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The Broad Street Pump

Why doesn't mosquito-borne Zika virus pose a widespread threat to Australia?

Dr Cameron Webb

Department of Medical Entomology

*Marie Bashir Institute of Infectious Diseases and Biosecurity, University of Sydney
NSW Health Pathology, Westmead Hospital, Level 3 ICPMR, Westmead*

Mosquito-borne disease is never far from the minds of those responsible for the health of local communities. The bites of mosquitoes threaten death and disease in many parts of the world but it's the emergence of a little known virus from an African forest, and its potential link between mosquito bites and birth defects, that's caused much recent consternation among the public, politicians and health authorities alike. With Australia experiencing annual activity of mosquito-borne disease¹, it is not unexpected that the potential introduction of a new pathogen would raise concern among the community. However, understanding the risks posed by exotic pathogens requires understanding the role of local mosquitoes in their potential spread.

Zika virus (ZIKV) is a mosquito-borne Flavivirus closely related to dengue, Yellow Fever and West Nile viruses. Discovered almost 70 years ago in a Ugandan forest, the virus generally only causes a mild illness. Symptoms include rash, fever, joint pain and conjunctivitis. Severe symptoms aren't common and the illness was never thought to be fatal.



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Until recently, ZIKV was rarely recorded outside Africa and Asia.² However, in the last decade, ZIKV outbreaks have occurred in the Pacific³ but the virus was generally always seen as the lesser of three mosquito-borne pathogens circulating throughout the region at the time. Despite some reports of more severe illness resulting from ZIKV, much greater attention was paid to the dengue (DENV) and chikungunya (CHIKV) viruses.

In mid-2015, ZIKV burst into the public health spotlight when it reached the Americas.⁴ Since the first ZIKV infection was identified, cases have been reported from over 20 countries or territories in the Americas with estimates from WHO that millions of people may eventually become infected.

Rapid spread of an emerging mosquito-borne pathogen is news enough but a sense of panic has surrounded the emergence of ZIKV with more serious consequences of infections, including *post-viral Guillain-Barré Syndrome* and a potential link to birth defects. Of most concern has been the rapid rise in rates of microcephaly in newborns in regions where ZIKV has been circulating. While causal link between ZIKV infection and microcephaly has yet to be determined,⁵ concern is great enough for WHO to declare a Public Health Emergency of International Concern.⁶ There is enough concern that the Australian Government Department of Foreign Affairs and Trade has issued warnings for those pregnant to delay or avoid travel to countries experiencing an outbreak of ZIKV.⁷

While there have been cases of person to person transmission of ZIKV via sexual contact,⁸ the primary route of transmission is through mosquito bites. The role of individual mosquito species has implications for both control of outbreaks and assessment of outbreak risk.

A suite of mosquito species, including *Aedes africanus*, *Aedes apicoargenteus*, *Aedes luteocephalus*, *Aedes vitattus*, *Aedes furcifer* and *Aedes hensilli*, have been implicated in the spread of ZIKV but the most important mosquito driving transmission internationally is the Yellow Fever mosquito, *Aedes aegypti*.² The Asian Tiger mosquito, *Aedes albopictus*, may also be likely to contribute to transmission in some regions.⁹ *Aedes aegypti* is also the only mosquito present on mainland Australia likely to play a role in local outbreaks and, as this mosquito is only found in northern regions of QLD, the risk of a widespread ZIKV outbreak in Australia is minimal. In fact, the most likely scenario is that should local transmission occur, it will be limited to small outbreaks around Cairns and Townsville. Small outbreaks of DENV occur in this re-

gion annually¹⁰ and the factors that drive these outbreaks are the same as those that may play a role in local ZIKV outbreaks.

There is little doubt there will be a steady trickle of travellers that test positive to ZIKV in Australia. There have been a number of infections reported in travellers arriving in Australia from Cook Islands¹¹ and Indonesia¹² in recent years and there is no reason there won't be occasional infections in travellers over the coming months. However, while travellers hold the key to the introduction of ZIKV into Australia, mosquitoes will be critical to local transmission.

