Framework for the surveillance, prevention and control of Murray Valley encephalitis virus in Australia

This framework has been developed by the National Arbovirus and Malaria Advisory Committee (NAMAC), endorsed by the Communicable Disease Network Australia and noted by the Australian Health Protection Principal Committee. The purpose of the framework is to provide nationally consistent guidance on the prevention and control of Murray Valley encephalitis. This information supplements the information provided in the Series of National Guidelines ('SoNGs') document for Murray Valley encephalitis.

This framework captures the knowledge of experienced professionals, and provides guidance on best practice based upon the best available evidence at the time of completion.

Readers should not rely solely on the information contained within these guidelines. Guideline information is not intended to be a substitute for advice from other relevant sources including, but not limited to, the advice from a health professional. Professional judgement and discretion may be required in the interpretation and application of these guidelines.

The membership of the NAMAC, CDNA and the AHPPC, and the Commonwealth of Australia as represented by the Department of Health ('the Commonwealth'), do not warrant or represent that the information contained in the Guidelines is accurate, current or complete. The CDNA, the AHPPC and the Commonwealth do not accept any legal liability or responsibility for any loss, damages, costs or expenses incurred by the use of, or reliance on, or interpretation of, the information contained in the framework.

Revision history

Version	Date	Revised by
1.0		

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Introduction

Murray Valley encephalitis virus (MVEV) is a mosquito-borne zoonotic virus that periodically causes disease in humans in Australia.

In 2011, the Australian Health Protection Committee requested the National Arbovirus and Malaria Advisory Committee (NAMAC) develop a national framework for the detection and management of MVEV in Australia. This framework has been developed by a working group of NAMAC and is intended to build on the existing 2005 National Guidelines for the Prevention, Management and Control of Murray Valley Encephalitis [1] The framework aims to provide an overarching approach for routine public health activities and response to MVEV at local, state and national levels, and considers future policy and research options for this arboviral disease.

Topics included are: the governance and legislative framework for communicable diseases and MVEV in Australia; disease information about MVEV; surveillance and detection of outbreaks; prevention and control activities; public health response plans including guidelines for public health response to human cases and investigation of outbreaks; and finally, policy and research options to further develop our understanding and approach to the disease.

The Framework is intended for use by the Australian Government, State/Territory and Local Governments and associated agencies.

Purpose

- To improve national coordination and collaboration on the management of MVEV
- To describe the current surveillance, laboratory, prevention and control activities for MVEV
- To provide clear direction to public health units in responding to human cases of MVEV infection including jurisdictional outbreaks (Series of National Guidelines – SoNGs)
- To define the steps in identifying and responding to MVEV outbreaks
- To assist in identifying current and future research and policy priorities for MVEV

Timeframe

It is anticipated that the timeframe for this framework be five years (2013 – 2018).

Governance and legislative frameworks

The roles and responsibilities for communicable disease control in Australia are shared between the Commonwealth, State, Territory, and Local Governments, each supported by relevant legislative frameworks. State and Territory Health Departments have primary responsibility for communicable disease prevention and control programs, and response to notifications of all notifiable diseases, including MVEV infection.

At the national level, the Commonwealth Department of Health (Health) works to coordinate communicable disease control activities and health emergency responses across the country, and provide public health leadership on matters of national importance. The development of

a national MVEV framework is consistent with the requirements for the National Health Emergency Response Arrangements to provide sub-plans for communicable diseases of national significance. The *National Health Security Act 2007* provides the legislative basis for communicable disease notifications in Australia and the exchange of health information between jurisdictions and the Commonwealth. The Act provides for the establishment of the National Notifiable Disease List, which specifies the diseases about which personal information can be provided to government departments. The National Health Security Agreement supports the practical operation of the *National Health Security Act 2007* including the transfer information of disease notifications from jurisdictions to the Commonwealth.

Commonwealth legislation is implemented through the Australian Health Ministers Advisory Committee (AHMAC) and its principal committee, the Australian Health Protection Principal Committee (AHPPC). AHPPC is supported by six national expert committees – the Communicable Disease Network Australia (CDNA), the Public Health Laboratory Network (PHLN), the Environmental Health committee, the National Health Emergency Management subcommittee, Antimicrobial Resistance subcommittee and the Blood Borne Virus and Sexually Transmissible Infections subcommittee. CDNA coordinates national surveillance and response to communicable disease outbreaks of national importance.

In 2001, Health established the National Arbovirus Advisory Committee (NAAC) as a technical advisory group to CDNA. In March 2003, NAAC became the National Arbovirus and Malaria Advisory Committee (NAMAC) when malaria was included in its terms of reference. NAMAC monitors arbovirus and malaria surveillance, strategic arbovirus and malaria disease management and vector control, and has a key role in making recommendations on the management of mosquito-borne disease. NAMAC provides expert technical advice to AHPPC through CDNA. It also assists in the detection, management and control of actual or potential outbreaks of arboviral and malarial disease. Members of the Committee have expertise in disease surveillance, virology, vector surveillance, vector control and quarantine, and represent agencies with a substantial interest in the area.

The role of States and Territories, as agreed in the National Health Security Agreement, is to develop, strengthen and maintain the capacity of the health sector to detect, report and respond to public health events; maintain communication networks with agencies and organizations within their jurisdictions to ensure an effective response to public health events and to receive information about events requiring a nationally coordinated public health response. The public health and communicable disease responsibilities for each State and Territory of Australia are enacted by their own pieces of public health legislation, typically Public Health Acts. Accordingly, the primary responsibility for public health action from a notification resides with State and Territory health departments.

Complementing the national role of NAMAC, most State and Territories manage their own mosquito-control and mosquito-borne disease programs and maintain interdepartmental taskforces or committees as part of a comprehensive response to animal or vector borne diseases.

To support States and Territories, the SoNGs have been developed by CDNA. The purpose of the SoNGs Guidelines is to provide nationally consistent guidance to public health units (PHUs) in responding to a notifiable disease event. These guidelines capture the knowledge of experienced professionals, and provide guidance on best practice based upon the evidence available at the time of completion. This framework includes a national guideline for MVEV infection (Appendix 2 MVEV SoNG).

The public health role of some local government is most often stated in terms of environmental health and engineering activities, for example waste management, prevention of infectious disease (including mosquito and vermin control), food safety and ensuring drinking water quality. These traditional concerns of local government are widely recognised and contribute to protecting the health of their communities. State and Territory Public Health Acts confer certain powers and responsibilities to local government, and there is significant variation between jurisdictions in both public health and local government legislation. With reference to MVEV, many State/Territory governments fund local government for a range of routine environmental health measures to mitigate the risk of mosquito-borne disease.

Disease background

MVEV is a mosquito-borne flavivirus that is found mainly in the tropical areas of northern Australia, eastern Indonesia and Papua New Guinea.[2, 3, 4] It was first isolated from patients who died from encephalitis during an outbreak in the Murray Valley in Victoria, New South Wales and South Australia in 1951,[5] though it is thought to have also been responsible for encephalitis occurring in eastern Australia in the early part of the twentieth century.[6, 7, 8, 9, 10, 11, 12] The only Australia-wide outbreak of MVEV infection was in 1974, primarily in the Murray-Darling basin, but cases were also reported in Queensland, the Northern Territory and Western Australia.[13] Large outbreaks also occurred in the Northern Territory in 1988 (3 cases), 1993 (6 cases), 2000 (4 cases), 2001 (3 cases) and 2011 (4 cases) and Western Australia in 1991, 2000 and 2011. Human cases, including encephalitis cases, occur in most years in the Kimberley region of Western Australia and the top two thirds of the Northern Territory, with sporadic cases further south in Western Australia (Pilbara, Gascoyne, Midwest, and Murchison areas, north of Perth), in Central Australia and in Queensland.[14, 15, 16]

MVEV infection in humans was not detected in south-eastern Australia again until 2008, with a single human case of encephalitis in Macquarie Marshes in NSW and widespread virus activity in southeastern Australia.[17, 18] In 2011 there was widespread flooding in south-eastern Australia with reappearance of MVEV in mosquitoes in NSW, Victoria and South Australia.[3] Cases of encephalitis were identified in humans from NSW, SA and possibly Victoria, in horses from all three states and in ducks in SA. This overlapped with a larger outbreak of encephalitis and non-encephalitic disease occurring in WA and the NT, again following heavy rainfall and flooding.

MVEV commonly infects humans without producing apparent disease (subclinical infection). It may also cause a comparatively mild disease with features such as fever, headache, nausea and vomiting. In a small proportion of all people infected (estimated 1:200 – 1:1000) meningitis or encephalitis of variable severity develops.[14, 19] In children, meningitis

or encephalitis may occur in up to 1:20 cases of infection, depending on the geographical location.[15, 16, 20] Signs of brain dysfunction such as drowsiness, confusion, seizures, weakness, tremor, ataxia and/or cranial nerve palsies indicate the onset of encephalitis. Based on the 1974 outbreak (which occurred primarily in south-eastern Australia) and studies in Western Australia and Northern Territory, it is estimated that the case fatality rate of encephalitic cases is about 15%–30%[16, 20] with long-term neurological sequelae occurring in 30%–50% of survivors and only 40% recovering completely.[13, 15, 16, 20, 21] There is no specific treatment available for MVE, and medical care is largely supportive. As a result, primary prevention (early warning, avoidance of mosquito bites and vector control) is extremely important.

Geographic distribution

Terminology

Endemic disease means a disease or infectious agent that is constantly present in humans within a specified geographical area or population group.[22] An epidemic disease is the occurrence in a community or region of human cases of an illness, specific health-related behaviour, or other health-related events clearly in excess of normal expectancy.[22] Applying the same principles to diseases with animal reservoirs, an epizootic is an outbreak of disease in an animal population, often with the implication that it might affect human populations. Enzootic disease means the disease or agent is constantly present in animals within a specific geographical area or population. Constantly present can still mean a disease has a seasonal presence, for example, a disease commonly observed every year but only during summer time can be referred to as enzootic.

As the primary activity of MVEV in Australia is thought to be between reservoirs and vectors, the terms used to describe disease activity in mosquitoes and reservoirs are enzootic and epizootic. In enzootic areas, regular disease activity occurs in vectors and reservoirs and may spill over into humans, and a single sporadic human case is not considered an outbreak, but outbreaks of cases in excess of normal disease expectancy may occur. In epizootic areas, a single human case of MVEV disease is considered an excess of normal disease expectancy and is typically referred to as an epidemic.

