Original articles

Assessing the threat of chikungunya virus emergence in Australia

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Abstract

Background: Chikungunya virus (CHIKV) is a major threat to Australia given the distribution of competent vectors, and the large number of travellers returning from endemic regions. We describe current knowledge of CHIKV importations into Australia, and quantify reported viraemic cases, with the aim of facilitating the formulation of public health policy and ensuring maintenance of blood safety.

Methods: Cases reported to the National Notifiable Disease Surveillance System (NNDSS) from 2002 to 2012 were analysed by place, month of acquisition, and place of residence. Rates of chikungunya importation were estimated based on reported cases and on the numbers of short-term movements.

Results: Between 2002 and 2012, there were 168 cases of chikungunya virus (CHIKV) imported into Australia. Victoria and New South Wales had the largest number of notifications. The main sources were Indonesia, India and Malaysia. The number of cases increased from 2008 to reach a peak in 2010 (n=64; 40%). Although Indonesia accounted for the majority of CHIKV notifications in Australia, travel from India had the highest CHIKV importation rate (number of imported cases per 100,000 travellers).

Conclusions: The Australian population is increasingly at risk from CHIKV. Arrivals from endemic countries have increased concurrently with vector incursions via imported goods, as well as via local movement from the Torres Strait to North Queensland ports. An outbreak of CHIKV could have a significant impact on health, the safety of the blood supply and on tourism. Case and vector surveillance as well as population health responses are crucial for minimising any potential impact of CHIKV establishment in Australia.

Keywords: Chikungunya, importation, risk, travellers, Australia, vectors, viraemic cases

Introduction

Chikungunya virus (CHIKV) is a mosquito-borne Alphavirus of the family *Togaviridae*. The virus is endemic in Africa, India, South-East Asia and the Western Pacific and is considered to be emerging or re-emerging in many regions of the world.[1-4] The disease was first detected in 1952 in Africa following an outbreak on the Makonde Plateau.[5,6] The name chikungunya is derived from the Makonde* root verb, meaning "to become contorted" or "that which bends up" in reference to the stooped posture developed when arthritic symptoms appear. The virus was originally observed in Central and East Africa, circulating in a sylvatic cycle between forest-dwelling mosquitoes, non-human primates,[4,7] with sporadic human cases. In urban centres of Africa and throughout Asia, CHIKV is transmitted from viraemic humans via mosquitoes to available non-immune human hosts.[8] Although it is not demonstrated that cross-protection after infection with other alphaviruses (Ross River—RRV, O'nyong nyong—ONNV viruses) occurs in humans, it has been shown in animal models.[9-12] Large outbreaks of CHIKV have become more frequent in many endemic regions, including a number of Indian Ocean and Pacific Island nations, including Papua New Guinea, as well as emergent cases in historically non-endemic areas, such as Italy.[13,14,15]

These outbreaks have led to considerable problems for public health authorities, not only in relation to adequate vector control and epidemiological surveillance but also on the sustainability of the blood supply.[16,17] For example, in La Réunion Island in 2005, in which more than 30% of the population was infected during an outbreak, local blood donation was suspended to prevent transfusion-transmitted infection and pathogen inactivation was introduced to avoid critical shortages in platelet components.[16]

Potential Australian CHIKV vectors include; *Aedes vigilax, Aedes procax, Coquillettidia linealis,* and *Aedes notoscriptus* [all competent RRV and Barmah Forest virus (BFV) vectors] as well as *Aedes aegypti* and *Aedes albopictus*.[18,19] However, except for the last two, transmission is unlikely due to limited contact between these vectors and people.[18] Currently, *Ae. aegypti* is distributed widely throughout northern and central Queensland, with Goomeri (235 km north of Brisbane) the southern limit near the coast and

* The Makonde Plateau is a border area between Tanzania and Mozambique. "Chikungunya" is from the Makonde language.

Charleville (740km north west of Brisbane) the south western limit.[20,21] *Ae. albopictus* is currently restricted to the Torres Strait Islands off Cape York.[22,23] However incursions of this species, which is a more cold-tolerant mosquito than *Ae. aegypti*, do occur. In India, during an outbreak in 2005-06, *Ae. aegypti* was the main vector associated with disease transmission.[24] However, in the Indian Ocean CHIKV outbreak in 2005-2006, a mutation in the virus increased the transmission ability of *Ae. albopictus*.[25] Because this mosquito can survive in temperate climates, it has become a worldwide concern as a CHIKV vector.