While dozens of mosquitoes are capable of spreading local mosquito-borne pathogens, such as Ross River virus,¹³ only one of the 300 or so mosquitoes found in Australia is critical for the transmission of ZIKV. *Aedes aegypti* is only found in northern QLD and its absence from major metropolitan centres greatly reduces the risk of a major outbreak of disease. Previous studies investigating the risk of exotic pathogen (e.g. CHIKV) spread has shown that some local mosquitoes may be capable of transmitting exotic virus under laboratory conditions¹⁴ but in reality, the risks are extremely low in the local environment.

For local mosquitoes to spread ZIKV, they must bite an infected traveller shortly after they arrive. In fact, that bite may have to happen within a couple of days of return, while the virus is still circulating in the blood of the traveller. While the chances of this happening are small, if it does, there is then a risk of a local outbreak occurring as the infected mosquito spreads the pathogen as they bite people who've never left the country.

This is the process that occurs when outbreaks of dengue occur in Far North Queensland.¹⁰ If we can get outbreaks of dengue, there is no reason we cannot, or won't, get a small outbreak of ZIKV in the future but if the worse happens and if ZIKV was to be transmitted by *Aedes aegypti* in the urban centres of Cairns or Townsville in north QLD, authorities are well placed to contain the outbreak as strategies are shared with the current strategic management of dengue outbreaks. This strategy involves reliable identification of DENV cases and rapid response by authorities to undertake mosquito control. Reducing opportunities for local mosquitoes by removing sources of standing water and the deployment of specially designed mosquito traps that target *Aedes aegypti* in combination with the judicious use of insecticides minimised the contact between infected individuals, local mosquitoes and the wider community.

Why doesn't mosquito-borne Zika virus pose a widespread threat to Australia? *(continued from page 2)*

The reality is that, due to the limited distribution of suitable mosquito species and the trickle of infected travellers entering the country, the risk of an outbreak of ZIKV in Australia is very low. Perhaps the real message here for Australian authorities is that they need to work diligently to keep exotic mosquitoes out of the country. While *Aedes aegypti* may not become established in southern cities, there is great potential that *Aedes albopictus* could become established in our major metropolitan centres and, as well as vector of ZIKV, DENV and CHIKV,¹⁵ it is a significant nuisance-biting pest. As highlighted by the emergence of ZIKV in the Americas, the movement of people and their belongings poses as great a future risk of exotic mosquito and pathogen increases in Australia as any change in climate. Local authorities should remain vigilant to ensure surveillance and strategic responses to exotic mosquito detections are in place.

Notwithstanding the threat of exotic mosquitoes and mosquito-borne pathogens, local mosquitoes and their ability to transmit pathogens between wildlife and people pose an annual public health concern. Ensuring local authorities promote awareness of the health risks associated with mosquitoes as well as the safe and effective strategies to avoid mosquito bites¹⁶ will be critical in protecting the health of Australians into the future.



For more information on this article,
contact **Dr Cameron Webb**
Email: cameron.webb@health.nsw.gov.au
or follow Cameron on Twitter: [@mosziebites](https://twitter.com/mozziebites)

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This is a revised version of an article that originally appeared in The Conversation on 26 January 2016 [<https://theconversation.com/does-zika-virus-pose-a-threat-to-australia-53557>].

Zika emergency status a cause for alert, not alarm

Dr Grant Hill-Cawthorne

Marie Bashir Institute for Infectious Diseases & Biosecurity, and School of Public Health, University of Sydney

Conversation 2/2/2016: <https://theconversation.com/zika-emergency-status-a-cause-for-alert-not-alarm-54042>

Overnight, World Health Organisation Director-General Margaret Chan declared the outbreak of Zika virus a public health emergency. So what does this mean?

This is the fourth time the WHO has declared a state of emergency. The first was in 2009 for the H1N1 virus. The second and third were in 2014 for outbreaks of polio and Ebola.

Headlines declaring this news might sound alarmist but this is not the WHO's intention. The alert is a political tool, to bring attention to people all over the world that this is an issue of concern.