Australia

Enzootic regions: MVEV is reported in mosquitoes and sentinel chicken flocks each season in northern Western Australia and the Northern Territory, with sentinel chicken antibody detections showing a rise in February and maintaining a high level of detection until June. In these regions sporadic human cases or small outbreaks of MVEV occur every few years, usually during or soon after the summer monsoon season (February to July) when the mosquito vector population is high.[1]

Epizootic regions: MVEV activity occurs only occasionally in southeastern Australia, where it has caused epidemics, particularly in the Murray Darling basin and usually after heavy rains and flooding in northern regions with associated rain and flooding extending into the south.[1]

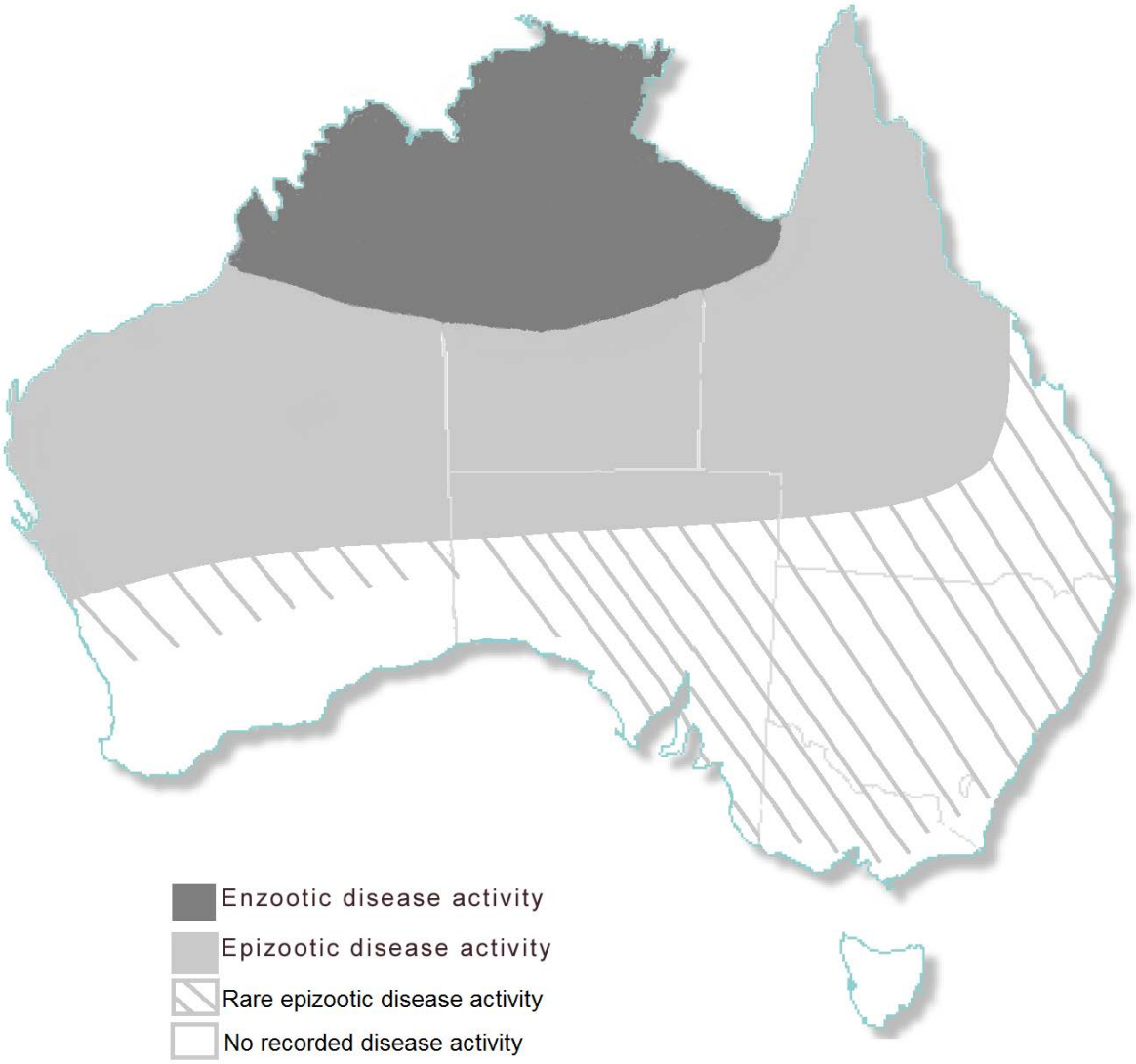

Figure 1 MVEV enzootic and epizootic regions in Australia

MVEV in the region

MVEV is enzootic in Papua New Guinea and eastern Indonesia (Papua and West Papua).[2]

Virology

MVEV belongs to Japanese encephalitis (JE) serological group within the genus *Flavivirus*, family *Flaviviridae*. It is closely related genetically and antigenically to JE virus, West Nile virus (including the Kunjin strain found in Australia) and several other flaviviruses. Alfuy virus (ALFV) which is classified as a subtype of MVEV, also occurs in Australia but it has not been associated with human disease.

MVEV transmission and life cycle

There is no evidence of person-to person transmission, either directly or via mosquitoes. Rare cases of intra-uterine transmission of flaviviruses have occurred as well as transmission by blood transfusion and needle stick injuries.[1] The ecology of MVEV is a complex

relationship between humans, vertebrate hosts, mosquito vectors and the environment, which is also applicable to most arboviruses.[4, 23]

Mosquito vectors

The primary vector during epidemics is the fresh water breeding mosquito *Culex annulirostris,* the common banded mosquito. Other mosquito species, including some *Culex* species and some *Aedes* mosquitoes may be involved in other aspects of MVE virus ecology.[24] *Cx. annulirostris*, is found throughout Australia (but is rare in Tasmania). In northern Australia it is active year-round, with its greatest numbers in the wet and post-wet season, in association with shallow flooded vegetated areas in the early wet season, and the larger vegetated swamps, flood plains, and poorly draining creek systems in the wet and post-wet season.[1, 4] Particularly productive areas are in waters of high organic levels associated with sewage and other waste water storage and treatment or disposal facilities. In the northern areas mosquito populations may be highest in the post wet season; however the greatest risk may be earlier in the season when populations are not necessarily high.

In southern regions of Australia, *Cx. annulirostris* tends to be a high-summer species associated with natural wetlands and irrigation waters. Adult mosquitoes may not be seen during the cooler months (when the adults are quiescent in harbourage and not laying eggs), emerging during mid- to late-spring as the weather warms, peaking in abundance in mid- to late-summer, and disappearing before winter. Typically, southern populations are dependent on spring and summer rainfall in non-irrigated areas but, as in northern regions, the species can be sustained in dry areas and produced in great numbers by sewage and other waste water storage and treatment or disposal facilities.[1, 4]

Susceptible hosts

The primary vertebrate hosts of the MVE virus are thought to be water birds such as herons and egrets, which act as reservoirs or amplifiers for infection. In particular, the Rufus (or Nankeen) Night Heron *(Nycticorax caledonicus)* is considered important. The principal virus cycle exists between these birds and the mosquito vectors. MVEV also infects a wide range of native and non-native animals,[25, 26, 27, 28, 29] but the role of these species in maintenance and transmission of the virus is unclear. Investigation at the time of the 1974 outbreak demonstrated infections in domestic fowls and wild birds.[27, 30, 31, 32] Although MVEV seroconversion in animals confirms a species can be infected with MVEV, it does not provide an indication of viral titre levels or the length of viral persistence during infection with MVEV. These two factors influence whether a particular species can be a major host in the MVEV life cycle.[4]

Humans can become infected if bitten by infected mosquitoes. Infection with MVEV is believed to confer life-long immunity although this is not thought to offer cross-protection against infection with other flaviviruses. There is no evidence of person-to person transmission, either directly or via mosquitoes.

Factors affecting the MVE life cycle

Meteorological events such as rainfall, temperature and humidity play a role in the transmission of MVEV. Mosquito abundance is affected by the availability of aquatic breeding habitats. Other factors such as temperature, wind speed and wind direction affect their distribution and life cycle. MVEV outbreaks may occur after unusually heavy and persistent rainfall and subsequent flooding.[4] Abnormal rainfall may increase the numbers of mosquitoes and lead to movement of infected birds from enzootic regions to epizootic regions.[20] The mechanisms by which outbreaks in south-eastern Australia commence are unclear. Activity outside the enzootic areas is believed to follow the migration of infected water birds into flood-affected areas.[33, 34]

Other factors that may affect the establishment and maintenance of MVEV life cycle include:

- Vector factors: density, longevity, feeding patterns, distribution, control mechanisms by humans
- Vertebrate host: range of host species, prior exposure to MVE virus, viral titre and duration of viraemia, movement and migration, mosquito avoidance mechanisms
- Environment: climate, weather, physical landscape such as presence of waterways, human interventions on the environment such as irrigation, swamp drainage
- Human: prior exposure to MVE virus, population distribution, lifestyle factors, use of prevention measures to avoid being bitten by mosquitoes

Epidemiology

MVEV infection was made nationally notifiable in 2001. Between 2001 and 2012, a total of 35 MVEV cases were notified in Australia, a rate of 0.1 cases per 100,000 population per year. Annual cases numbers ranged between 0 cases (2003, 2007 and 2010) to 16 cases in 2011 (Figure 2).

In both enzootic and epizootic areas, the most frequently reported months of onset were March, April and May.

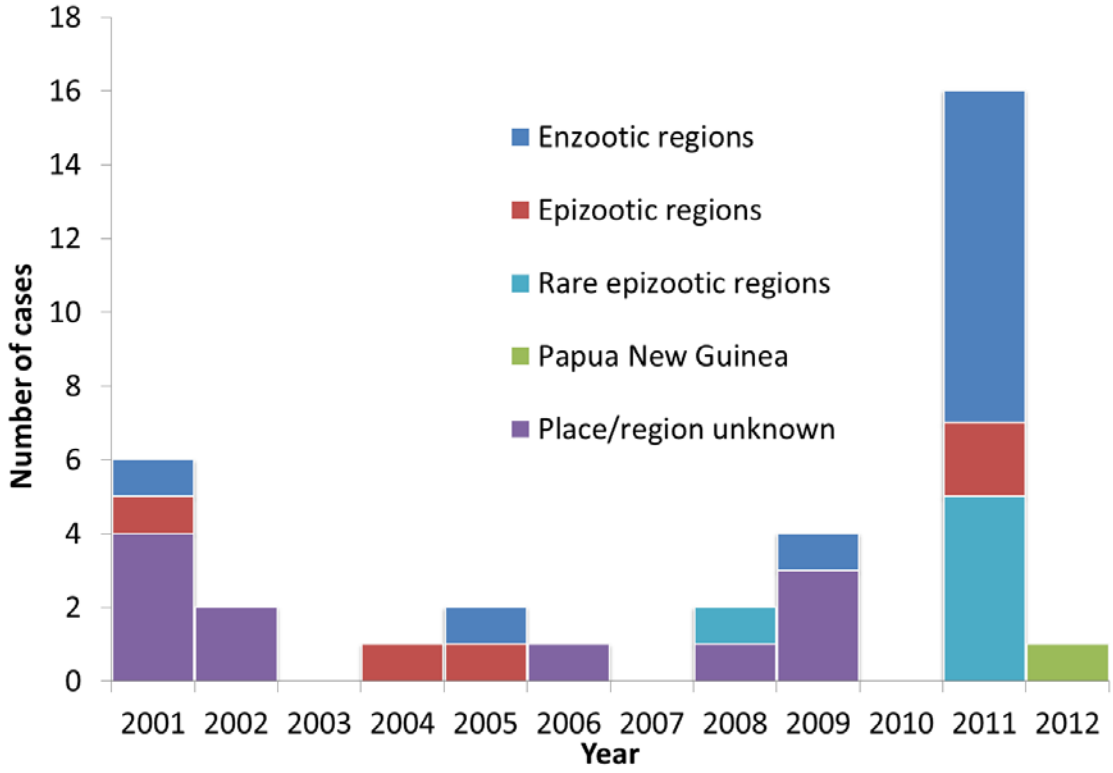

Figure 2 Human cases of MVEV infection, Australia, 2001 to 2011, by local disease epidemiology, year and quarter diagnosed (Source: NNDSS)

Clinical features and natural history of disease

Given the relative infrequency of human MVEV cases in Australia, the summary of clinical features largely represents a case series from the 1974 outbreak and ongoing community-based studies and case-follow up from enzootic regions in NT and WA.

