

Emerging Infections in Australia

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Abstract

Over the last 10 years, novel infectious agents including Equine Morbillivirus, Lyssavirus, Barmah Forest Virus, Rickettsia honei and two as-yet-unnamed bunyaviruses have been identified as causes of human disease in Australia. Previously described agents, such as Japanese B Encephalitis virus, Dengue virus, Ross River virus, Orientia tsutsugamushi, Rickettsia australis, Burkholderia pseudomallei, Mycobacterium ulcerans and Trichinella pseudospiralis, have increased their geographical distribution over the last 20 years. Widespread antibiotic use has also resulted in selection for, and dissemination (especially in hospitals) of, multiresistant bacteria such as multiple-resistant Staphylococcus aureus (MRSA), expanded-spectrum β -lactamase (ESBL) producing gram-negative bacteria, penicillin-resistant pneumococci and vancomycin-resistant enterococci (VRE).

Ann Acad Med Singapore 1997; 26:609-15

Key words: *Burkholderia pseudomallei, Dengue virus, Equine Morbillivirus, Lyssavirus, Multiresistant bacteria*

Introduction

In recent years, several novel infectious agents which cause human disease have been described in Australia. Whether their apparently sudden appearance represents true "emergence" (such as the crossing of species barriers) or reflects improved diagnostic capabilities for long-present diseases is not established. In many cases, the ecology and epidemiology of these infections are not currently well understood and it is uncertain whether they will become significant health threats to the Australian community or visitors. In addition, a number of diseases which have been recognised to occur in Australia in the past have appeared to increase in incidence or geographical extent recently. In the absence of good longitudinal data, however, it is not clear whether this is a real or perceived phenomenon. If the increased notifications of these diseases are due to a true rise in incidence, this may relate to increased travel to previously remote areas, environmental changes resulting in creation of new areas of endemicity or expansion of residential communities into areas (i.e. wetlands) currently endemic for exotic pathogens.

Novel Pathogens

Equine Morbillivirus (EMV)

The outbreak of a fatal respiratory illness affecting horses on a property near Brisbane was shown to be

caused by a previously undescribed morbillivirus.¹ Two of the stable staff developed an influenza-like illness after close contact (including extensive exposure to respiratory secretions) with the equine index case. The first patient recovered and had equine morbillivirus antibodies demonstrated in his sera collected on days 10 and 20 of his illness. The second patient developed severe pneumonitis requiring intensive medical support. He eventually improved prior to his sudden death from a cardiac dysrhythmia. This patient was also shown to be seropositive for the equine morbillivirus on days 7 and 13, and EMV was cultured from a kidney specimen obtained at autopsy.

Initial attempts to identify the natural reservoir for the virus were unsuccessful, but further studies revealed that 15% of flying foxes in a cohort of animals from eastern Australia were seropositive for EMV antibodies.* Eventually the virus was demonstrated by immunofluorescence (IF) of tissues obtained from a Pteropus flying fox.³

An additional human case subsequently occurred in a patient who developed mild meningitis shortly after he performed an autopsy on 2 horses that had died (one of a respiratory illness and the other of a neurological illness) on his property.⁴ While he initially appeared to respond to antibiotics, a year later he developed fatigue and irritability which progressed to encephalitis associ-

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ated with status epilepticus. He subsequently died and EMV was detected by polymerase chain reaction (PCR) in his serum collected at the time of his initial illness and also in cerebrospinal fluid (CSF) and brain tissue collected at the time of his second admission. His serum had low titre EMV antibodies at the time of the initial illness and higher titres were detected in the late phase of his illness.⁴ Both horses involved in this case had EMV demonstrated in tissues by IF and nested PCR.⁵

The mechanism of transmission of EMV from flying foxes to horses has not yet been elucidated. These cases graphically illustrate that novel infectious agents can suddenly appear in Australia and the rapid detection of such novel pathogens requires ongoing support of existing scientific resources in Australia.