It's estimated there are more than four million people living in areas populated by the Yellow Fever mosquito, which is responsible for spreading the disease. We need to communicate the risks to these people. We need the global community to get on board to aid in control efforts in South America and the other areas affected by the Zika virus.

In particular, this is an opportunity for expertise to be shared across the globe, for research money to be directed to diagnostics and vaccine development and for an increase in international aid money required to control mosquito populations in some of the poorer affected countries.

Declaring Zika virus a public health emergency has happened relatively early in the outbreak compared to the comparable declaration for Ebola virus. But this simply reflects the acknowledged need by the world community to deal with these emergencies more quickly.

The emergency alert is also a call to arms to focus on research in this area, particularly to establish a causal link between the Zika virus and the reported subsequent birth defects, especially microcephaly (reduced head size and brain damage).

The WHO's briefing overnight made clear that the emergency of international concern is not for Zika itself, but for the cluster of microcephaly cases and its suspected link to the Zika virus.

As the WHO pointed out, Zika itself is not a clinically serious condition.

The US has added Zika virus to its research agenda. The affected countries within the Global Research Collaboration for Infectious Disease Preparedness, a body of infectious disease experts and funders, are meeting this evening to discuss what resources can be diverted to help in diagnostic and vaccine development.

Explainer: what is microcephaly and what is its relationship to Zika virus?

Professor Lyn Gilbert

Marie Bashir Institute for Infectious Diseases & Biosecurity and Centre for Value Ethics and Law in Medicine, University of Sydney

Centre for Infectious Diseases & Microbiology Westmead Hospital, Westmead

Conversation 5/2/2016: <https://theconversation.com/explainer-what-is-microcephaly-and-what-is-its-relationship-to-zika-virus-54049>

This week the World Health Organisation declared Zika virus a public health emergency of international concern.

Despite high rates of infection, the outbreak would not have been particularly alarming – since the infection is usually asymptomatic (80% of cases) or mild and self-limiting – had it not been for the sudden and (apparently associated) increase in numbers of infants born with microcephaly.

What is microcephaly?

Microcephaly is a condition in which the infant's head is smaller than "normal" for the infant's age and gender, because of delayed or arrested brain growth. There is no universally agreed definition.

Most authorities suggest it should be defined by a head circumference of two – but some say three – standard deviations or more below the average.

It is often first diagnosed by ultrasound examination during pregnancy. The incidence of microcephaly – in the absence of Zika virus infection – is difficult to determine.

Apart from the lack of an agreed definition or definitive diagnostic test, there is probably significant under-reporting of the condition. State-based surveillance in the United States – where Zika virus is not endemic – suggests it occurs in between two and 12 infants per 10,000 live births. Rates vary from 0.5 to 19 in 10,000 live births in different states.

Explainer: what is microcephaly and what is its relationship to Zika virus? *(continued from page 4)*

If the incidence were similar in Brazil, where about three million infants are born each year, this would represent 600-3,600 cases a year. This is more than estimates based on recent review of birth certificates – approximately 0.5 per 10,000 live births.

Some of the approximately 4,000 cases reported in Brazil during 2015 may have been due to increased awareness and reporting – although there appears to have been a real increase also.

Microcephaly is often associated with other developmental abnormalities and with varying degrees of intellectual and developmental delay, seizures, and visual and hearing loss. In severe cases it can be life-threatening.

Causes

There are many recognised causes of microcephaly including a number of other infections in pregnant women. These include rubella, cytomegalovirus (a common virus that causes asymptomatic infection or a mild glandular fever-like illness in otherwise healthy people and severe disease in people with severe immune suppression such as AIDS), herpes simplex virus infections, syphilis and toxoplasmosis (a parasitic disease).

Chikungunya, a virus spread by the same mosquito responsible for spreading Zika (the *Aedes aegypti*, or yellow fever mosquito), has also been shown to cause brain damage in infants of women infected during pregnancy in a naïve population (one without previous exposure to the virus).

Noninfective causes of microcephaly include a variety of genetic disorders, maternal exposure to drugs, alcohol, chemical toxins and radiation and severe malnutrition.