MVEV commonly infects humans without producing apparent disease (subclinical infection). It may also cause a comparatively mild disease with features such as fever, headache, nausea and vomiting. In a small proportion of all people infected (estimated 1:200 – 1:1000) meningitis or encephalitis of variable severity develops.[14, 19] The incubation period is usually 7 to 12 days but can between 5 and 28 days. The incubation period is followed by a prodromal period of 2-5 days typically including fever and headache.[3, 13, 15, 20, 34] Other non-specific symptoms can include neck stiffness, nausea, vomiting, diarrhoea, a macular rash and cough.[15] Neurological features can include lethargy, irritability and confusion. Encephalitis or meningitis occurs in up to 1:20 cases in children depending on the geographical location.[15, 16, 20] Seizures most commonly occur in children, but they have also been reported in adults.

While the severity of clinical disease is highest in infants and older persons, severe disease is well recognized in healthy young people. Inapparent or undiagnosed infection is more common at other ages. The case fatality rate of MVEV disease with encephalitis is about 15-30%, with long term neurological sequelae observed in 30-50% of survivors and only 40% recovering completely.[3, 13, 15, 16, 20]

MVEV disease with encephalitis in humans can present anywhere in Australia because the patient may first become ill after returning to their home, having been infected up to 28 days previously in northern Australia, or areas where there is evidence of MVEV activity. As a consequence, the possibility of the MVEV infection should be considered initially in any patient presenting with encephalitis in Australia.

Laboratory diagnosis

Testing for MVEV infection in humans

Laboratory diagnosis of MVEV infection requires either isolation of the virus, detection of MVEV RNA, a fourfold rise in MVEV IgG titres between acute and convalescent serum samples, or IgG seroconversion or significant rise in antibody level, or detection of MVEV IgM in serum or cerebrospinal fluid (CSF) (in the absence of cross-reactive antibodies). At the time of writing, detection of IgM in serum is only considered laboratory evidence of infection if the patient has encephalitis.[35]

Virus isolation from blood is only possible in the early acute phase of the illness prior to the appearance of antibodies. MVEV has only been isolated from a small number of human cases, and none since 1974. The precise duration of MVEV viraemia is unknown[3] experience with the closely related West Nile virus suggests it could be less than 14 days from the time of infection.[3, 36]

As a result, most infections are diagnosed serologically. Most reference laboratories have developed in-house MVEV serological tests that detect total antibody by haemagglutination inhibition, IgG by immunofluoresence assays (IFA) or enzyme immunoassay (EIA), and IgM by IFA or EIA. It is thought that MVEV IgM appears 4 to 9 days after disease onset, again based on the documented experience of West Nile virus, and can persist for months or even years.[3, 20, 36]

Due to high levels of background flavivirus infection in humans residing in enzootic areas, and the long-term persistence of IgM, it is important to demonstrate rising titres of IgG or to have a positive viral detection test (culture or PCR) to confirm acute infection. If confirmatory laboratory evidence is unavailable or inconclusive, then a detailed exposure and clinical assessment is required to determine the likelihood of recent infection. As there is broad cross-reactivity in antibodies to the flaviviruses, assigning a particular virus as the cause based on serology requires a test that is sufficiently specific.

Recommended testing procedures for suspected human cases are included in Appendix 3, the MVEV SoNG in Section 8 Laboratory testing.

The Public health Laboratory Network of Australia (PHLN) provides a laboratory case definition for flavivirus infection, available from http://www.health.gov.au/internet/main/publishing.nsf/Content/cda-phlncd-flavivirus.htm

Testing for MVEV in vertebrates and vectors

There is a network of laboratories across Australia that provide a range of testing for MVEV activity in vertebrates and vectors, including serological testing, mosquito identification and viral isolation from mosquitoes.

In principle, testing for MVEV and seroconversion to MVEV in vertebrates and vectors is similar to the testing in humans. Ideally, the virus itself would be isolated or cultured, and complementing this, serological evidence of infection would be available. However there are challenges with interpretation of flavivirus tests in vertebrates largely related to their diagnostic specificity not being fully validated in the presence of clinical signs and symptoms in certain species of unwell animals. This is further discussed in the Surveillance section, under Vertebrate Surveillance.

Surveillance

The complex transmission cycle of MVEV means that a number of surveillance mechanisms can be utilised to predict MVEV activity. Mechanisms for monitoring MVEV activity include surveillance of human cases, surveillance of MVE virus activity in vertebrate hosts, vector surveillance including monitoring of mosquito vectors for abundance, virus isolation or detection from mosquitoes, and climate surveillance. A recent development has been the evaluation of a new surveillance tool involving testing of honey baits in special mosquito traps by a PCR method for MVEV presence.[37]

The appropriate surveillance tools for monitoring MVEV activity may vary from jurisdiction to jurisdiction. Factors such as whether the area is enzootic or epizootic, the frequency of human disease, the geography and climate, the availability of laboratory facilities and other infrastructure, competing public health concerns and the availability of public health resources will influence what surveillance mechanisms are appropriate.

Human surveillance

The objectives of human surveillance are:

- to detect and guide immediate action and control measures for MVEV outbreaks
- to monitor the epidemiology of MVEV
- to identify geographic areas for targeted interventions or research
- to identify risk factors and high-risk populations

States and Territories report MVEV infections to the National Notifiable Disease Surveillance System (NNDSS) maintained at Health. Since 2001, States and Territories have reported against a national surveillance case definition. National surveillance case definitions are regularly reviewed and updated and therefore it is important that readers consult the Health website (www.health.gov.au/casedefinitions) to ensure they are reading the most up to date case definition. A revised national surveillance case definition for MVEV infection was implemented on 1 July 2010 and is included in this document as an example only (Figure 3).

During the MVEV risk season and depending on the areas at risk, surveillance can be enhanced to include surveillance for hospitalized cases of encephalitis and for patients who have IgM antibodies to MVEV. This can be achieved with general alerts to key health care personnel such as primary care providers, infectious disease physicians, neurologists, hospital infection control personnel, and diagnostic laboratories.

Although not specifically or routinely used for MVEV surveillance, some jurisdictions maintain syndromic surveillance systems, including surveillance of presentations to emergency departments. Such systems could be tailored to look for syndromes such as “fever and headache” and utilised for enhanced surveillance in the setting of confirmed or suspected human cases.

Complementing notifiable disease data, CDNA conduct fortnightly teleconferences during which recent and local disease outbreaks are discussed. These meetings can include discussion of suspected cases of diseases with significant public health impact such as MVEV. This mechanism provides for early warning and action, or preparation for action, in response to surveillance signals for MVEV.

Given the small number of human cases of MVEV disease that have been reported in Australia, epidemiological research has provide additional information about risk factors for infection, high-risk populations and supported identification of geographic distribution. Examples include longitudinal studies in Indigenous communities in Western Australia [14] and seroprevalence studies of rural residents in south-eastern Australia.[38, 39]

In the setting of MVEV activity or an outbreak, opportunistic laboratory based surveillance for MVEV infections can include testing of serum from patients from at risk areas. MVEV infection was one of several infections included in the national voluntary passive reporting scheme, LabVISE, although given the inclusion of symptomatic and asymptomatic infections it is likely the true number of cases was overestimated by this system.[40]

Figure 3 National Surveillance Case Definition for MVEV

A confirmed case requires **Laboratory definitive evidence** AND **clinical evidence.**

Laboratory definitive evidence

1. Isolation of Murray Valley encephalitis virus

OR

2. Detection of Murray Valley encephalitis virus by nucleic acid testing

OR

3. IgG seroconversion or a significant increase in antibody level or a fourfold or greater rise in titre to Murray Valley encephalitis virus

OR

4. Detection of Murray Valley encephalitis virus-specific IgM in cerebrospinal fluid in the absence of IgM to West Nile/Kunjin, Japanese encephalitis and dengue viruses

OR

5. Detection of Murray Valley encephalitis virus-specific IgM in serum in the absence of IgM to
West Nile/Kunjin, Japanese encephalitis and dengue viruses. This is only accepted as laboratory evidence for encephalitic illnesses.

Confirmation of laboratory result by a second arbovirus reference laboratory is required if the case occurs in areas of Australia not known to have established enzootic/endemic activity or regular epidemic activity.

Clinical evidence

1. Non-encephalitic disease: acute febrile illness with headache, myalgia and/or rash

OR

2. Encephalitic disease: acute febrile meningoencephalitis characterised by one or more of the following:

focal neurological disease or clearly impaired level of consciousness an abnormal computerised tomograph or magnetic resonance image or electroencephalogram, presence of pleocytosis in cerebrospinal fluid
OR

3. Asymptomatic disease: case detected as part of a serosurvey should not be notified.

Case definitions found at the Health website (www.health.gov.au/casedefinitions)

Vertebrate surveillance

The general purpose of vertebrate surveillance (mainly captive birds, wild birds, other animals such as horses) is to utilise information about seroconversion to MVEV in animals as indicators that transmission is occurring to vertebrates, ideally as an early warning for potential risk of disease transmission to humans.

Surveillance to detect MVEV should focus on the bird and mosquito components of the enzootic transmission cycle. Non-human mammals, particularly equines, may also serve as effective sentinels because a high intensity of mosquito exposure makes them more likely to be infected than people.

Sentinel chickens

The purpose of sentinel chicken surveillance is to utilise seroconversion in captive bird species as indicators of local MVEV activity, as an early warning for potential risk of disease transmission to humans. Chickens have long been successfully used in flavivirus surveillance as they are readily fed upon by *Culex* vector mosquitoes, and captive birds can be serially bled, making the geographic location of infection definite. Collection of specimens is inexpensive compared with the costs of wild bird surveillance. However, sentinel flocks detect only focal transmission, and thus multiple flocks must be positioned in representative geographic areas.

At the time of writing, sentinel chicken surveillance programs are active in five jurisdictions: Western Australia, the Northern Territory, New South Wales, South Australia and Victoria. The flocks in Western Australia and the Northern Territory are tested all year round but those in New South Wales, South Australia and Victoria are tested only in the warmer months (usually mid-spring to mid-autumn), during the main MVEV risk season. Typically chicken flocks in NT and WA seroconvert each rainy season whilst seroconversion in southeastern chicken flocks is less common. For example, in 2008 sentinel chickens in Victoria showed evidence of antibodies to MVEV for the first time in 30 years.[41] State representatives post results on the National Arbovirus and Malaria Surveillance Website, a secure website managed by NAMAC. A yearly summary of the program is presented in the journal *Communicable Diseases Intelligence*.[42]

Wild birds

Wilds birds provide the opportunity for sampling important reservoir host species and may be used both for early detection and for monitoring virus activity. Due to the need to track and trap wild birds, this is a much more resource intensive surveillance mechanism and the results are not necessarily easy to interpret. Similarly, unless the same sero-negative birds can be bled and tested on a frequent basis, this type of surveillance is generally more useful in guiding further research into potential hosts rather than as an indicator of current MVEV activity.