Lyssavirus

Fruit bats from New South Wales and Queensland were recently identified as carrying a previously unknown Lyssavirus.⁶ A case of progressive fatal encephalitis developed in a patient from Rockhampton in Queensland who had contacts with many animals, including insectivorous bats, and had recently sustained multiple scratches from a fruit-bat.⁷ Her serum contained lyssavirus antibodies and PCR of CSF using lyssavirus-specific primers was positive for a 250 base pair product. Because of the genetic relatedness of the lyssavirus to classical rabies virus, rabies immunoglobulin was administered to the patient which transiently stabilised her condition, but it did not prevent the eventual fatal outcome. A Lyssavirus Expert panel was convened by the Australian Commonwealth Health Department and they have released directives for prevention of infection⁸ with this virus and urged clinicians to consider the diagnosis in cases of unexplained encephalopathy occurring in eastern Australia. Recently, the virus has been isolated from an insectivorous bat from New South Wales (NSW).⁹ The likely importance of this new pathogen as a threat to

human health, particularly in people with close contact with bats, is currently undetermined.

Flinders Island Spotted Fever

A general practitioner on Flinders Island (which lies between the Australian mainland and Tasmania) recognised a spotted fever-like illness in 26 people over a span of 15 years.¹⁰ Serological cross-reactivity with several spotted fever species, including *Rickettsia australis*, was documented.¹¹ Subsequent isolation¹² and genetic analysis of the causative organism¹³ confirmed this to be a novel spotted fever rickettsia and it was named *Rickettsia honei* in honour of the eminent Australian rickettsiologist Frank Hone. The vector for *R. honei* transmission (presumed to be an ixodid tick), its reservoir host (possibly reptiles) and its full geographic distribution are yet to be proven.

Bunyaviruses

Bunyaviruses, which include hantaviruses and the agent of Rift valley fever, are well recognised causes of human and animal disease worldwide. Gan-Gan is an arbovirus from this family, and it is well known to be an infrequent cause of epidemic polyarthritis in Australia.¹⁴ Several novel bunyaviruses have been isolated from arthropods in Australia's tropical north in the last decade.¹⁵ Seroconversions and significant rises in titres to two novel bunyaviruses have recently been documented in patients from the Northern Territory with febrile illnesses.¹⁶ Serological testing of the general population and domesticated animals have suggested a widespread distribution of these viruses. Bunyaviruses need to be considered as possible causes of acute febrile illnesses in patients exposed to arthropods in Northern Australia.

Barmah Forest Virus (BFV)

This alpha virus is transmitted by similar mosquito vectors to Ross River Virus (RRV). It may cause an acute exanthema and accounts for about 10% of cases of epidemic polyarthritis in Australia.¹⁷ The first clinical cases occurred in eastern Australia¹⁸ but subsequent outbreaks have identified new foci of endemicity in the Northern Territory¹⁹ and Western Australia.²⁰ While the epidemiology is not fully understood, it appears to be similar to RRV.

Previously Identified Pathogens

Japanese B Encephalitis (JE)

This flavivirus causes a severe encephalitis with a high mortality and frequent and serious sequelae in many parts of continental Asia.²¹ Until very recently, there was no evidence for this virus extending east of Wallace's line which separates South East Asian from Australasian flora and fauna.¹⁴ This was thought to be due to the pre-existence of endemic Australian flaviviral encephala-

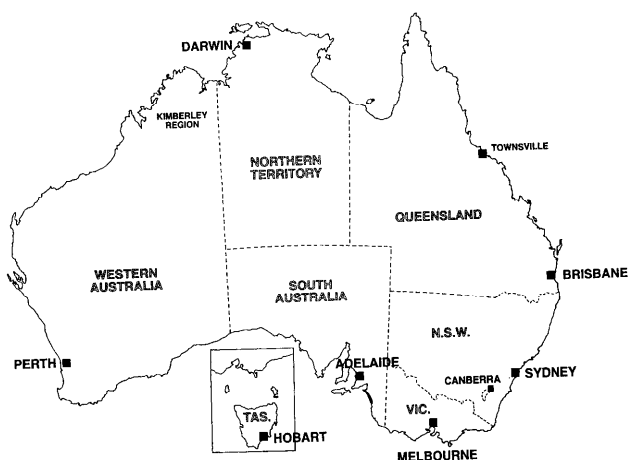


Fig. 1. Emerging infections in Australia.

