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Sydney Emerging Infections and Biosecurity Institute (SEIB) publication*

The Broad Street Pump

Climate change and the future risks of mosquito-borne disease in Australia

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With predicted changes in rainfall and temperature, together with sea level rise, associated with climate change, increased mosquito-borne disease risk is a potential concern in Australia. However, of potentially greater importance is the way we manage current risks associated with endemic disease-causing pathogens, their vectors and reservoir hosts.

Concern generally surrounds a potential expansion in the geographic range of mosquitoes and with it the risk of human disease, particularly "tropical" diseases such as malaria and dengue, associated with increased temperatures and rainfall. Generally, the risks of these mosquito-borne diseases are not considered to be elevated based on predictions of climate change alone and, notwithstanding the introduction of exotic vector species or pathogens, the future mosquito-borne disease risks will be primarily related to shifts in the activity of endemic disease-causing pathogens. However, there are many factors that determine local risks including the availability of suitable mosquito habitats, abundant vector populations, availability of reservoir hosts and activity of disease-causing pathogens. *Continued next page.....*

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** The articles in this issue are summaries of presentations at the recent CIDM-PH & SEIB 'Arboviruses, Public Health and Recent Floods Symposium'. Presentations can be found on the CIDM-PH website at www.cidmpublichealth.org*

Events

- SEIB 2011
23-24 November 2011
- CIDM-PH Colloquium
2 December 2011

Climate change and the future risks of mosquito-borne disease in Australia

The risks of increased activity of Ross River virus, Barmah Forest virus, Murray Valley encephalitis virus or Kunjin virus may be primarily influenced by seasonal shifts in rainfall that drive both local mosquito populations and the activity of reservoir hosts. In addition, warmer weather may extend the peak periods of mosquito activity, increasing potential public health risks into either the spring or late autumn. However, the complexities involved in determining outbreaks of mosquito-borne disease are currently not well understood and computer modelling has not been shown to be reliable in accurately predicting outbreaks historically. Predicting future outbreaks, taking into account the regional uncertainties of predicted climate change, is unlikely to be effective.

While there is no doubt that climate can influence mosquito and reservoir host activity, many other social, cultural and economic factors influence human activity and their exposure to disease-causing pathogens. Perhaps it will be the way in which health authorities, and other stakeholders, manage mosquito-borne disease risk that may prove to be more influential in determining future public health risks. An effective surveillance strategy

should be the keystone of regional, state and federal mosquito-borne disease management. Without an understanding of mosquito and disease-causing pathogen activity, the effectiveness of both pro-active and reactive management strategies may be compromised.

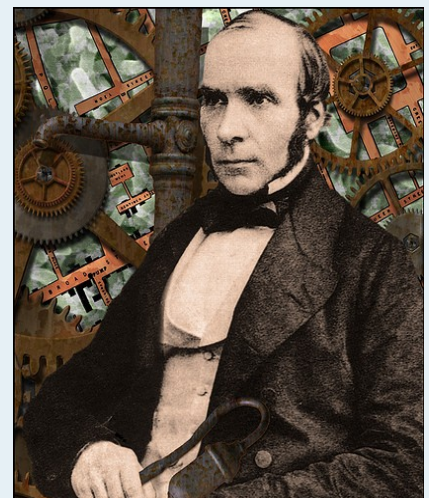
While annual broadscale mosquito control programs are unlikely to be routine, mosquito control itself should not be completely ignored as a potential component in integrated management plans. Community education campaigns involving the use of public health warnings, highlighting the public health risks of mosquitoes, and information on personal protection strategies will remain the primary tool in reducing mosquito-borne disease risk. However, sustainable strategies may also include informed design of urban development and wetland rehabilitation projects so that mosquito risk can be minimised.

In summary, managing future mosquito-borne disease risk will require integrated regionally specific strategies built on appropriate surveillance and research activities together with cooperation between all stakeholder authorities.