Is Zika to blame?

Although Zika virus has not yet been definitively proven to be the cause of the increased numbers of infants with microcephaly in Brazil, there is strong circumstantial and epidemiological evidence that it is, at least partly, responsible.

Many of the mothers of affected babies in Brazil reported an illness consistent with Zika virus infection in early pregnancy. However, this was often mistaken for dengue and not confirmed by laboratory tests.

The peak incidence of microcephaly occurred in the same geographic region (northeastern Brazil) about a year after an outbreak of dengue-like illness, with fever and rash, started. Six months later Zika virus was identified as the cause.

There have been several reports of detection of Zika virus genetic material (nucleic acid) in amniotic fluid, placentas, tissues of infants who have died with microcephaly and in live-born infants, with or without microcephaly, of mothers who have had Zika virus infection during pregnancy. It is highly likely that maternal Zika virus infection can damage the developing foetal brain. But the level of risk is unknown.

The other major uncertainty about Zika virus infection and microcephaly is the level of risk at different stages of pregnancy. Because the infection is so frequently asymptomatic or easily mistaken for other viral infections, the number of pregnant women infected and the stage of pregnancy at which infections occur are unknown.

For most intrauterine (within the uterus) infections that cause foetal damage (such as rubella or cytomegalovirus, for which these risks are well-known), the risk of the foetus being infected from the mother is relatively low in early pregnancy and increases with increasing gestation.

However, if foetal infection does, in fact, occur early in pregnancy, the foetus is more likely to be severely affected than if it occurs in the later stages of pregnancy. This is yet to be determined for Zika virus infection.

Hopefully, studies and enhanced surveillance of Zika virus infection and birth defects will provide answers to these questions. These are underway in Brazil.

In the meantime, while overall rates of Zika virus remain high, pregnant women are being advised to defer travel to Zika-affected countries if possible. Those who live there are advised to defer pregnancy or take extra precautions to avoid mosquito bites.

“Although Zika virus has not yet been definitively proven to be the cause of the increased numbers of infants with microcephaly in Brazil, there is strong circumstantial and epidemiological evidence that it is, at least partly, responsible”.

Zika virus, spread through mosquitoes, causes widespread panic in Brazil, as the rest of the world cautioned before Olympics

Dr Grant Hill-Cawthorne

Marie Bashir Institute for Infectious Diseases & Biosecurity, and School of Public Health, University of Sydney

The Advertiser (Adelaide) 28/1/2016: <http://www.adelaidenow.com.au/news/zika-virus-spread-through-mosquitoes-causes-widespread-panic-in-brazil-as-the-rest-of-the-world-cautioned-before-olympics/news-story/ec72adce5e57a4d28bd2deaa8dd4db3a>

1. What is Zika virus?

Zika virus is a Flavivirus, which means it is closely related to yellow fever, dengue, West Nile and chikungunya viruses. All of these viruses are transmitted by mosquitoes and so they are collectively referred to as arboviruses (arbo meaning ARthropod-BORne). There are two types, or lineages, of Zika virus – the African and the Asian lineages. Recent genetic studies have shown that the one currently causing a panic in South America belongs to the Asian lineage.

2. Where has it come from?

We have known about Zika virus since the 1950s but up until recently it has always been located in a small belt around the equator in Africa in Asia. However, in 2014 we got the first reports of the virus spreading across the Pacific Ocean to French Polynesia and then in 2015 onto Central and South America and the Caribbean.

3. Is it an old disease or a new disease?

Zika virus was first isolated from a monkey in the Zika Forest near Entebbe in Uganda in 1947. The word “Zika” means overgrown and it is a large swampy forest with at least 40 species of mosquitoes. It was first seen in humans in Nigeria in 1968. However, it is likely to have been around for much longer than this. Zika virus has been infecting humans across Africa and Asia for at least the last 50 years.