The Australian Wildlife Health Animal Network (AWHN) facilitates collaborative links in the investigation and management of wildlife health in support of human and animal health, biodiversity and trade. AWHN utilises wildlife health data sources both within governments (such as those data from Australia's states and territories) and sources outside of governments (such as those provided by university researchers or zoo wildlife hospitals). Other sources include the Australian Registry of Wildlife Health; and specific targeted projects such as the avian influenza wild bird surveillance program.

Other animals

No formal surveillance mechanisms are active to monitor the diagnoses of MVEV in animals. The National Arbovirus Monitoring Program (NAMP) is an integrated national program jointly funded by the livestock industries and governments to monitor the distribution of economically important arboviruses of livestock and their vectors in Australia. These viruses include bluetongue, Akabane and bovine ephemeral fever (BEF). The cornerstone of the program is the maintenance of a national network of sentinel cattle herds from which regular blood samples are taken and tested for these viruses. In addition, potential insect vectors are trapped and identified to monitor changes in their location and abundance. Although NAMP does not routinely record animal infections with MVEV, these systems have the potential to provide additional information about the activity of MVEV or other flaviviruses. Collections of sera from these programs could be tested for MVEV, although the value of testing of other sentinel animals is yet to be fully determined. Both the Australian Animal Health Laboratory (AAHL) and the State and Territory veterinary laboratories are involved in surveillance programs.

Monitoring MVEV activity in other animals tends to be opportunistic. Animals (particularly horses) presenting with symptoms of encephalitis (ataxia) or arthritis (stiffness or swollen joints) may be tested for Ross River, Kunjin and MVE viruses. Rising Kunjin virus IgG titres and Ross River virus IgM reactivity have been occasionally demonstrated in animals showing signs of disease, where more common causes of disease have been excluded. MVEV has been isolated from the cerebrum and spinal cord of a Queensland horse with encephalitis,[43] and in early 2011, MVEV and KUNV antibodies were detected in a small number of horses across Victoria.[44]

Given horses are considered incidental hosts in the transmission cycle of WNV and JE viruses,[45] it is reasonable to expect that they could be incidental hosts in the MVEV transmission cycle. However the extent of their role in MVEV transmission is yet to be fully defined. As a result, the significance of positive MVEV results in horses (specifically as it relates to human health risk) is currently unknown, but seropositive animals may provide additional surveillance data on which to base risk analyses.

Enhancing emerging zoonotic disease surveillance data from animals

The Australian Government Department of Agriculture, Fisheries and Forestry funded a pilot project in the 2008–2009 financial year to determine how surveillance of zoonotic infections in animals can add to the understanding of the epidemiology of emerging zoonoses in humans, using MVEV as a model. [42] Project partners include Health, AWHN and Animal

Health Australia. Initial findings of this report supported the use of chickens for surveillance, and also recommend the use of young cattle and horses for general MVEV surveillance. Eastern grey kangaroos also showed a high prevalence of antibody to MVEV, making them a potential source for monitoring outbreaks and retrospectively determining the extent of an outbreak.

Vector surveillance

The purpose of mosquito surveillance is

- to use data on mosquito populations and virus infection rates to assess the threat of human disease
- to identify geographic areas of high risk
- to identify larval habitats for targeted control
- to monitor the effectiveness of mosquito control interventions

Vector surveillance includes mosquito trapping for identification and enumeration of mosquitoes to monitor population sizes and composition. There are some models or predictive indicators involving mosquito numbers that are used in some jurisdictions to assist predictions of possible MVEV activity.[46] Virus isolation from trapped mosquitoes is necessary to define whether MVEV is actually present, but can be difficult to deliver in a timely fashion in some jurisdictions. Mosquito surveillance tends to occur in the context of mosquito management programs and therefore surveillance signals can trigger mosquito management responses and/or broader public health responses. For example, a threshold number of mosquito larvae per dip might trigger larviciding or source reduction in a known breeding site, or a threshold mean number of adult *Cx. annulirostris* per EVS/CO2 trap might trigger adulticiding (residual or fogging or both).

A recent development has been the evaluation of a new surveillance tool involving testing for MVEV presence by a PCR method using honey baits in special mosquito traps.[37] Where possible, honey bait trap mosquito virus surveillance could be set up in the area to monitor for MVEV activity, as an adjunct to other methods, and for the purposes of comparison and refinement of the method. The sensitivity, cost-effectiveness and technical feasibility of honey bait traps are still being established, but these have the potential to be a very useful tool in the future.

Climate surveillance

The purpose of climate surveillance is to predict MVEV activity by signalling meteorological conditions that have been associated with an outbreak of MVE in humans in the past. The abundance of mosquito vectors is dictated principally by rainfall patterns (and irrigation practices in inland regions), physical and biological parameters in swamp lands, and temperature. Meteorological monitoring is therefore used by some states for the prediction of MVE virus activity. Regular monitoring of rainfall patterns, temperature, the Southern Oscillation Index via the Bureau of Meteorology website (http://www.bom.gov.au/) and river

flow data (e.g. Murray Darling Basin Commission http://www.mdbc.gov.au/) is also undertaken by some States. In some jurisdictions there are models or predictive indicators involving rainfall that are used to predict likely MVEV activity.[46, 47]

In general, climate surveillance complements information from the animal and vector surveillance systems, as hypotheses postulated to date, such as Forbes and Nicholls hypotheses, have not reliably predicted increased MVEV activity.[17] However, future research may refine and validate predictive modelling, such that climate and weather modelling can be used to inform surveillance approaches.

Vertebrate, vector and climate surveillance in States and Territories

The most up-to-date information about mosquito-borne disease surveillance and control activities in each jurisdiction is summarized in the NAMAC Annual Report, published in the *Communicable Diseases Intelligence* journal on the Health website (http://www.health.gov.au/internet/main/publishing.nsf/content/cda-pubs-cdi-cdiintro.htm)

Prevention and Control

The objectives of prevention and control of human MVEV infection are to minimise the risk of human exposure to infected vectors and minimise the impact of MVEV infection during transmission seasons or outbreaks.

To minimise the risk of human exposure to infected mosquitoes, prevention and control activities include environmental management and vector control; and public health communication strategies that encourage humans to avoid mosquito bites.

To minimise the impact of MVEV infection during a particular season or during an outbreak, the same principle of reducing human exposure to mosquito bites applies and can required additional environmental and public health measures.

Routine environmental management, including vector control

Routine environmental management and vector management programs support the ongoing prevention of mosquito-borne disease in Australia. Broadly speaking, mosquito control programs exist in most States and Territories and only parts of these are directly related to MVEV infection. Their existence, however, contributes to the reduction of mosquito-borne disease in Australia. Similarly, State or Territory programs and sometimes local governments are responsible for environmental management strategies, some of which are related to environmental conditions relevant for MVEV activity such as urban planning, drainage, wastewater management, flood relief and community education about water storage and management on personal properties.

Integrated mosquito management (IMM)

Mosquito management is carried out to protect community health and well-being by reducing risks of mosquito borne disease and reducing the pain, annoyance and economic loss (to business or property values) caused by mosquito biting. Personal protection

measures are effective in preventing the transmission of mosquito borne diseases, and local governments should consider mosquito reduction strategies depending on the level of mosquito nuisance and environmental impact if chemical use. If the Local Government is considering either biological control or application of pesticides/chemical for mosquito control, they need to seek advice from their respective environmental authorities on required licenses, obligations and approved methods.

Treatment of mosquito breeding sites may increase risks to the environment, in particular wetland ecosystems. Ecosystems are complex and many of the implications of mosquito management intervention have not been comprehensively studied. Therefore the precautionary principle should be applied when designing shire by shire mosquito management programs.

Integrated mosquito management (IMM) attempts to solve existing problems and to prevent or mitigate future problems, requires community involvement, and recognises the importance of stakeholder coordination. It locates the use of physical, chemical and biological methods within a broader context of educational and planning strategies. It is underpinned by health, environmental and socio-economic values.

Core principles of IMM are:

- Integrated mosquito management includes mosquito reduction, personal protection, community education and land use planning.
- Mosquitoes are an integral part of the ecosystem and their treatment may have positive and negative environmental impacts.
- While disease control is the primary focus, reduction in nuisance value of mosquitoes is a legitimate aspect of improved community wellbeing.
- Effective mosquito management requires a holistic approach and the cooperation and coordination of all stakeholders.
- Coordinated programs and on-going monitoring are necessary for effective mosquito management in the long term.
- Treatment of mosquito larvae or adults is an on-going activity.
- Treating larvae is generally more effective and targeted than treating adult mosquitoes.

Approaches to mosquito management can be direct or indirect. Direct interventions include the removal of breeding habitat by physical modification, the introduction of biological controls (e.g. predatory fish) or the application of pesticides. Indirect approaches reduce human-mosquito conflict, for example utilising planning mechanisms to create adequate buffers around wetlands and educating the public to avoid mosquitoes. Another important indirect approach is for mosquito managers to actively liaise and collaborate with other departments/authorities to ensure that storm water and wastewater management, the planting and harvesting of aquatic vegetation, the design of roads, prevention of animal and vehicle access, and the impact of land use (e.g. mining, irrigation, farming) are undertaken in such a way as to minimise the potential for mosquito breeding.

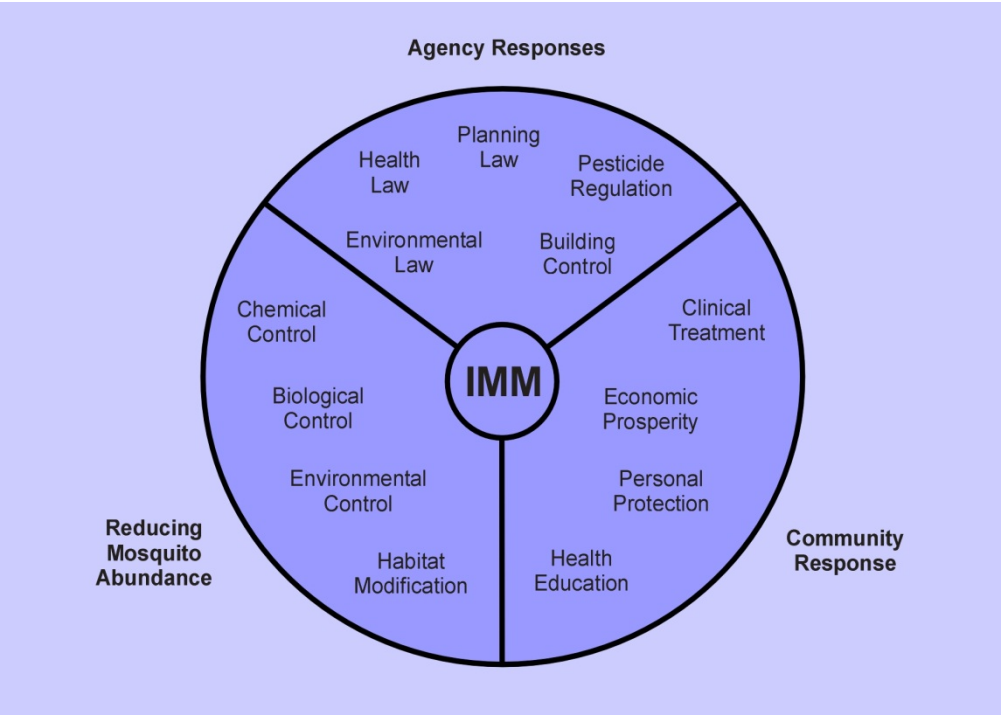

Figure 4: Integrated mosquito management

Public Health Response Plans

Public health response for MVEV infection in humans should be rapid, informative and appropriate for the event that occurs. As MVEV activity varies in each mainland State and Territory, the response should be initiated by the relevant State/Territory Health Departments and adjusted to local conditions. In addition, there may be times when a nationally coordinated outbreak response is required.