The genus *Alphavirus* contains seven antigenic complexes. CHIKV belongs in a complex with ONNV, BFV, Semliki Forest (SFV), RRV, Sindbis (SINV), and Mayaro viruses (MAYV); members of the complex cause rheumatic manifestations including arthralgia.[26,27] For CHIKV infections the extrinsic incubation period (EIP) appears to be short in *Ae. albopictus*, as little as two days after the infective blood meal.[28] However, the EIP can be as long as 15 days when taken as time to reach maximum transmission efficiency.[29] The intrinsic incubation period ranges from 1 to 12 days (typically 2–4 days).[13] This period is followed by sudden onset of high fever, severe myalgia and arthralgia, with headaches, a skin rash and photophobia.[15,30,31] The symptoms usually resolve within 1-2 weeks but arthralgia may persist for weeks or months following the acute illness.[27] Infections may rarely be complicated by encephalopathy and hepatic failure.[30] CHIKV can also be transmitted to neonates by vertical transmission.[32,33] During recent epidemics in the Indian Ocean region, maternal-foetal transmission, severe neonatal disease, and adult mortality were reported.[34,35]

CHIKV infection is diagnosed on the basis of clinical and epidemiological criteria and can easily be confused with disease caused by other alphaviruses such as SINV, RRV and BFV, as well as dengue virus infection (Flavivirus) and hence requires laboratory confirmation. The most commonly used methods for laboratory diagnosis are serological tests and the quantitative reverse transcription-polymerase chain reaction (qRT-PCR) that detects the presence of viral RNA in serum.[36,37]

In Australia, the principal CHIKV vectors are present in suitable environments near susceptible populations. In addition, countries endemic for CHIKV are frequently visited by tourists, which eventually may result in chikungunya infectious cases in visitors or residents returning to Australia.[38-41] At present, the risk of CHIKV becoming established in Australia is restricted to areas where the vectors are present in sufficient density (Torres Strait Islands for *Ae. albopictus* and North Queensland for *Ae. aegypti*). CHIKV transmission in Queensland and the Torres Strait islands would have significant population health implications, including a potential impact on the supply of fresh blood components. In this study, we undertook an analysis of imported CHIKV cases in order to understand importation pathways and assess the risk of chikungunya emergence in Australia.

Methods

Chikungunya surveillance system

Chikungunya is notifiable in all Australian States and Territories except the Australian Capital Territory. It is not currently nationally notifiable, but a national case definition was implemented in 2010, and Australia's National Notifiable Diseases Surveillance System (NNDSS) includes a separate disease category for chikungunya. Before 2010, cases of chikungunya were sent to the NNDSS under the disease group "arbovirus Not Elsewhere Classified (NEC)" and the Northern Territory still maintains this practice.

Case definition

Under the Communicable Diseases Network Australia (CDNA) surveillance case definition for CHIKV, a confirmed case requires definitive laboratory evidence before notification.[42] Definitive laboratory evidence is:

- isolation of CHIKV
- detection of the virus by nucleic acid testing
- seroconversion or a significant rise in antibody level to chikungunya virus, in the absence of a corresponding change in antibody levels to RRV and BFV or
- detection of CHIKV-specific IgM, in the absence of IgM to RRV and BFV.

If the suspected case has not travelled to an endemic or epidemic country, then confirmation by a second reference laboratory is required.

Data collection

Notification data

Data on notifications of CHIKV infection were extracted from the NNDSS (8 February 2013). These data were subject to retrospective revision and may vary from that reported in published NNDSS reports and reports of notification data by states and territories. Notifications of chikungunya under "arbovirus NEC" were included. 'Diagnosis date (month and year of diagnosis)' represents the onset date, or where the date of onset was not known, the earliest of specimen collection date, notification

date, or date notification was received. Data span 1 January 2002 to 31 December 2012. 'Place of acquisition' was based on where the infection was believed to have been acquired, and the incubation period and time spent in a location or the place of recent travel. Data on place of acquisition were obtained from the NNDSS, and checked (up to 30 June 2011) and completed by State and Territory data managers for National Arbovirus and Malaria Advisory Committee (NAMAC) annual reports. Where insufficient information was available on the country or region of acquisition, 'Overseas – unknown/inadequately described' was recorded. Place of acquisition is usually obtained through public health follow-up of each case. 'State/Territory' is the state or territory of residence of the case. Cases residing in one jurisdiction but diagnosed in another are notified by the state of residence. Duration of travel was not recorded.

Overseas travel data

We accessed overseas arrivals and departures tables from the Australian Bureau of Statistics (ABS) website for 2008 to 2012.[43] Earlier years were not analysed because there were fewer than five cases of CHIKV per year before 2008. We analysed the number of short-term movements (resident departures and visitor arrivals) from Indonesia, Malaysia and India, the three main sources of importation identified. Monthly data are complete from January 2008 to December 2012 inclusive.