4. What sparks an outbreak?

For an outbreak of an infectious disease to occur you need three components to be present: an organism that can be transmitted (Zika virus) a vector or route of transmission (mosquitoes), and a susceptible host population (humans). In South America all three of these components are present with a very large mosquito problem (as can be seen from recent dengue and chikungunya virus outbreaks) and a population of people who have never been exposed to the virus and therefore do not have immunity. Lots of other factors may also be at play for example, changes in mosquito distributions due to climate change, genetics of people making them more susceptible, close living conditions, etc. Infectious disease outbreaks are often unpredictable and this emphasizes why we always need to be vigilant and spend money on infection surveillance in all countries.

5. What are the signs and symptoms of the virus?

Around 80% of people infected with the virus do not experience any symptoms. However for the rest it typically presents with a mild headache, followed by a rash, mild fever, joint pains and conjunctivitis (pink eye). It is usually mild and there have been no reported deaths. While there have been only around 4000 confirmed cases in Brazil, estimates have placed the true figure closer to 1.5 million cases in the past year.

However, there have been two concerning aspects that have appeared in the recent outbreaks. In French Polynesia there were 73 cases of a relatively rare condition called Guillain-Barré syndrome. This is a rapidly progressive muscle weakness due to damage to the peripheral nervous system. A quarter of people affected by GBS go on to experience weakness of their breathing muscles and need artificial ventilation.

The other, even more concerning, aspect is a significant increase in cases of microcephaly in Brazil. Microcephaly means “small head” and can stem from a number of conditions that cause abnormal growth of the brain. Children affected often have impaired intellectual development and may have neurological defects and seizures. Brazil usually sees 150 cases per year, but has recently reported 3000–4000 cases in the past year, occurring in the same timeframe as the spike in Zika virus cases.

6. How can you prevent yourself from contracting the virus?

As this is a mosquito-borne virus the best protection is to not be bitten by mosquitoes. This means using effective insect repellents containing DEET or picaridin, wearing long-sleeved shirts and trousers and treating your clothes with permethrin. In addition the number of mosquitoes in and around your house can be reduced by emptying standing water from containers such as flowerpots and buckets and making sure there are not puddles in your garden where mosquitoes can breed.

The CDC and DFAT have advised women who are pregnant or planning to become pregnant to avoid a list of 22 countries across Central and South America and the Caribbean where transmission is highest.

Zika virus, spread through mosquitoes, causes widespread panic in Brazil, as the rest of the world cautioned before Olympics *(continued from page 6)*

7. What kind of mosquito carries the virus? Can you catch it from any mosquito?

The *Aedes* group of mosquitoes can transmit the virus. The most efficient transmitter is the day-biting mosquito *Aedes aegypti*, which exists in Australia in tropical areas such as far north Queensland. The global distribution of this virus is increasing due to global trade and travel and climate change.

8. How is the virus spread? Can someone who has been in Brazil, come back to Australia and pass it on?

In 2009 there was a case of an infected biologist passing on Zika virus to his wife via sexual transmission. In 2015 Zika virus genetic material has been detected in the amniotic fluid and placenta of infected mothers, suggesting that mother-to-child infection could occur. There have been a number of travellers returning to Australia infected with the virus over the last few years. In theory it could be transmitted via the *A. aegypti* mosquitoes present in Australia in the same way that limited outbreaks of dengue virus are seen in Queensland. Therefore it is important to continue with mosquito-control problems in far north Queensland to prevent this possibility.

9. Is there a vaccine?

Not yet but scientists in Texas and Brazil are now putting in a lot of effort to develop one. They won't be starting from scratch – a very effective vaccine already exists for the related yellow fever

virus and lots of work has been done on dengue and West Nile fever virus vaccines. However, there are still a lot of unknowns about Zika virus so it will be at least a year before a vaccine is likely to go into large clinical trials.

10. Will the fact the disease is in Brazil have any effect on the Rio Olympics?

Very likely. This is certainly a big worry to the Brazilian authorities who have deployed nearly a quarter of a million troops to hunt down and clear mosquito breeding grounds. There is a significant risk of attendees, both spectators and athletes, taking the virus back to their home countries and secondary outbreaks occurring where the mosquitoes are present. The Australian Olympic Committee has already warned members of the national team who may be pregnant during the games to reconsider going.