This section describes:

- general principles of responding to MVEV surveillance signals
- specific considerations in the event of a national or regional outbreak of MVEV disease

Specific guidance for investigation and response to notified human cases of MVEV infection is contained within the guidelines for public health units in responding to notification of MVEV disease in humans, the MVEV SoNG (Appendix 2). The Series of National Guidelines (or SoNGs) are developed by the Communicable Disease Network Australia to provide nationally consistent guidance to publichealth units (PHUs) in responding to a notifiable disease event. These guidelines capture the knowledge of experienced professionals, and provide guidance on best practice based upon the best available evidence at the time of completion.

Specific guidance for environmental health practitioners for emergency interventions and control activities is included in Appendix 3. These describe options for escalated vector control activities.

In addition, some jurisdictions might conduct seasonal mosquito avoidance public health awareness campaigns that contribute to minimising risk of exposure to MVEV and other mosquito-borne diseases.

General principles of responding to MVEV surveillance signals

The underlying principle of public health interventions for MVEV is that early warning should provide opportunities to prevent further transmission of infection to humans and minimise the physical, social, and economic impact of human MVEV outbreaks.

The need for public health interventions is determined by assessing data from the various surveillance mechanisms, and assessing the risk of MVEV activity and risk of transmission to humans. As there is no specific treatment for MVEV infection, prevention remains the most important strategy for reducing the impact of the disease.

Based on the current surveillance mechanisms in Australia, there are four main surveillance signals that will necessitate consideration of public health interventions from perspective of public health authorities. These signals are

- Abnormal vector numbers during transmission risk periods

- Detection of MVEV in trapped mosquitoes
- Evidence of recent infection in animals, and/or
- Evidence of recent infection in humans.

The components of a public health response to the presence or risk of MVEV activity include:

- Risk assessment
    - Likelihood and consequences of localized or widespread disease activity in animals or vectors
    - Likelihood and consequence of transmission of infection to humans
- Laboratory testing
    - Confirmation of the diagnosis (repeat samples) and consideration of sending samples for reference testing interstate
- Surveillance
    - Targeted or enhanced surveillance of humans, animals or vectors
- Vector control
    - Targeted or enhanced vector control strategies – escalation or new intervention
- Communication plan
    - To stakeholders and partners
    - To health professionals and hospital networks
    - To the public (accompanied by public health measures) and can include targeted public education on personal mosquito protection and reducing exposure risk behaviours
- Research
    - Implementing relevant research plans according to the situation

An overview of public health interventions in response to these signals is described in Table 1.

Occasionally, weather events such as flooding and climate surveillance data may prompt public health responses; however, most often these complement the mosquito, animal and human surveillance signals. The range of responses to the surveillance signals will be influenced by the location of the event (epizootic / enzootic for disease), assessment of risk

based on triangulation with other sources of surveillance information, State/Territory based arboviral response plans, and the public or media interest or profile of the event.

Table 1 Responding to MVEV surveillance signals

Surveillance signal	Abnormal numbers of vectors	Detection of MVEV in mosquitoes	Recent MVEV seroconversion in animals	Evidence of recent MVEV infection in humans
Aim of responding to signal	To provide early notification to relevant human and animal public health agencies and implement appropriate public health control measures			
Risk assessment	Consider location, type and distribution of abnormal vector numbers, relative abundance of mosquito vectors, consistency with previous surveillance data, current and ongoing weather conditions	Consider location of positive samples in relation to humans, history of flavivirus test results from this trapping site, relative abundance of mosquito species, comparison with mosquito trapping data from other sites, current and future weather conditions, history of MVEV outbreaks in the region	Location of positive animal or chicken sample in relation to humans, history of test results from this site, triangulate with vector surveillance information, current climate conditions, time of year and future weather outlook, history of MVEV outbreaks in the region	Case investigation – includes confirmation of onset date, symptoms, laboratory tests, possible source of infection. Case exposure history – probable location of exposure, triangulate with animal and vector surveillance data if available, current climate conditions, time of year and future weather outlook, history of MVEV outbreaks in the region (**Appendix 2** MVEV SoNG contains detailed case investigation steps)

Laboratory testing	If applicable, continue routine testing of vectors for presence of MVEV	Confirm the diagnosis by repeating PCR tests on the positive sample or by virus culture and isolation, consider interstate reference testing if applicable	Re-bleed animal or chicken, considering need for extra number of samples, consider interstate reference testing if indicated. Confirm diagnosis by repeating tests on previous weeks samples, the first positive test and serum from repeat bleeds; and referring specimens to human reference laboratories	Confirm the diagnosis by repeating tests on previous serum samples (if available), first positive and convalescent samples, arrange for convalescent samples if single bleed has been reported; consider reference testing if indicated
Surveillance	Assess information from other surveillance mechanisms; consider targeted or enhanced surveillance of human cases or animal seroconversions			
Vector control	Consider escalation of existing mosquito control activities or implementation of integrated mosquito management to reduce larvae and adult vectors (**Appendix 3** details emergency vector control response options)			
Surveillance signal	**Abnormal numbers of vectors**	**Detection of MVEV in mosquitoes**	**Recent MVEV seroconversion in animals**	**Evidence of recent MVEV infection in humans**
Communication	**Stakeholders and partners**			

	Notify Public Health Unit and/or State/Territory health department	Notify Public Health Unit and/or State/Territory health department Notify NAMAC representative	Notify Chief Health Officer or delegate[1] Notify NAMAC representative	Notify Chief Health Officer or delegate Notify NAMAC representative
	Public Health Units to inform: Directors of Communicable Disease Control or equivalent Relevant local government depending on public health operation plans	Public Health Units to notify/brief/inform: Chief Health Officer and/or senior Staff	Public Health Units to notify/brief/inform: Senior departmental staff, Minister for Health, media liaison unit[1] Notify CDNA secretariat who will inform other jurisdictions Local government depending on public health operation plans Laboratory representative – from human or animal laboratory and/or interstate reference laboratory	Public Health Units to notify/brief/inform: Senior departmental staff, Minister for Health, media liaison unit Notify CDNA secretariat who will inform other jurisdictions Local government depending on public health operation plans Laboratory representative – from human or animal laboratory and/or interstate reference laboratory

[1] These measures may not apply in an area of enzootic disease activity.

	Health professionals		
	Depending on the risk assessment, targeted communication to GPs, hospitals, specialists to increase awareness of MVEV infection and/or encephalitis, advice about symptoms, signs and/or relevant investigations – including instructions for referral of laboratory specimens		
	Public		
	Routine mosquito avoidance prevention measures could be reinforced	A public health warning (via media release) could be issued and advise residents of the need to take additional precautions to avoid mosquito bites; and provide relevant information about presenting to doctors if symptomatic.	Immediate media release stating: *MVEV infection has occurred in person, aged XX resulting in encephalitis, which appears to have been acquired in X; depending on local conditions, this may be an isolated infection or may be the beginning of an outbreak in XX, recommendations for personal protection are XX*
	An example of triggers for the escalation of public messages is provided in **Appendix 5.**		
Research	Implementing relevant research plans according to the situation **Appendix 6**		

Outbreaks and epidemics

In some jurisdictions, one case of MVEV infection will be considered an epidemic, in other jurisdictions sporadic cases of MVEV are expected, and increased numbers of cases or evidence of clustering in place or time might provide the trigger for an outbreak response. Analysis of case exposure history will assist in determining whether there is any clustering of cases. A public health alert including education on avoiding mosquitoes may be indicated.

The steps of defining and closing an outbreak (**Figure 5**) would be similar in response to escalating outbreaks in enzootic areas or to an epidemic (a single case) in epizootic areas.

Figure 5: Declaring and closing outbreaks

Define an outbreak

1. Assembling outbreak response team

Consider assembling an outbreak response team. In States or Territories this may consist of Public Health staff, medical entomologists, and state or local government EHOs. Staff experienced in arbovirus control should be consulted. Should the outbreak response team require expert advice it can contact NAMAC through the secretariat.

2. Defining outbreak response teams

Define outbreak response team, regional and State/Territory reporting lines, roles and responsibilities. An outbreak management team (OMT) ideally would include essential stakeholders from disease control, epidemiology, entomology, vector-control, environmental health, animal health, infectious disease, primary health care, laboratory, health promotion and communications personnel.

Outbreak closure

Three considerations for outbreak closure are: scaling down the response based on outbreak information, deciding when to declare an outbreak is over, and planning operational debrief including an outbreak report.

Scaling down response: Pool information from collaborating agencies to determine when risk has declined sufficiently (eg decreasing numbers of positive testing in animals or in mosquito surveillance, total reduction in number of mosquitoes, change in weather, decrease in number of humans cases).

When/how to conclude: No evidence of new human infections acquired in the preceding 6 weeks and environmental conditions that won't support further transmission; AND; no new seroconversions in sentinel animals for one month.

Debrief: Within a reasonable time frame of the outbreak concluding, all parties involved in the outbreak should meet to debrief and determine possible improvements for future responses. In the case of an outbreak in multiple jurisdictions, the debrief should be coordinated by CDNA or AHPPC as appropriate. Plan closure should include a write-up of the debrief. A descriptive report and a publication of the outbreak should take place if noteworthy.

Appendix 4 contains a brief guide to outbreak investigation and management. This is supported by Appendix 5, which contains examples of escalating public health warnings or measures in an outbreak setting.

Roles and responsibilities in an outbreak of national concern

In situations where human cases of MVEV infection are occurring in multiple jurisdictions or extensively in south eastern Australia, there will be a need for national leadership and coordination by AHPPC, CDNA and Health.

The *National Health Security Act 2007* provides for the National Health Security Agreement between the Commonwealth and State and Territory governments, setting out arrangements to support its practical operation. The Agreement has been developed to establish a framework for events requiring a coordinated national response and describes the roles of the States and Territories, Commonwealth and AHPPC (including its sub-committees) in coordinating a national response.

