). Similar investigations were undertaken by the Queensland State Government animal health authorities following the diagnosis of the disease in a single horse in Cairns in 1999 (K.J. Dunn, personal communication). These studies demonstrated that no spread of HeV had occurred beyond the known infected premises. In Australia, the media and professional awareness programmes have been used to create a high awareness among government and private veterinarians, and all those who keep horses, of the possibility that horses can become infected with this lethal zoonotic virus. The disease is officially notifiable under regulations in all States of Australia and all animal carers have an obligation to report suspicions of unusual animal disease to animal disease control authorities.

Prophylaxis and treatment

No vaccines are available to control HeV disease and no antivirals are suitable for use in infected animals, even if this were a financially viable option. The outbreak of the disease in Brisbane was controlled by a stamping-out programme involving slaughter of all known infected horses, quarantine of premises, controls on the movement of horses within a defined disease control zone, and serological surveillance to determine the extent of infection. Serological testing revealed no other known infected premises. Similarly, serological testing was used to determine the extent of infection on the infected premises and elsewhere in the incidents in Mackay and Cairns. No other infected horses were identified on the premises, suggesting that infection did not spread beyond the horses affected initially (two horses on the Mackay property and one horse on the Cairns property).

Perspectives

The isolation of three previously unrecognised zoonotic viruses in Australia in the 1990s (HeV, Australian bat lyssavirus and Menangle virus), the natural hosts of which appear to be bats of the family Megachiroptera, and perhaps Microchiroptera, was totally unexpected and provided an Australian perspective to the world-wide concept of emerging diseases. The recognition of these viruses began with the speedy discovery of HeV as the cause of an unusual disease in horses which was zoonotic (12). This was followed rapidly by the demonstration of the role of bats as the probable natural host of the virus (21), in addition to the disturbing finding of the variable symptoms in infected humans and the possible delayed sequelae to infection (10). Subsequently, research aimed at acquiring a better understanding of the biology of HeV in bats led to the discovery of Australian bat lyssavirus (4) and the recognition that Menangle virus was probably also a bat virus (14). Each of these zoonotic viruses were new to human and veterinary medicine and presented challenges to disease control authorities not only because the viruses were new, but also because a co-ordinated effort was required between human and animal health authorities and institutions. In addition, it was necessary to develop means and resources for studying a wildlife species which is difficult to access.

Hendra virus disease was not only new to human and veterinary medicine but the virus was also new to virology. Analysis by Hyatt and Selleck (9), Yu et al. (23) and Wang et al. (16) found that the virus was unique and probably was the first recognised member of a new genus within the Paramyxoviridae family. This prompted thoughts about whether other members of this putative genus exist, a question answered with the emergence of Nipah virus. Given the extensive distribution of Megachiroptera in Asia, Australia and the surrounding islands, additional members of this proposed genus may be discovered in the future.

The problem of natural zoonotic virus infections in bats is not easily solved. Awareness of these infections is important, as is ensuring that the knowledge and means exist to prevent, or at least significantly diminish, opportunities for 'spillover' of such viruses from the natural host into humans and other animal populations. How 'spillover' of HeV occurs is not known, although based on the Australian experience, it is sporadic and uncommon. Current data suggest that additional natural hosts of HeV are unlikely to exist in Australia. Consequently, 'spillover' of the virus must occur from bats to horses, although whether this is direct, or through intermediaries, requires further study. Some time
may elapse before this can be determined, as the conjunction of events leading to 'spillover' seem to occur infrequently.

It is also apparent that HeV does not transmit readily between horses. Opportunities for more widespread transmission between horses existed during the incidents in Brisbane, Mackay and Cairns, but did not occur. In the incident in Brisbane, disease spread to only one contiguous property and this seemed to involve direct horse-to-horse contact. The explosive outbreak of disease on the index property in Brisbane may be inconsistent with this concept, although the sequence of events relating to the management and husbandry of the horses before and during the early stages of the outbreak is not known. There are suspicions that iatrogenic spread of the virus may have occurred. Nipah virus, in contrast to HeV, spreads readily between pigs, perhaps by aerosols generated during coughing, as the virus multiplies in the respiratory epithelium and is present in exudate in the airways of affected pigs (H.A. Westbury and D. Middleton, unpublished data). This feature has neither been observed in horses naturally infected with HeV, nor in horses, cats or guinea-pigs experimentally infected with the virus. Whether this is characteristic of the respective viruses or of the host (pig or horse), is not known at this time. However, a strain of HeV with the propensity to spread among horses in the way that Nipah virus spreads in pigs would significantly change current perspectives of HeV.

