

Lessons to be Learnt from the Nipah Virus Outbreak in Singapore

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The Nipah virus story in Singapore began on March 13 this year. From this date and for the next week, a number of abattoir workers developed illnesses with fever and predominantly neurological signs and symptoms. All those who came down with this mysterious disease were closely associated by occupation with the pig industry. At the same time, a similar outbreak was occurring in Perak and Negri Sembilan, Malaysia. As 80% of the pigs slaughtered in Singapore came from Malaysia, it was logical for clinicians, veterinarians, epidemiologists and laboratory personnel to come to the conclusion that the disease on both sides of the causeway was similar and linked to pigs from the Perak and Negri Sembilan farms.

Calling upon close working relationships and friendships with other virologists in Kuala Lumpur and Australia, contact was established between the Singapore medical professionals involved in the outbreak and the CDC (Centers for Disease Control) in Atlanta and their field officers in Kuala Lumpur. Clinical samples of blood as well as post-mortem tissues from the single patient who died from the illness were sent to CDC, Atlanta, and a further lot was sent to the CDC team in Malaysia, where it was quickly established that 11 of the specimens sent were positive for IgM antibodies against Hendra virus (the paramyxovirus found in horses in two outbreaks in Queensland, Australia and named after the town in which it first appeared.) In addition, it was also established by immunohistochemistry that the brain, lung and kidney of the patient who died contained a paramyxovirus closely related to the Hendra virus, and was found to be identical to the virus responsible for over 300 cases in Malaysia (and around 100 deaths). This virus, first isolated by the Malaysian virologist, Dr Chua Kaw Bing, was later named Nipah virus.

The Ministry of Health and the Primary Production Department (PPD) of the Ministry of National Development and the Ministry of the Environment rapidly instituted steps which effectively contained the outbreak. Already in place over the years was an integrated control programme to allow only pigs from pig farms accredited by the PPD to be exported to Singapore. Accreditation involves regular inspection to ensure such farms are well managed with good disease control programmes and hygiene. The PPD would only accept consignments accompanied by a health certificate issued by the Department of Veterinary Services in Malaysia, certifying that the pigs

exported were healthy. On arrival at the abattoir, the pigs are inspected upon being unloaded. Unhealthy looking pigs are rejected; only healthy ones are sent for slaughter. After slaughter, the carcass and organs of each pig are again inspected by PPD officers before being released. Pigs are tattooed so as to make it possible to identify the farm of origin.

In the early phase of the viral encephalitis outbreak in October, 1998, it was thought that the cases were due to Japanese encephalitis (JE) which is endemic in Malaysia. Control measures taken to prevent JE included banning of imports from affected farms in Malaysia, fogging the abattoirs in Singapore to destroy the mosquito vectors for the disease and increasing the frequency of spraying to eliminate mosquito larvae. A serological survey on imported pigs in January, and again in March 1999 was carried out and this confirmed that there was no active JE infection. Vaccination of abattoir workers against JE was begun in mid-February. When the outbreak spread to Negri Sembilan, the ban on the import of pigs was extended to all farms in Negri Sembilan and the Kinta Valley in Perak on 3 March. These measures, whilst appropriate for the control of JE, did not prevent the incursion of the then unknown virus, and indeed, the first Singapore patient was warded on 13 March. After the disease was notified on 17 March, a further extension of import ban to include all farms north of Johore was instituted on 18 March. The next day, following confirmation that the Singapore abattoir worker who died was not infected with JE, together with reports that a Hendra-like virus was isolated from human cases in Malaysia, the PPD immediately instituted a total ban on all Malaysian pigs, horses, dogs, cats and other mammals. Abattoirs were closed and thoroughly disinfected. Abattoir workers and their contacts were screened. The PPD believes that those infected with Nipah virus appeared to have contracted the disease from a point source – a batch of pigs from Negri Sembilan before the ban on imports of pigs from Negri Sembilan and Perak was imposed on 3 March. Interestingly, these pigs did not show any clinical signs of illness and post mortem meat inspection did not reveal any unusual findings in the carcasses. The last patient was admitted to hospital on 19 March. The total ban on importation of pigs seems to have been the crucial step leading to the cessation of the epidemic in Singapore. Preventive control measures in the hospitals were instituted and included medical personnel employing strict infection

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control standards, contact and airborne precautions when caring for all patients associated with abattoirs.

Imports of pigs resumed at the end of April only from an accredited pig farm in Indonesia after porcine sera samples from this farm sent for testing to the Australian Animal Health Laboratory (AAHL) were shown to be negative for Nipah virus.