If considered a national outbreak of MVEV infection (large outbreak of national importance or multiple States/Territories involved):

- AHPPC coordinates a strategic response, convenes outbreak management team or emergency response committee
- CDNA coordinates and implements surveillance and response
- Health coordinates national data management and reporting to support CDNA surveillance and response
- States and Territories are responsible for operations in their jurisdictions
- NAMAC representation should be included in outbreak management teams, and provides expert advice to AHPPC, through CDNA.
- NAMAC coordinate liaison with veterinary personnel through the Office of the Chief Veterinary Officer within the Department of Agriculture, Fisheries and Forestry.
- Health coordinates media and communication
- If requested by States/Territories, Health coordinates additional resources

The National Health Emergency Arrangements (NatHealth)

The NatHealth Arrangements direct how the Australian health sector (incorporating state and territory health authorities and relevant Commonwealth Agencies) would work cooperatively and collaboratively to contribute to the response to, and recovery from, emergencies of national consequence.

The NatHealth Arrangements may be utilised in response to a domestic or international event that:

- impacts or threatens to impact two or more states and/or territories and across jurisdictional borders;
- has the potential to overwhelm or exhaust a state and/or territory's health assets and resources; or

- its scale or complexity warrants a nationally coordinated response.

The NatHealth Arrangements may also be utilised for an international health emergency such as a border health event or overseas health emergency affecting Australian interests, Australian nationals or other designated persons.

Policy and Research

Evidence-based public health policy is essential for development and delivery of disease prevention measures, reductions in health disparities and improvements in the health of vulnerable populations. Policy development is linked to continued investment in research and applied research that allows evaluation of current measures and promotes innovation of new disease prevention interventions.

Policy

National and jurisdictional policy for arboviral disease control needs to be evidence based, coordinated, relevant and supported by legislative frameworks. Considerable progress has been made in the last decade including the establishment of NAMAC, introduction of legislation that supports sharing of information and national coordination of outbreaks, and the development of national surveillance case definitions and nationally consistent response guidelines for public health units managing human cases of MVEV infection. States and Territories have continued to support and improve their own MVEV surveillance, prevention and control activities.

Policy framework

A jurisdictional arbovirus or MVEV policy or plan would ideally address the following:

- Formal establishment of an interdepartmental committee or taskforce (by agreement or Memorandum of Understanding) to oversight surveillance, prevention and control of mosquito-borne disease, including MVEV. Membership should represent animal health, environmental health, laboratory representatives and public health authorities
- Coordination of human, vertebrate and vector surveillance activities including mechanisms for cross-border surveillance
- Coordination of laboratory capacity and sharing of resources between human and animal laboratories
- Communication protocols in response to certain events (ie surveillance signals) – to intrastate, interstate and/or national counterparts
- Standard outbreak management plans including roles and responsibilities, allocation of funds for investigation and response
- Mechanisms to coordinate human, animal, vector and ecological research priorities

Research

The intermittent MVEV activity in humans in Australia has meant that opportunities for outbreak-based research have been limited. To assist in identifying current and future research priorities for MVEV infection, based on existing knowledge and knowledge gaps about MVEV in Australia, NAMAC proposed a range of human, vector and animal research opportunities. The types of research required that could be conducted during or in-between human outbreaks include: human serological and clinical studies, veterinary clinical and epidemiological studies, virological studies; entomological studies; climate and environmental studies; laboratory investigations; evaluation of public health interventions; and opportunities to develop data sharing mechanisms.

For example, a combination of research studies would improve knowledge of the current and future geographic distribution of MVEV, vector and vertebrate host relationship and range, virus persistence mechanisms, laboratory diagnosis, disease risk factors and the effectiveness of prevention activities.

A detailed description of the proposed research activities is given in Appendix 6.

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Appendices

1. Planning a mosquito management program
2. MVEV SoNG: Guidelines for public health units in responding to notified case of MVEV disease in humans
3. Emergency interventions and control for environmental health practitioners
4. Outbreak investigation and management
5. Triggers for escalation of public messages (example)
6. MVEV research priorities

Appendix 1 Planning a mosquito management program

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Introduction

The management of mosquitoes is rarely as simple as taking one approach (e.g. the application of larvicide) to achieve an acceptable level of control. In general, an effective mosquito management program will be based on an integrated approach, that combines various methods to minimise interaction between mosquitoes and the public and to reduce the risk of mosquito-borne disease, and yet will be environmentally and economically sustainable over the long-term.

Mosquito populations will fluctuate from year to year (as well as seasonally) in response to changing environmental conditions. Therefore there will need to be corresponding flexibility in the resources available to the program.

Approaches to mosquito management can be direct or indirect. Direct interventions include the removal of breeding habitat by physical modification, the introduction of biological controls (e.g. predatory fish) or the application of pesticides. Indirect approaches reduce human-mosquito conflict, for example utilising planning mechanisms to create adequate buffers around wetlands and educating the public to avoid mosquitoes. Another important indirect approach is for mosquito control managers to actively liaise and collaborate with other departments/authorities to ensure that storm water and wastewater management, the planting and harvesting of aquatic vegetation, the design of roads, prevention of animal and vehicle access, and the impact of land use (e.g. mining, irrigation, farming) are undertaken in such a way as to minimise the potential for mosquito breeding.

This chapter provides a generic framework and checklist to assist people developing a mosquito management plan. Related elements and considerations for mosquito management plans have been grouped together with a brief explanation about their significance to mosquito management.

This information is a brief coverage of the issues only, and it is intended that reference should be made to other chapters in this manual for more detailed treatment of the various aspects of mosquito management.

Where do I start?

Knowing just where to start with a mosquito management plan may seem daunting, especially if there is little or no evidence of a previous program in your region. However, in most cases there is some information that will help you get underway. This can be used to decide when and where to start with surveys to define and manage the problem.

Existing information

As a starting point, contact colleagues in your own and other organisations, including previous incumbents. The following will provide important clues about the sources and extent of mosquito impacts:

- Previous mosquito surveys or reports if they exist (within agency or from other government departments)
- Public complaints (most local governments keep a complaints register)
- Disease reports and case follow-up information (from disease control or public health units)
- Geographical survey:
    - location of man-made water infrastructure (belonging to council and other agencies) (e.g. sewage lagoons, constructed wetlands, rainwater and effluent re-use tanks, roadside drains and culverts)
    - maps, aerial photographs
    - local knowledge
- Land ownership & responsibilities (council planners, jurisdictional land registry department)
- Applicable environmental legislation (council planners; environmental agencies)

Baseline mosquito surveys

If there is no prior information about mosquito breeding sites, seasonal productivity and the most prevalent species, then the following baseline surveys will be essential.

- Larval surveys: survey all potential mosquito breeding habitats, natural and man-made
- Adult surveys: undertake adult mosquito trapping in a range of natural and domestic locations
- Timing of surveys: surveys should follow breeding triggers [e.g. rainfall, tides, human manipulation of water sources (irrigation, dam releases, backyard sprinklers, effluent re-use)] to maximise the effectiveness of the survey to locate breeding sites
- Prioritise surveys in areas closest to residential and recreational areas and work out from there

Determining mosquito management needs and options

The analysis of existing information and baseline mosquito surveys (above) will allow you to decide whether, when, where and how mosquito management should be undertaken.

Necessity (the need for control):

- Cases of mosquito-borne disease
- Severe nuisance (complaints, impact on quality of life)

Timing:

- Likely season(s) of nuisance and disease risk
- Triggering environmental conditions or human activities
- Timing of monitoring and treatments (larviciding/adulticiding) or other interventions in relation to season, breeding triggers, activity of life stages of the target species

Priority sites from nuisance and public health perspectives:

- Proximity of breeding sites to human habitation
- Productivity of sites (size of breeding area and density of larvae)
- Pest and disease vector status and biology of mosquito species emanating from site

Options for management within available resources:

- Cultural – will the public respond to encouragement about personal preventive measures?
- Physical (source reduction) – can the site be modified or removed to prevent breeding?
- Chemical – larvicides (ground and aerial applications)
- Chemical – adulticides (fogging and residual surface adulticides)
- Biological – is it possible and appropriate to introduce mosquito predators (e.g. fish) to the site?

In-principle support

- Obtain initial in-principle support for a program based on the above (later, the organisation will need to accept the program as part of the core business plan to ensure ongoing commitment to funding and support)

Operational aspects

Once you've decided on the broad approach you will need to determine necessary resources, stakeholder support and involvement, and then implement the program.

Determining budget and resources

- Manpower - personnel required to undertake the management options identified above
- Equipment – chemical application, earthworks, PPE, etc
- Chemicals, prices, number of treatments, area to be treated
- Advertising, educational and promotional material
- Vehicles

Approvals and collaboration

- Identify key partners/stakeholders
- Seek environmental approvals
- Seek aboriginal heritage and native title approvals
- Inform other departments/agencies about proposed program and liaise over potential conflicts (e.g. with agricultural biocontrol programs)
- Advise other departments/land-owners of management responsibilities and options

Public education, advice and warnings

The public have a key role and responsibility in any integrated program to manage mosquitoes. It is important that communities are kept informed and become stakeholders in achieving a successful program.

- Develop information displays and material for letter drops
- Undertake school and community education
- Promote the program and your key messages using local media
- Disseminate warnings when environmental and mosquito monitoring indicate a risk of mosquito-borne disease is likely
- Advise the public of planned chemical and physical mosquito control activities
- Inform and educate the public about their responsibilities for personal preventive measures and backyard mosquito control (e.g. septic tanks, rainwater tanks, fish ponds, roof gutters, pot plant saucers, tyres and other water-holding 'containers')

Determining the effectiveness of the program

- Post-treatment monitoring of larvae and adults
- Monitor public complaints
- Occasional inspection of physically modified sites

- Measure the coverage and impact (on behaviour) of your publicity and warnings
- Monitor human case notifications (although this may not necessarily indicate the effectiveness of the program because disease transmission depends on more than just adult mosquitoes)

Support and resources to make a mosquito control program happen

Effective mosquito management is an ongoing commitment for the agency concerned. This means dedicating some time to ensuring the program is supported and adequately resourced over the long term.

Organisational commitment

- Secure long-term commitment to program from council/agency by adoption of strategic plan
- Achieve recognition of fluctuating nature of funding requirements
- Achieve recognition that program will evolve and grow over time
- Ensure local councillors, politicians and community are aware of and supportive of your program
- Promote the need for adequate buffers between residential areas and high risk areas for nuisance and disease vectors with planning staff in your agency

Program funding

- Secure funding for current financial year
- Obtain commitment to long-term funding in line with the agency's adoption of your strategic plan
- Seek opportunities for collaborative funding (e.g. DOH CLAG funding program, mining companies, local industry)
- Investigate the possibility of developer contributions to funding control of mosquitoes affecting new residential subdivisions

Document program activities and procedures

Deliberately develop an institutional memory of the program to prevent loss of knowledge and information when staff leave or are promoted through the organisation.

- Maintain thorough records/archive files on the mosquito management program
- Document activities and write an annual report/summary
- Archive copies of maps, aerial photos, equipment manuals, chemical labels and other operational resources

- Integrate your program onto your agency's Geographic Information System, if it has one

- Ensure that other staff receive training in running the program so that back-up is available when needed (e.g. during annual leave), and to avoid the loss of your knowledge and experience if you resign

Ongoing refinement of the program

There will be an ongoing and indefinite need to review and refine the program. Additional breeding sites will be found and some others may be created by human activities. Alternative approaches to mosquito management may become available or desirable (e.g. due to the development of resistance to a particular chemical group).