litides (predominantly Murray Valley Encephalitis Virus). In 1995, three cases of JE, two of which were fatal, occurred on Badu island in the Torres Strait (which separates Australia from Papua New Guinea).²² Serological surveys confirmed widespread virus activity in residents and animals (particularly pigs) of the "outer islands" of the Torres Strait but not in the islands closer to the Australian mainland. It was hypothesised that spread of JE was from the New Guinea mainland (where there has been evidence of serological activity but no clinical disease or viral isolations) via infected mosquitoes and/or birds.²² An aggressive vaccination campaign was instituted in the Torres Strait because of concern that this dangerous virus may become established in Australia. Interestingly, despite previous concerns in Australia about reactions to this vaccine, few problems were experienced with its widespread use in this outbreak. Whether there is a potential for spread to the Australian mainland in the future is not known, but a study of migrating birds is in progress and may shed light on this issue.

Dengue Fever

The flavivirus which causes this clinical syndrome was endemic in most of tropical Australia until the 1950s when a campaign to eradicate the mosquito vector *Aedes aegypti* was instituted after 15 000 cases occurred between 1953 and 1955 in the Townsville region of northern Queensland.²³ No further cases were seen until 1981 when an epidemic affected a large part of northern Queensland.²⁴ Repeated outbreaks due to type 1 virus have occurred since in the area between Townsville and Cairns.²⁵ More recently, epidemics of type 2 virus have occurred,¹⁴ raising the prospect of dengue haemorrhagic fever (DHF) or dengue shock syndrome (DSS) appearing in this population (which has had previous exposure to another serotype of dengue). In fact, a case of Grade III DHF did occur during the Charters Towers outbreak of 1992 which included 190 cases of acute dengue.²⁶

Ross River Virus (RRV)

This arbovirus is transmitted by the bite of several species of salt marsh mosquitoes and causes acute illness with epidemic polyarthritis that has a tendency towards chronicity.¹⁷ Macropods (i.e. kangaroos and wallabies) appear to provide a significant reservoir of virus. Until recently, the vast majority of cases occurred in the tropical regions of Australia. Recent epidemics drew attention to extension of its distribution to South Australia²⁷ and the presence of a new endemic focus in the south west of Western Australia.²⁸ This infection is likely to be an ongoing problem as new housing developments are often located near wetlands harbouring suitable mosquito vectors. The chronic nature of many cases may result in significant economic losses to these communities.^{18,27}

Australian Spotted Fever (ASF)

The first case of this disease was reported in 1946²⁹ from northern Queensland. A large outbreak occurred shortly thereafter in soldiers camped on the nearby Atherton Tableland and the illness was named North Queensland Tick Typhus.³⁰ Subsequently, the term Queensland Tick Typhus (QTT) was used. The causative organism was isolated from one of the original cases, found to be distinct from other Australian agents of typhus³¹ and was subsequently called *R. australis*. The vectors are Ixodid ticks and the main hosts are small marsupials.³²

Further cases were reported over the next three decades from Southern Queensland³³ and Sydney³⁴ suggesting that ASF may be a less misleading term for this disease than QTT.³² There has been an apparent increase in notifications of ASF³² over the last decade and the first fatal case was described in 1990.³⁵ Recent cases,¹³ including a cluster,³⁶ were reported from East Gippsland near Melbourne. It is now proven that *R. australis* is distributed down the entire eastern seaboard of Australia, and suitable Ixodid vectors for transmission are found all the way over to the south coast of Western Australia.³⁷ It is likely, therefore, that additional foci of ASF may be identified.

Murine Typhus

Hone³⁸ first reported this disease in Adelaide, South Australia, in 1922 and he was the first clinician to associate this disease with rodents and their ectoparasites (predominantly *Xenopsylla* species). Subsequent outbreaks were reported from Queensland³⁹ but most cases occurred in Western Australia.⁴⁰ Despite an absence of notifications during the 1960s and 1970s, sporadic cases^{41,42} and clusters have been reported in the last six years.⁴³