Diagnosis of HeV disease is relatively uncomplicated. The gross pathology in the lungs is suggestive, and the microscopic pathology is distinctive especially if giant syncytial cells are present in the endothelium of blood vessels. These cells can be immunostained, as can virus or viral components in ultrathin sections of affected tissues used for EM. The virus grows readily in a range of cell cultures and rapidly induces a syncytial-type CPE. It can be readily visualised in these samples by EM, following negative staining. The virus can be detected in infected cell cultures or fresh, formalin-fixed and paraffin embedded tissue samples from affected horses using molecular virological techniques. Thus, presumptive diagnosis of the disease can be made using conventional histopathological or immunohistochemical techniques at regional animal health laboratories with confirmation of the diagnosis made at central laboratories with access to virus isolation, EM and molecular virological techniques. The key component to diagnosis, as with most diagnoses, is the awareness of the disease by veterinarians and other animal health professionals working in the field. This has been achieved with HeV disease because the significant zoonotic potential of the virus has demanded changes in the handling of horses and disease diagnosis in horses, particularly where respiratory disease is present, and in areas inhabited by bats.

Infection due au virus Hendra chez les équidés

H.A. Westbury

Résumé

L'auteur retrace la découverte d'une nouvelle maladie des équidés, non décrite auparavant, et fait le point sur les études consacrées à son étiologie. L'agent causal, qui porte aujourd'hui le nom de virus Hendra, est le virus de référence pour la constitution d'un nouveau genre proposé au sein de la famille des Paramyxoviridae. Agent de zoonoses létales, il est à l'origine d'infections naturelles chez l'homme et les équidés ainsi que d'infections expérimentales chez le chat, le cobaye domestique et la souris. Par ailleurs, ce virus est responsable d'infections naturelles, dans la plupart des cas sans signes cliniques apparents, chez les mégachiroptères, qui en sont l'hôte naturel. Le virus se transmet facilement entre les différentes espèces de mégachiroptères ; il se transmet plus difficilement entre chevaux, dans des conditions naturelles et expérimentales, ainsi qu'à l'homme. On ignore encore le mode de transmission entre les chauves-souris et les équidés. Trois épisodes dus au virus Hendra ont été signalés chez des équidés en Australie — deux en 1994, entraînant la mort de 15 chevaux ainsi que deux décès humains, et un en 1999, causant la mort d'un seul...

Mots-clés

Enfermedad causada por virus Hendra en el caballo
H.A. Westbury

Resumen
El autor da cuenta del descubrimiento de una enfermedad equina hasta ahora no descrita y explica los estudios realizados para determinar la etiología de la enfermedad. El virus causante de esa enfermedad, denominado ahora “virus Hendra”, es el virus de referencia de un nuevo género que se ha propuesto añadir dentro de la familia Paramyxoviridae. Se trata de un agente zoonótico letal, capaz de infectar en condiciones naturales al hombre y el caballo y en condiciones experimentales a gatos, cobayas y ratones. En condiciones naturales el virus también infecta a los megaquirópteros (en general de forma subclínica), que constituyen su huésped natural. Este virus, que parece transmitirse fácilmente entre especies de megaquirópteros, no presenta la misma facilidad de transmisión entre caballos, tanto en condiciones naturales como experimentales, ni tampoco del caballo al ser humano. Se desconoce el mecanismo por el cual se transmite de los murciélagos al caballo. En Australia se han registrado tres incidentes de enfermedad equina causada por el virus Hendra, dos en 1994 que causaron la muerte de quince caballos y de dos seres humanos, y uno en 1999 que se saldó con la muerte de un solo caballo. El virus Hendra guarda parentesco con el virus Nipah, el agente que provocó brotes de enfermedad y mortalidad en seres humanos, cerdos, perros y gatos en Malasia en 1998 y 1999.

Palabras clave

References