Periodically, review achievements and results from several consecutive seasons to identify emerging trends or risks. Join the Mosquito Control Association of Australia and attend their conferences to continue to develop your professional skills and knowledge in this field (see website below).

Further reading

WA Department of Health (2009) Mosquito Management Manual. Contact Mosquito-Borne Disease Control Branch at WA DOH to obtain a copy.

Mosquito Control Association of Australia Inc. (2008). Australian Mosquito Control Manual. For purchasing details, see the Mosquito Control Association of Australia website http://www.mcaa.org.au

Appendix 2 MVEV SoNG Guidelines for public health units in responding to notified case of MVEV disease in humans

The CDNA SoNG for MVEV . The purpose of the SoNGs Guidelines is to provide nationally consistent guidance to public health units (PHUs) in responding to a notifiable disease event. These guidelines capture the knowledge of experienced professionals, and provide guidance on best practice based upon the evidence available at the time of completion. This framework includes a national guideline for MVEV infection.

The CDNA SoNG for MVEV can be accessed on the Department of Health website (http://www.health.gov.au/internet/main/publishing.nsf/Content/cdna-song-mvev.htm).

Appendix 3 Emergency interventions and control for environmental health practitioners

Emergency intervention and control activities are undertaken to minimise the risk from MVEV infection (and other mosquito-borne diseases) when an elevated risk to public health has been identified or an outbreak is in progress.

A primary aim of the environmental health practitioner under these circumstances is to minimise interactions between biting adult female mosquitoes (in the case of MVEV, *Cx. annulirostris*) and the community/individuals. As with routine mosquito management, an integrated (multi-faceted) approach is essential – no single technique or method is likely to eliminate the risk. Key elements of this part of a program will include:

- Targeted knock-down of or reduction in contact with existing adult mosquito (*Cx. annulirostris*) populations is essential in situations where there is already evidence of MVEV transmission – for example following a confirmed human case(s) or seroconversions in chickens. Cases or seroconversions means there are infected adults in the environment and reducing human exposure to these is essential:
    - ULV or thermal fogging – undertaken with appropriate chemicals, equipment and at best time of day to ensure contact with flying adult mosquitoes (ie sunset and first hours of evening for *Cx. annulirostris*).
    - Application of residual surface adulticides to harbourage areas or as a barrier around perimeter of small communities surrounded by extensive natural mosquito breeding habitat.
- Upscale larval mosquito control and source reduction – to reduce supplementation of adult mosquito populations that may in turn prolong potential for elevated arbovirus activity.
    - Source reduction can include filling or draining depressions, clearing weeds from drains, filling in stormwater sumps
    - Chemical larval control using microbials such as Bti or insect growth regulators (IGRs such as methoprene)
- Ongoing communications plan - prominent publicity and warnings, including advice on importance of and effective approaches to mosquito avoidance. Requires a thorough communication strategy to ensure all sections of the community are reached (e.g. social media, tourists, indigenous community, FIFO, etc).
- Provision or availability of personal repellents, bednets, mosquito control devices such as mosquito lanterns, residual surface adulticides available to households for barrier or harbourage sprays in high risk locations with limited personnel resources.
- Ensure personal protective items (especially repellents) are available in the community (through supermarkets or other outlets).
- Enhanced monitoring of mosquito populations and virus surveillance to ensure accurate assessment of ongoing risk and efficacy of interventions.
- Coordinate/integrate local program with neighbouring jurisdictions and State and Commonwealth Health Departments.

What products are available for use?

A range of larvicides and adulticides are available in Australia and councils may purchase site/location specific products. In general terms these are selected from the below list however other products may also be utilised depending on local need.

- Larval control: microbials (*Bacillus thuringiensis* var. *israelensis*), IGRs (S)-methoprene, surfactants.
- Adult control: adulticide fogging of maldison, pyrethroids, pyrethrin**.** Perimeter, barrier or harbourage residual insecticide such as bifenthrin or lambda-cyhalothrin or alpha-cypermethrin
- Weed control (herbicide): glyphosate

Appendix 4 Outbreak investigation and management

In some jurisdictions one case of MVEV infection will be considered an epidemic, in other jurisdictions sporadic cases of MVEV are expected, and increased numbers of cases or evidence of clustering in place or time might provide the trigger for an outbreak response. Analysis of case exposure history will assist in determining whether there is any clustering of cases. A public health alert including education on avoiding mosquitoes may be indicated.

The steps of defining and closing an outbreak would be similar in response to escalating outbreaks in enzootic areas or to an epidemic (a single case) in epizootic areas.

Define an outbreak

1. Assembling outbreak response team

Consider assembling an outbreak response team. In states or territories this may consist of Public Health staff, medical entomologists, and state or local government EHOs. Staff experienced in arbovirus control should be consulted, consider the need for NAMAC representation. If the outbreak response team require expert advice it can contact NAMAC through the secretariat and ensure NAMAC representation on the outbreak response team for multi-jurisdictional outbreaks.

2. Defining outbreak response teams

Define outbreak response team, regional and state/territory reporting lines, roles and responsibilities. An outbreak management team (OMT) ideally would include essential stakeholders from disease control, epidemiology, entomology, vector-control, environmental health, animal health, infectious disease, primary health care, laboratory, health promotion and communications personnel.

Responding to outbreaks includes investigation and management. Although they occur concurrently, they are presented separately.

Outbreak investigation

The goal of the investigation is to identify the source of infection and potential risk factors for illness, thereby informing public health action.

Below are the steps to be taken in identifying the source of an outbreak. Most of these steps will occur concurrently.

1. Humans

1.1 Assessment of a possible case should include:

- Clinical presentation: Signs and symptoms and their compatibility with MVEV infection
- Laboratory tests: Ensure that relevant tests are conducted and confirm the results. Consider the need for confirmatory laboratory tests in a second laboratory.

- Exposure to MVEV: Travel to an endemic region, outdoor activity (bushwalking, camping and proximity to wetlands and other significant mosquito breeding areas), mosquito self-protection precautions and memory of being bitten.

- Time frame: Onset of symptoms and compatibility with incubation period and possible contact with vectors and potential transmission localities.

- Connections: Consideration of any illness (including mild illness) in patient's contacts (those who have shared similar exposures during the patient's incubation period).

1.2 Case finding/enhanced surveillance:

- Consider conducting risk assessment to define the population at risk.

- Contact local hospitals and general practices to advise them of the case/s and to ascertain whether other people are possibly affected, noting usual symptoms.

- Consider milder and non-encephalitic forms of disease.

- Consider media involvement to assist in alerting the community to the case/s.

- Identify serum surveys of people younger than last regional outbreak (if there has been one).

- Enhanced human surveillance could include recognition of milder non-encephalitic illness by reviewing data from existing emergency department syndromic surveillance systems (such as PHREDSS in NSW), communicating regularly with GPs and hospital emergency departments to ask about encephalitis and other compatible symptoms.

2. Vectors

- Review previous studies of vector species and their spatial and temporal abundance to identify at-risk areas.

- Review breeding site locations near at-risk areas and their current productivity.

- Consider an extension of routine surveillance (eg additional sites, more extensive or frequent sampling).

- Evaluate relative numbers and population densities of vector species in at-risk areas.

- Evaluate relative population densities of vector species at waterbird habitats and breeding areas.

- Confirm whether mosquito trapping has occurred at a distance relevant to the outbreak location.

- Ascertain the results of any virus isolations (by tissue culture or viral antigen detection by PCR) that have been done from these mosquito-trapping locations.
- Consider the role of mosquito species in urban virus transmission.
- Consider any evidence of vertical (transovarial) transmission.

3. Vertebrate hosts

- Review sentinel chicken results from other locations to identify at-risk areas.
- Extend serological/virological survey to other vertebrate hosts acting as a reservoir of infection, especially water birds, and possibly passerine birds and whatever mammals are in the at-risk environment (this may be inappropriate in endemic areas).
- Consider number, location, breeding status, and movement of other hosts in relation to residential areas.
- Consider an extension of current sentinel chicken surveillance.

4. Virus: isolates in human and vector species

- Analyse previous virus isolation or honey card data from region.
- Collect and identify virus from at-risk areas.
- Molecular analysis of virus isolates.

5. Environmental factors

- Examine relevant weather data including local and regional rainfall, temperature, humidity and wind strength and direction, and projected weather patterns. Look at present and historical flooding patterns and likely extent or persistence.

Outbreak management

Management is differentiated from investigation in these guidelines, although both are likely to occur concurrently. Below are the actions that should be taken to prevent further spread of the outbreak.

1. Human disease management

No specific treatment is available for MVEV disease and care is largely supportive. Given the potential for neurological deterioration, patients with encephalitis should ideally be managed in hospitals with the facilities for artificial ventilation. Management of patients should be discussed with a physician with experience in MVEV disease, and if indicated, general clinical guidelines should be developed, in collaboration with infectious diseases physicians.

2. Reducing/preventing transmission

To reduce/prevent virus transmission, interruption of human/mosquito contact should be attempted by:

2.1 Vector control:

The goal is suppression of the vector mosquito population in the affected areas close to relevant communities, both larval and adult, with emphasis on the higher productivity breeding sites near residential areas of major towns. Once virus activity and human cases are confirmed, adult populations must be attacked and reduced if transmission is to be interrupted; larval control will reduce the recruitment of new adults to the population (and can be important in that regard) but will not prevent new human infections by adults already carrying virus. Typically, this requires attacking the adult mosquito populations in or near towns and communities with insecticides applied as aerosols or fogs at the time of adult activity (e.g. early evening).

As mosquito control activities are likely to be carried out by people other than state/ territory Environmental Health Officers (for example, local council workers), ensure appropriate training of these people. Consideration should be given to doing this prior to an outbreak (if one is predicted or expected).

2.2 Human avoidance of mosquitoes:

Consider involvement of the media to help educate people on how to avoid mosquito contact. Media methods should include posters in public places, newspaper articles and commercials on TV or radio.

Information to be communicated by media and others involved in the outbreak response could include:

- Personal protection measures particularly after sunset, during the evening and at night; the use of long sleeves and trousers, socks, mosquito repellents, bed nets, house screens, screened tents when camping, barrier or perimeter sprays and mosquito control devices.

- Avoid going outside in the evening and at night during the risk season when mosquitoes are biting, particularly in the two hours after sunset.

- Avoid mosquito-prone areas during the risk season after sunset, during the evening and during the night.

- Consider closing outdoor recreation areas at night.

2.3 Enhancing surveillance

- Human surveillance should be enhanced to help identify new cases.

- Vector and animal surveillance should also be enhanced.

- Encourage people with symptoms to present to a doctor.

In the event of a very high incidence of MVEV infection in a particular area or region, health departments and the *International Health Regulations* (2005) National Focal Point in Health (health.ops@health.gov.au) should be notified so that further investigation of potential vectors, reservoirs and co-infected people can be organised. The National Focal Point will assess the need to notify the WHO of the outbreak under the IHR (2005).

Appendix 5 Triggers for escalation of public messages (example)

During an expanding outbreak, public health authorities might need to escalate recommended public health measures and associated public messaging. The five potential triggers or decision points are provided below as an example. They are more relevant for epizootic regions of Australia, for example south-eastern Australia rather than for enzootic areas in Western Australia or the Northern Territory.