Scrub Typhus

This potentially fatal infection is caused by the intracellular pathogen *Orientia* (previously *Rickettsia*) *tsutsugamushi* and is transmitted by Leptotrombidium mites, with bandicoots and rodents acting as reservoir hosts. Paine and Nye in 1927⁴⁴ described the first Australian case, which occurred in Northern Queensland. The bulk of Australian cases continue to occur in this location but recently a new epizootic focus was discovered in Litchfield Park, a popular tourist spot, near Darwin.⁴⁵ This area has recently had its first fatal case.⁴⁶ A separate endemic focus in the western Kimberly region of Western Australia has also been suggested by a recently reported case of scrub typhus.⁴⁷

Burkholderia pseudomallei (Meliodosis)

This gram-negative bacillus causes acute septicaemia or severe pneumonia with a high mortality rate.⁴⁸

Most cases occur in the monsoon season but chronic and relapsing disease may present at other times. The epidemiology revolves around environmental reservoirs in soil and water, cutaneous inoculation and compromised hosts (especially the presence of diabetes or alcoholism).⁴⁹ The Northern Territory and northern Queensland have long been recognised as endemic areas, but in recent times cases have been reported from sub-tropical Queensland⁵⁰ and temperate Western Australia.⁵¹ There has been an apparent increase in melioidosis as 37 cases were seen between 1960 and 1979 in the Northern Territory⁵² but the 1990-1991 wet season in Darwin produced 33 cases.⁴⁸ In addition, cases in the Kimberley region of Western Australia have been very infrequent in the past, however, over the last 12 months at least 5 cases have been transferred to hospitals in Perth for treatment.

Bacillus anthracis (Anthrax)

Anthrax was imported into Australia in infected bone-meal and the disease was first reported in animals in 1847 in New South Wales.⁵³ From there it subsequently spread to southern Queensland, western Victoria, South Australia, Tasmania⁵³ and Western Australia.⁵⁴ Widespread vaccination programmes greatly diminished the occurrence of anthrax in animals and sporadic human cases became very infrequent. In January 1997, an outbreak occurred in northern Victoria which subsequently affected 38 dairy properties and resulted in one human case of cutaneous anthrax in a knacker worker.⁵⁵ Public health measures, including mass vaccination of cattle, rapidly brought the outbreak under control. Unfortunately, the recent ban on importation of Australian beef by several countries suggests that it has not been appreciated that the current outbreak occurred in a dairy region. Unusual environmental conditions (a very dry summer followed by heavy rain) may have played a role in the latest outbreak. Because of the organism's ability to persist in soil for very long period,⁵⁶ it is likely that sporadic cases will continue to occur in endemic areas of Australia.

Mycobacterium ulcerans

This agent produces chronic progressive skin ulceration and was first recognised in patients from Bairnsdale in the Gippsland region of eastern Victoria.⁵⁷ Subsequently it was recognised as a cause of chronic (Buruli) ulcer in most tropical regions of the world. Over the last 10 years several new foci have been recognised in areas close to Melbourne, including one at Phillip Island where a contaminated irrigation system was implicated in the spread of the organism.⁵⁸

Schistosomiasis

Although the causative parasites of this disease are not

endemic in Australia, a rapid increase in the number of travellers returning from Africa have caused a dramatic increase in locally-diagnosed cases of schistosomiasis (Bilharzia).^{59,60} For example, in Western Australia the annual number of notifications of cases has increased 464% between 1993 (11 cases) and 1996 (51 cases). In our own Infectious Diseases unit, we have seen 48 cases since 1994 with the vast majority having acquired *Schistosoma haematobium* infection from Lake Malawi. Although most cases are uncomplicated and respond adequately to a single course of praziquantel, unusual presentations (pyrexia of unknown origin, genital masses, cervicitis, and testicular abnormalities) and occasional relapses occur. In addition, 23% of cases have had co-infections with other tropical pathogens (including *Entamoeba*, *Strongyloides* and *Taenia*) so formal infectious diseases assessment with staging of disease is important prior to therapy.