11. Is it likely to make its way to Australia?

It already has come to Australia in returning travellers but there have not yet been any reports of transmission within the country. This is a possibility in areas that see limited outbreaks of dengue virus, for example, and so it is important for everyone to be vigilant and take precautions against mosquito bites in at-risk areas.

CONTACT US

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CIDM-PH

Centre for Infectious Diseases and Microbiology - Public Health
Mailing Address: PO Box 533
Wentworthville NSW 2145
Phone: (612) 9845 9870
Website: www.wslhd.health.nsw.gov.au/CIDM-PH
Email: WSLHD-CIDM-PH@health.nsw.gov.au
Contact: Ms Lou Orszulak

MBI

Marie Bashir Institute for Infectious Diseases & Biosecurity
Mailing Address: Level 4, Westmead Millennium Institute for Medical Research
176 Hawkesbury Road, Westmead NSW 2145
Phone: (612) 8627 3402
Website: www.sydney.edu.au/mbi/
Email: mbi@sydney.edu.au
Contact: Ms Christine Aitken

In the media....

Comments

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Forbes: <http://www.forbes.com/sites/judystone/2016/01/19/how-can-we-slow-the-epidemic-of-zika-infections/#533ffbd6418d>

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Dr Grant Hill-Cawthorne (left), Professor Lyn Gilbert and Dr Cameron Webb talk about the Zika virus at Sydney University.

Photo: Kate Geraghty

Upcoming Events....

RESEARCH SYMPOSIUM HONOURING PROFESSOR LYN GILBERT *Advancing Control of Communicable Diseases through Innovation and Translational Research*

REGISTRATIONS ARE OPEN

The Centre for Infectious Diseases and Microbiology Laboratory Services, Pathology West (ICPMR), the Centre for Infectious Diseases and Microbiology - Public Health (CIDM-PH), the Marie Bashir Institute, University of Sydney (MBI), and the Centre for Research Excellence in Critical Infections, University of Sydney (CRE Critical Infections) are proud to co-host this wonderful event to celebrate a lifetime of Professor Lyn Gilbert's achievements with a research symposium **Advancing Control of Communicable Diseases through Innovation and Translational Research**.

Confirmed Invited Speakers

- Professor Chris Baggoley, Chief Medical Officer of Australia
- Professor Ian Gust, University of Melbourne
- A/Professor Jeremy McAnulty, NSW Ministry of Health
- Professor Dennis Clements, Global Health Institute, Duke University USA
- Professor Peter McIntyre, NCIRS, University of Sydney
- Professor Suzanne Garland, Royal Women's Hospital, Melbourne
- Professor Saul Tzipori, Tufts University, Boston USA
- Professor Paul Johnson, University of Melbourne and Austin Health
- Professor Ian Kerridge, University of Sydney

Date: Friday, 18th March 2016

Time: 8.30am - 5.00pm

Location: John Loewenthal Auditorium, Westmead Hospital, Sydney

Symposium Program: www.sydney.edu.au/mbi

Symposium Registrations: www.sydney.edu.au/mbi

RSVP: 1 March 2016



An evening dinner function will also be held to honour Prof Gilbert.

In conjunction with The Westmead Association, the Centre for Infectious Diseases and Microbiology - Public Health (CIDM-PH), Centre for Infectious Diseases and Microbiology Laboratory Services (CIDMLS ICPMR), Marie Bashir Institute for Infectious Diseases and Biosecurity University of Sydney (MBI), and CRE in Critical Infection University of Sydney, we would like to invite you to you to attend a celebration dinner honouring Professor Lyn Gilbert, on Friday 18th March 2016, at 'The Tearoom, Queen Victoria Building, Sydney'.

Date: Friday 18 March 2016

Time: 7.30pm

Cost: \$125pp

Where: The Tearoom, Queen Victoria Building Address: 455 George Street, Sydney

RSVP & Payment:

Mrs Georgette Hanna Phone: 02 9845 7983 Email: georgette.hanna@sydney.edu.au