“An effective surveillance strategy should be the keystone of regional, state and federal mosquito—borne disease management”

Why the Broad Street Pump?

In 1854, Dr John Snow observed that most cases that occurred in the first few days of an explosive cholera epidemic, in London, occurred in close proximity to Broad St. parish pump, from which 89% of people who died, regularly drew water. He persuaded the vestrymen of the local parish of St. James to remove the handle of the pump whereupon “the plague immediately abated”. His circumstantial evidence would not have been upheld in a court if the parish had refused his request (or later sued him for loss of revenue). Today he would need a sophisticated laboratory to provide proof of his suspicion.



Laboratory Diagnosis of Arboviruses

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Arboviruses exhibit a broad range of clinical symptoms commonly found in numerous non-arboviral infectious diseases. It is for this reason that laboratory diagnosis is critical in confirming clinical suspicion.

The most accurate and definitive means of achieving a diagnosis is by isolating the virus – but in reality this is achievable in <40% of cases. The advent of antigen detection by ELISA and PCR has improved this success rate but as the majority of arboviruses are not human pathogens these have limited usefulness in arbovirology.

The most common means of achieving a diagnosis is serology. It is important to note that antibody is produced whether or not the patient is ill and the presence or absence of antibody cannot indicate a disease state nor can it predict outcome.

There are two types of serologic diagnosis – presumptive (single sample high titre or IgM positive) and definitive (a seroconversion or fourfold or greater rise in titre).

- Serology uses a variety of techniques such as:
- Neutralisation (most sensitive and specific),
 - Haemagglutination inhibition (moderate sensitivity, cross-reactive),
 - Complement fixation (specific but short-lived),
 - Immunofluorescence (moderate sensitivity, cross-reactive, can distinguish antibody class) and
 - ELISA (very sensitive, can distinguish antibody class, can be specific or cross reactive depending on design).

Each of these techniques measures antibody of different class and function which appear at different times in the course of an infection. It is this temporal occurrence that makes serology valuable.

For those who can remember their first year immunology figure 1 will be familiar.

In this representation IgM is specific, short-lived and produced once. It is followed by the appearance of IgG which is also specific and lasts presumably for life. Sadly this is frequently not an accurate representation of real life particularly in respect of arboviruses.

Figure 2 shows the antibody profile in Ross River virus infection. As you can see IgM can be produced for long periods (18 to 48 months) post infection which makes it less useful as an indicator of recent infection. IgG antibody (detected by immunofluorescence or ELISA) is long lived but not specific. HI antibody (which detects a mix of IgG and IgM) is cross-reactive with other closely related alphaviruses making diagnosis problematic in the absence of patient history. The viraemia is of low level and short duration (< 3 days) making detection via culture, PCR or ELISA difficult. While the humble CF antibody may be the most useful in terms of detecting a short lived antibody only one lab in the country is able to perform it. *Continued next page...*