Trichinella pseudospiralis

Trichinella spiralis is endemic in many countries of the world where consumption of inadequately cooked infected meat (especially pork) may result in either inapparent infection or disease (which may include fatal cardiac and neurological complications).⁶¹ This pathogen has never been endemic in Australia. A related species, *Trichinella pseudospiralis*, was originally described in Europe⁶² but later was shown to be present in Tasmanian mammals.⁶³ Human disease due to this nematode was not proven until the recent description of *T. pseudospiralis* myositis occurring in a botanist who had eaten marsupial meat whilst on a field trip in Tasmania.⁶⁴ Unreported cases of locally-acquired trichinosis have occurred in Australia⁶⁴ and some of these may have been caused by *T. pseudospiralis*.

Multiple-resistant Staphylococcus aureus (MRSA)

In the 1960s, only sporadic cases of MRSA were reported in Australia but over the next 20 years it became established in the major hospitals of eastern Australia.⁶⁵ Brisbane, Sydney and Melbourne have the highest notification rates in Australia but these have remained stable over the last 10 years.⁶⁵ Because of aggressive and effective infection control procedures, MRSA never became established in Western Australian hospitals. Over this period, however, a new methicillin-resistant strain (non-multiple resistant or NMRSA) has appeared in Western Australia, possibly due to increased use of third generation cephalosporins in rural Western Australia. Although readily treatable with oral medications at present, this strain appears to have established a community reservoir and acquisition of further resistance mechanisms^{67,68} would create major therapeutic problems.

Penicillin-Resistant *Pneumococci*

Penicillin-resistance in pneumococci has become common in many countries and empiric regimens for treatment of meningitis have had to be revised to take this into account.⁶⁹ In Australia, carriage of strains with even intermediate penicillin-resistance (which in non-meningeal infections can usually be adequately treated by increasing the dose of penicillin) was infrequent (0.7%) in 1980/1991.⁷⁰ By 1989/1990, invasive isolates with intermediate penicillin-resistance accounted for 1.9% of the strains tested in a multi-centre study of metropolitan hospitals.⁷¹ When the same survey was repeated in 1994/1995, isolates with intermediate penicillin-resistance had risen to 3.7% of strains tested and isolated cases of high-level resistance were being encountered.⁷² It will not be long before penicillin alone will not be adequate for empiric therapy of pneumococcal meningitis in Australia.

Expanded-Spectrum (β -Lactamase (ESBL) Producing Organisms

These strains were first reported in Australia in 1990.⁷³ Since then antibiotic selection pressure (particularly from the widespread use of third-generation cephalosporins) has resulted in an increased frequency of isolates⁷⁴ including institutional outbreaks.⁷⁵ It is likely that they will become increasingly important as nosocomial pathogens in Australia with potentially significant cost implications for the future.

Enterohaemorrhagic *Escherichia coli*

These strains of *E. coli* are associated in many parts of the world with bloody diarrhoea and haemolytic-uraemic syndrome which occurs mainly in children. A recent outbreak in South Australia resulted from contaminated salami and produced 21 cases (including one fatality).⁷⁶ In North America the O157:H7 serotype has accounted for most cases, but the O111 serotype causes most infections in Australia.⁷⁷ Modern food technology utilising mass production methods and continuing government cuts in public health and inspection service funding suggests that further outbreaks are likely to occur.

Vancomycin-resistant *Enterococci* (VRE)

VRE have become major nosocomial pathogens in North America over the last decade.⁷⁸ The first VRE isolate in Australia was reported in 1995 from Melbourne and occurred in a liver transplant recipient.⁷⁹ Further sporadic cases have been seen in hospitals in Sydney and Perth. Because of the selective effect of third generation cephalosporins (and, to a lesser effect, vancomycin) for this organism, and Australia's extensive use of these agents, it is possible that this will become an important nosocomial pathogen in this country.

Conclusion

Because of increasing tourism to previously remote parts of tropical Australia, it is important to identify new endemic foci for previously recognised agents of serious infections. We also need to further characterise the ecology of newly discovered pathogens. Increased overseas travel and the potential for illness in returning travellers requires Australian hospitals to acquire expertise in diagnosis and treatment of tropical infections. In addition, increasing hospital use of broad-spectrum antibiotics in compromised hosts will continue to select out increasingly resistant nosocomial pathogens and lead to therapeutic and health economic difficulties.

Acknowledgements

The author would like to thank Drs M Balme and J McCarthy for their helpful review of this manuscript.

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