Over 1000 specimens have been collected from abattoir workers (including those who came down with any illness in March), horse handlers, all laboratory, medical and veterinary personnel who came into contact with pigs and patients and patient specimens and are awaiting testing.

One laboratory medical technician has been trained by the CDC team in Kuala Lumpur in the laboratory diagnosis of Nipah virus (antibody testing) and plans are being laid for doing the testing of sera in Singapore when a source of viral antigens is secured, and proper facilities for testing are in place. It should be kept in mind that this is a level 4 organism, (WHO definition: a pathogen that usually causes serious human or animal disease and which may readily be transmitted from one individual to another directly or indirectly. Effective treatment and preventive measures are not usually available).

What do we know of the outbreak and the disease? Much still needs to be discovered. That a paramyxovirus was responsible and that it affected pigs and was transmitted to persons in close contact with these pigs is known. This virus is closely related to the Hendra virus that was discovered in 1994 in Australia. The fruit bat in Australia is the natural host of the Hendra virus. It is not known whether the Nipah virus was introduced into Malaysia or is indigenous. It has also been found in horses, dogs, cats and bats, but it is not known how and from whom the pigs got infected. Fortunately, transmission from pig to man requires a close association, and the infection in man seems to meet with a dead end. None of the patients with the illness seems to have passed it on to a second human contact. This is probably why the ban on importation of pigs in Singapore led to such a rapid cessation of the outbreak.

The lessons we have learnt from this sobering outbreak are that we have to be ever-vigilant for zoonotic diseases. The pig alone may transmit bacterial diseases like anthrax, brucellosis, *Clostridium perfringens* type A, erysipelas, leptospirosis, pasteurellosis, salmonellosis, *Streptococcus suis*; viral diseases like Japanese encephalitis, swine influenza, vesicular diseases, and now Hendra and Nipah viruses; parasitic diseases like *Taenia solium*, trichinosis, toxoplasmosis and ringworm just to mention a few.

The recent Hong Kong avian influenza is another case in point; in that instance, culling of domestic chickens was needed to stop the H5N1 outbreak in Hong Kong, there was extensive cleaning up of the fowl markets in Hong Kong, vigilance and increased epidemiological surveillance has been instituted and work is continuing on an international scale to produce a vaccine. Again it was fortunate that transmissibility of the virus seemed to be low; however, the propensity for reassortment of the influenza virus

makes it imperative that surveillance for all new strains of influenza is continued. These are only two examples of emerging diseases; others are bovine spongiform encephalopathy which resulted in the culling of thousands of cattle, and haemorrhagic fevers like marburg and ebola which have no cure and no vaccine.

Since April, there have been no further cases in Singapore. For now, the outbreak seems to have been contained. However, for the prevention of Nipah virus and other zoonoses, we must continue, as we have in the past, to inspect all livestock at the point of origin and when they arrive, to take proper precautions for workers and make sure that facilities for their slaughter are maintained at the highest level of hygiene possible. For those who come down with these zoonoses, we must ensure that facilities for the care of patients with high level (dangerous) organisms are available, that all health care and veterinary care personnel have adequate protection, and that laboratories are equipped with P3 or P4 facilities to handle these dangerous organisms. A breakdown or neglect in the use of safety precautions because one is not aware that one could be exposed to dangerous organisms can lead to an outbreak of tragic consequences.

It goes to the credit of all those involved that the Nipah virus outbreak was contained so quickly, as most of the safety facilities and procedures were quickly instituted, or already in place. Acknowledgement must also go to all those who gave aid and advice, and established the diagnosis for this epidemic, particularly Professor SK Lam in Malaysia, and Dr Brian Mahy and the CDC team in Atlanta and their field team who were stationed in Kuala Lumpur and also in Singapore and AAHL.

We have established an early reporting system that gives rapid warning in situations like this, and close collaboration has been established between the Ministries of Health, National Development and the Environment. This was an important contributing factor in the limiting of the number of human cases of Nipah virus in Singapore. However, we need to continue to be vigilant. Links with international communicable disease teams have proven to be invaluable and must be continued. Training and attachment with such groups for the local team could be formalised so that we will have a stronger team with expertise in dealing with emerging diseases. This will immensely improve the skills of those who in this instance had to deal with this outbreak and prepare them for all eventualities to ensure that everything that can be done will be done rapidly to safeguard public health in similar situations that may arise in the future.

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