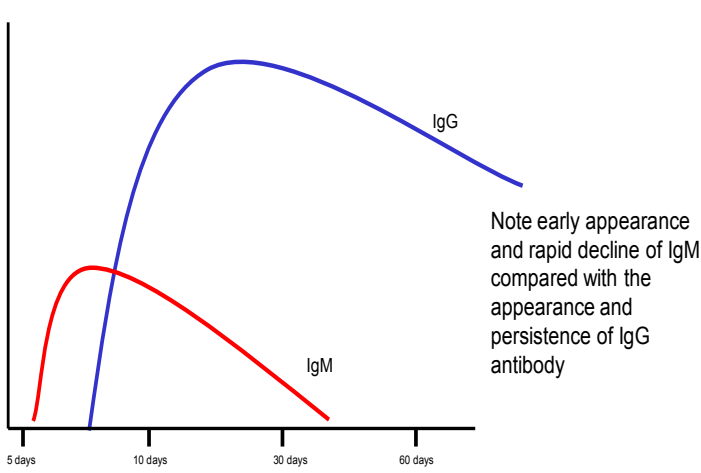


Figure 1

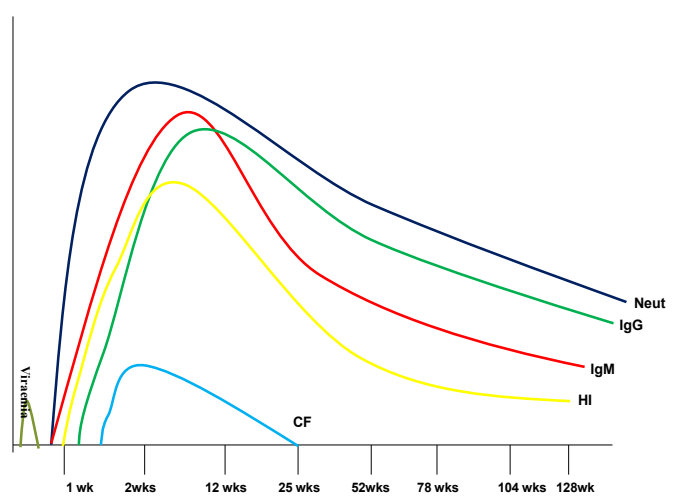


Figure 2

Associate Professor Ben Marais



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Ben joined the SEIB team from the first of July 2011 and is based at the Children's Hospital Westmead. He is a Paediatric Infectious Diseases specialist who recently transferred from Stellenbosch University, South Africa. He was part of a very active and multidisciplinary research team in Cape Town that focussed mainly on tuberculosis (TB). He has been involved in collaborative research projects in India, Bangladesh and sub-Saharan Africa and has considerable experience in international child health.

He will help to fulfil the remit of SEIB (to reduce the risks from, and global impact of, emerging and re-emerging infectious diseases) through his own research program, his involvement in strategic planning and by establishing local and international networks, representing SEIB on relevant national and international professional bodies and coordination of multidisciplinary protocol development.

Laboratory Diagnosis of Arboviruses

Results are only useful if they are consistently accurate, reproducible, specific and have a clinically relevant sensitivity. The most commonly used serologic technique is IgG and IgM antibody detection by ELISA. Unfortunately there is a general lack of standardization with ELISA in arbovirology. There is no correlation between reporting units of ELISA tests so interpretation is crucial and often attempted in the absence of clinical and travel history and there is widespread use of IgM as a screening assay which can be flawed particularly with viruses such as Ross River virus.

Problems with individual ELISA tests largely relate to their design and standardization. This has led to the recognition of high false positive and false negative rates which in turn has led to laboratory generated outbreaks rather than genuine outbreaks.

The persistence of genuine IgM impacts on both patient diagnosis and management but it also generates inaccurate reporting data leading to laboratory generated outbreaks.

All these problems can lead to a loss of clinician and public confidence. It is not however all doom and gloom, laboratory diagnosis isn't the answer to every problem but it does provide valuable information if used appropriately and wisely. It can still provide a wealth of information to clinicians, epidemiologists and government regarding the incidence and prevalence of disease in a community; it allows risk to be determined to ensure health dollars are spent wisely.

Finally there are simple ways in which clinicians and referring laboratories can improve laboratory diagnosis by:

1. Providing relevant clinical and travel histories
 - Doesn't have to be extensive
 - Should include onset dates, travel dates, countries visited, vaccination history.
2. Consider geography before ordering arbovirus tests
3. Have realistic expectations of laboratory tests – all of them have limitations.