Example triggers for escalation of public messages

The response to the threat of MVEV infection relies on warnings and personal behaviours, not enforced exclusions. These are, after all, populated areas and mosquito avoidance should be emphasised. State-wide communications will be undertaken in response to the first sentinel chicken conversions of the season in enzootic areas, and co-ordinated multi-jurisdictional communications may be considered in response to a case in an epizootic area, or for escalating outbreaks in an enzootic area.

(1) If one human case of MVEV infection is confirmed this will be reported to the public immediately and the public will be informed of the risk i.e. one human case detected implies further asymptomatic infections.

(2) If two cases are detected but in different local government areas (LGA) at the same time (ie onsets within one week of each other), protection messages as above will be re-emphasised

(3) If two or more cases are detected in one local government area at the same time strengthen warnings particularly in relation to mosquito avoidance measures including avoiding evening outdoor events (see note)

(4) If two or more cases are detected in one LGA and one case in another at the same time, re-emphasise protection messages as in (3) above

(5) If two or more local government areas each have multiple cases at the same time, consideration will need to be given to advising against non-essential travel to the area until the risk has lessened. Because this will have major consequences for the economy and for services in the area this would be a matter for consideration by Cabinet.

Note that numbers alone are not trigger points. Both numbers and time should be taken into account as this reflects the status of active disease transmission. This approach is consistent with other jurisdictional and international practice. It should be noted that local government areas (LGAs) in NT and rural areas of WA cover a wide geographical area, and the LGA guidelines above might not be relevant.

The Centers for Disease Control and Prevention in the United States uses a classification now called “travel health precaution”. This is used in relation to a disease outbreak which is occurring in a widespread geographic area, and is used to provide accurate information to

travellers about the status of the outbreak and specific precautions to reduce their risk of infection. The next level of warning, called a “travel health warning” is a recommendation against non-essential travel to the area. This level is only used for a widespread, serious outbreak of disease of public health concern that is expanding outside the area or populations that were initially affected.

Appendix 6 MVEV research priorities

Serological studies:

To better understand the geographic spread of the outbreaks, and the incidence of infection in the community, serosurveys need to be undertaken in different population groups. Serosurveys should include at least state level details of past residential addresses. The major groups/areas are:

1. Single serum sampling:

    (a) For people born since the 1974 outbreak, sera should be collected to test for antibodies to MVEV, KUNV, ALFV, and untyped flaviviruses (this latter group would differentiate those who may have received Yellow Fever or JE vaccines, and people who have seroconverted to dengue while on holiday). The samples could be collected as part of blood bank activities, as private pathology samples, etc. Positive samples from this could be either IgM or IgG, and often both as IgM antibodies often last up to 60+ days. It would also be worth considering accessing other serosurveys and specimen banks eg National Centre for Immunisation, Research and Surveillance, or antenatal clinic attenders (as a marker of community disease – these samples are kept for a year).

    (b) Stored samples from diagnostic laboratories can be used to look for changes in population seroprevalence across the risk season, as has been done for the pandemic influenza serosurveys [48].

    (c) Single serum samples collected from all ages to test for antibodies to the same viruses as in (a), but knowing some may have been exposed to MVEV or KUNV in 1974, or during the very occasional periods of virus activity since 1974, but if so, it would be expected that their current antibody levels would be relatively low, and possibly below detection, but any re-exposure could lead to a rapid IgG anamnestic response.

2. Paired serum sampling:

    (a) If possible, paired serum samples should be collected from community members, again collected by various ways such as blood bank, private and public pathology, etc (these sources will not necessarily have paired sera; to get paired sera, it may be necessary to recall patients in a prospective study). This would give an excellent opportunity to determine whether virus transmission is still continuing, what symptoms if any positive subjects remember having (symptom recall is poor – it is better done prospectively, but if done quickly, some information might still be gathered). Consider engaging with existing sentinel surveillance medical practices to send blood samples from patients, or liaising directly with GPs and public health units in affected areas to coordinate paired serum sampling. These and other serological samples could be collected as part of the clinical studies for milder infections (see below under clinical studies).

(b) If doing specific groups eg. horse handlers, then matched (age, gender, location etc) control groups are needed.

3. Veterinary investigations:

(a) Equine sero-surveys need to be undertaken retrospectively and prospectively where this is possible using local veterinarians, veterinary hospitals, or opportunistic blood specimens. Prospective collections would be better than opportunistic collections which could be biased. Both single serum specimens and, where possible, paired specimens should be collected for testing. It would be worth considering the use of broad flavivirus testing initially, and then examine those which are flavivirus positive to determine the virus responsible for infection.

(b) If any free range goose farms, duck farms or chicken farms are available (in NSW these are mostly east of the Great Dividing Range), it would be a good idea to determine their serological status to investigate the limits of activity. The length of time that food birds are maintained, free range or otherwise, is usually short, between 6 and 8 weeks. It would be best to liaise with industry groups for access.

(c) Attempts should be made to link up with wildlife investigators to undertake serological studies on wildlife. This could be with naturalists who are trapping animals, kangaroo shooters, or indeed any group who have an interest in wildlife of any sort and who have the means to collect blood specimens for serology. This could/should be undertaken in collaboration with the Australian Wildlife Health Network, or with University zoology departments. This information and the potential involvement of other wildlife species in transmission of MVEV or KUNV is important for understanding future epidemic activity.

(d) Longitudinal studies should be undertaken to determine the length of persistence of antibodies (IgM and IgG)

Clinical studies:

- The major clinical studies should reflect on presenting symptoms, investigation findings and the clinical progression of disease, and how this relates to short and long term outcome. If possible it would be useful to know the time at which the serological response is first detectable, if not already positive, and the time of likely exposure. These investigations could be linked with existing encephalitis studies.

- A prospective study to investigate clinical spectrum of milder cases of MVEV. General Practitioners and laboratories in areas where cases might be expected to occur could be alerted to possible encephalitis cases and milder forms of infection, especially fever of unknown origin, usually but not always accompanied with rash and/or headache and photophobia, and that blood specimens should be taken for serology and where possible, repeat samples collected 2-4 weeks later

- National guidelines for the investigation and management of patients with suspected or proven flavivirus encephalitis could be considered.

Veterinary clinical and epidemiological studies:

- To improve the understanding of the clinical features of MVEV and KUNV infections in horses, consider case series to compile clinical data from equine infections in south-eastern Australia

- Experimental infection of horses would also be a useful way to assess the virulence of the isolates and determine some of the early features of equine infections, as well as being able to assess whether horses also have good anamnestic responses if subsequently (or previously) exposed to a related virus. This is an area which could be important for understanding infections later, and to determine whether infection with one flavivirus leads to a wider protective immunity on re-exposure to related viruses.

- Experimental infection of ducks and geese would provide better information on the effect of these viruses on other species.

- Evaluate the performance of sentinel chickens and honey trap cards as an early warning system, based on the WA and NT sentinel chicken experience in both endemic and epidemic activity which can be enhanced with data from NSW and Victoria, and Qld health research on honey cards.

- There is good evidence that cattle can act as sentinels for JE virus, and as these closely related viruses share many characteristics, it would be useful to know whether cattle in areas where there have been equine cases also show serological evidence of infection. Indeed this type of study could provide very useful surveillance information both now (to determine the geographic range of these viruses in the current circumstances) and in the future *in lieu* of sentinel chickens.

- Longitudinal studies need to be undertaken in different animal species to determine the longevity of the immune response (IgM and IgG).

- Undertake serosurveys of waterbirds from northern Australia through to central and southern Australia and studies of the migration patterns of these birds in wet seasons to investigate the role of water birds in transferring virus from northern Australia to southern Australia (which may explain epizootic activity in central Australia, south-eastern Australia, and possibly further south in Western Australia).

Virological studies:

- The most important issue to resolve early on relates to the phylogenetic relationships of the various MVEV and KUNV isolates from equines and mosquitoes. Sequence studies may provide information on the origin of MVEV isolates and whether there are any differences to previous isolates from different years and regions.

- Developing phenotypic studies *in vitro* and *in vivo* for example comparing culture characteristics of new and old KUN/MVE isolates, animal/mosquito/human isolates, in different primary and continuous cell cultures; in mouse virulence; and in monoclonal antibody patterns.

Entomological studies:

- Although *Culex annulirostris* mosquitoes represent the major vector species, other species, such as *Cx. palpalis* in northern Australia, may also be important. This should be investigated where possible.

- Investigate the possibility that virus activity in epizootic areas is related to wind-borne distribution of mosquitoes from enzootic areas.

Climate and environmental studies:

- The environmental conditions in areas where there have been evidence of viral activities (equine cases, human cases, mosquito isolations, other indicators such as known seroconversions) need to be collated in each State or Territory to better understand the environmental drivers of virus seasonality or incursion and amplification, and then considered in terms of the wider climatic conditions, and in risk factors for either or both human and equine infections. Current models predicting MVEV outbreaks should be assessed to see if they fulfil these conditions, or whether they can be refined or need to be re-thought.

- Other environmental factors need to be considered – length of time of flooding in areas of virus activity, distance of flooding/obvious mosquito breeding to areas of virus activity, and any wildlife changes particularly unexplained wildlife deaths.

- Investigating existing potential examples of "mini-enzootic foci" in the Pilbara region of Western Australia, where regular flavivirus activity is detected in the absence of extensive rainfall and flooding.

Laboratory aspects:

- There is currently no agreed testing format (there is an agreed results interpretation format) for either serology or isolates of virus or PCR which is common across different human and veterinary laboratories in different states. While an agreed format might be beneficial, it is not essential if the relative performance of the assays in different laboratories is comparable and this may be deemed to be an essential requirement, possibly overseen by the PHLN. There is also a need to have confirmatory testing of isolates where possible. Most experience of testing for clinical cases of MVEV resides in PathWest as the vast majority of cases over the past three decades have occurred in WA and the NT and have been tested there, and thus PathWest may be able to provide material to assist in quality assessment of the testing methodologies. However, several states have experience with sentinel chicken testing, notably WA, NSW and Victoria. While this is not exactly a 'research' area, there is a good reason to explore this from a public health perspective.

- The performance of the epitope-blocking EIAs for diagnosis of human and animal infection should be formally assessed. Standardised controls and cut-off values should be developed.

- Expansion of the epitope-blocking EIAs in order to allow identification of antibodies to the less common (ALFV, EHV, STRV, KOKV, JEV) and exotic (SLEV, TBEV, etc) flaviviruses should be undertaken.

- A comprehensive and regular external quality assurance program should be provided to assess testing protocols and performance?

Publicity and Communication Interventions:

- Research into interventions and social responsibility, including publicity messages and warnings should be reassessed for effectiveness, penetration and timeliness.

    - Can we effectively educate people via public health warnings? Should there be regular educational messages even when there isn't activity in order to keep people "primed"?

    - Do people get the correct messages? Do they act on the information?

    - Can messages be targeted more effectively?

Data sharing:

- To maximize the use and integration of various data sources, the possibility of on-line sharing of data eg sequence data, clinical data, vet and human data could be examined.