Equine Arbovirus Outbreak of 2011

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A number of arboviruses within the *Togaviridae* and *Flaviviridae* families cause devastating neurological disease in both man and the horse. In the Americas, the three equine encephalitis alphaviruses within the *Togaviridae* family, Eastern (EEE), Western (WEE) and Venezuelan Equine Encephalitis (VEE) viruses are well known zoonoses causing significant seasonal morbidity and mortality in the incidental (except VEE) equine and human hosts. Most recently the flavivirus, West Nile Virus (WNV) swept across the United States, at its peak in 2003, 9,862 cases of WNV disease were diagnosed in humans and 264 deaths associated with the virus, whilst in horses over 20,000 were infected with the virus with a case fatality of between 30-40% decimating many horse populations. In Australia, until recently, the flavivirus Japanese Encephalitis (JE) virus, seen throughout Asia causing neurological disease and death in man and horses, was seen as the most significant arbovirus threat to the horse, with the virus seen in pigs in the Torres Strait Island, but yet to emerge on the mainland.

In 2011, the wet spring and summer coupled with a mild autumn resulted in an abundance of mosquitoes throughout Australia and an observed increase in neurological and musculoskeletal diseases in horses associated with arboviruses. Horses displaying unusual neurological signs (such as; reluctance to walk, stiff gait and ataxia) or muscle or joint soreness were first observed in February in NSW and Victoria and later in South Australia, particularly in horses housed along the Murray River. A small number of cases in Queensland and Western Australia were also reported overall 879 horses were clinical affected in this outbreak with 79 horses dying as a result (~9%). In Victoria and NSW cases were widespread, with two distinct outbreak in Victoria one in the North, the other in central Victoria which eventually merged overtime. The epidemic peaked earlier in Victoria compared to NSW (March compared to April/May in the latter) with epidemic curves largely following the numbers of mosquitoes (*Culex* spp. mostly) in affected areas. Three zoonotic arboviruses commonly seen in Australia were involved in

the outbreak, two flaviviruses, Murray Valley Encephalitis (MVE) virus and Kunjin (KUN) virus and an alphavirus, Ross River (RR) virus. Neurological disease seen in this outbreak was caused by MVE or KUN viruses, whilst the muscle and joint soreness observed primarily in central Victoria was caused by RR virus. The most striking feature of this outbreak was the severity of clinical signs and high case fatality rates observed. Experimentally MVE produces mild clinical signs in the horse with anecdotal reports of increased neurological disease in horses in Northern Victoria, associated with the 1974 MVE epidemic in humans (Kay et al. 1987; Studdert et al. 2003). KUN rarely causes severe neurological disease in man and has only once been isolated from a horse with neurological disease (Badman et al. 1984). The incidence of these diseases in humans, however, did not seem to reflect that seen in horses in the outbreak.

The potential increase in virulence of Australian KUN virus coupled with the promise of more climatic conditions favouring mosquito proliferation in southern parts of Australia where both human and horse population density is high is of concern. Proactive measures to reduce mosquito numbers and reduce the risk of exposure to mosquitoes through prudent stabling and effective rugging of horses and use of insect repellents is needed to lessen the future impact of arboviral diseases in Australian horses. The use of a WNV vaccine used to protect horses in the United State could be explored in Australia as a preventative measure to lessen the disease risk presented by the emergence of the closely related KUN virus as a significant pathogen of Australian horses.

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KAY, G.H., POLLITT, C.C, FANNING, I.D., and HALL, R.A. (1987). The experimental infection of horses with Murray Valley encephalitis and Ross River virus. *Aust Vet J* **64**: 52-55

STUDDART, M.J., AZUOLAS, J.K., VASEY, J.R., HALL, R.A., FICORILLI, N., and HUANG, J.A., (2003). Polymerase chain reaction tests for the identification of Ross River, Kunjin and Murray Valley encephalitis virus infections in horses. *Aust Vet J* **81**: 76-80

Upcoming Events...

- SEIB 2011
23-24 November 2011, Sydney Law School, University of Sydney. For more information, contact: seib@sydney.edu.au
- CIDM-PH Colloquium
2 December 2011, Westmead Education & Conference Centre, Westmead Hospital. The annual CIDM-PH Colloquium provides a forum for CIDM-PH staff and students to showcase their research and project outcomes. For more information, contact: lou_orszulak@wsahs.nsw.gov.au

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