Data analysis

Short-term resident departures and visitor arrivals in Australia have been analysed for the study period.[43] Short-term resident departures (STRD) are defined as Australian residents intending to stay abroad for less than 12 months. Short-term visitor arrivals (STVA) are defined as overseas visitors intending to stay in Australia for less than 12 months. Short-term movement is defined as less than one year in duration.

The total and mean number of short-term movements (STRD and STVA) per year have been calculated for Indonesia, Malaysia and India, and were used to determine the percentage increase in these travel categories from 2008 to 2012. Importation rates based on short-term resident departures alone, and short-term resident departures summed with visitor arrivals over the period 2008 to 2012 have been calculated per 100,000 persons.

We used short-term movement information as these data include the country departed to or arrived from, whereas such information is not included with long-term movement data. We selected short-term visitor arrivals (overseas visitors intending to stay less than one year), and STRD (Australian residents intending to stay abroad less than one year). STRD were used rather than returns, because short-term resident returns are not available by country. We assumed near equivalence of STRD and short-term resident returns. But short-term resident returns may be fewer than STRD if some people decide to stay longer than one year, or die overseas. We assumed that numbers in these categories (longer than intended stay and overseas deaths) would be low.

Results

Number of CHIKV notifications

Since 2002 there have been 168 CHIKV notifications in Australia, 160 of which were during the study period (2008 to 2012). There was no clear seasonality in importation rate, although importations were slightly more common in the period October to April (Figure 1). In 2010, case numbers were highest in October (14 cases, comprising 22% of notifications for the year). The number of cases peaked in 2010 (n= 64) accounting for 40% of cases during the study period. In 2011 and 2012, 38 and 16 cases were reported, respectively.

Source of CHIKV importations

All CHIKV cases in Australia were acquired overseas. The three most common countries of acquisition were Indonesia (28.0%), India (18.5%), and Malaysia (10.0%) (Figure 2). The remaining 43.5% were from other countries, and of these 15.0% were unknown or inadequately described at the time of notification.

State of residence

Of the 160 cases, the majority (57.0%) returned to the two most populous states, Victoria and New South Wales (Table 1). Except for the Australian Capital Terrority, in which CHIKV is not notifiable, all states and territories reported cases. India and Indonesia respectively accounted for 26.0% and 24.0% of cases reported from Victoria and New South Wales.

Predicted number of imported cases based on short-term travel data

Over the study period, there was an increase in SDRD and STVA arrivals for the three main source countries for CHIKV infections (Figures 3 and 4). From 2008 to 2012, the number of STRD to Indonesia increased (+140%) as did, to a lesser extent, departures from India (+57%) and Malaysia (+36%). The number of STVA also increased from 2008 to 2012 (+54% for Indonesia and Malaysia, +35% for India).

We utilised STRD as well as visitor arrival numbers, along with notification source data, to estimate CHIKV importation rates in travellers returning from Indonesia, India and Malaysia. Our analysis

Figure 1: Number of reported cases of CHIKV, 2008 to 2012, by month and year

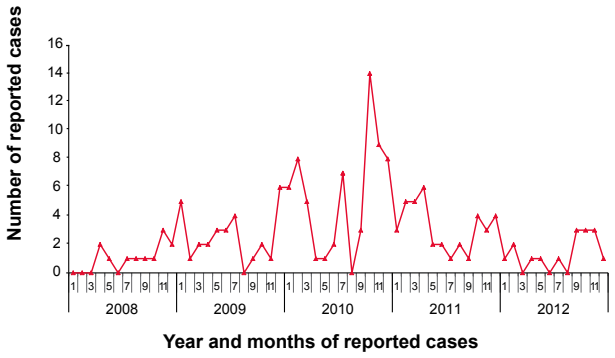


Figure 2: Number of reported cases of CHIKV, 2008 to 2012, by country of origin and year

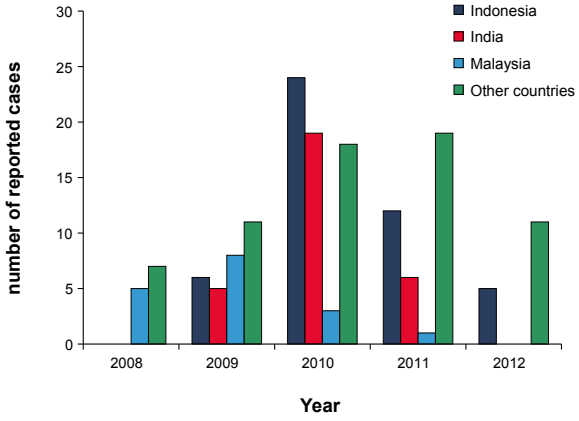
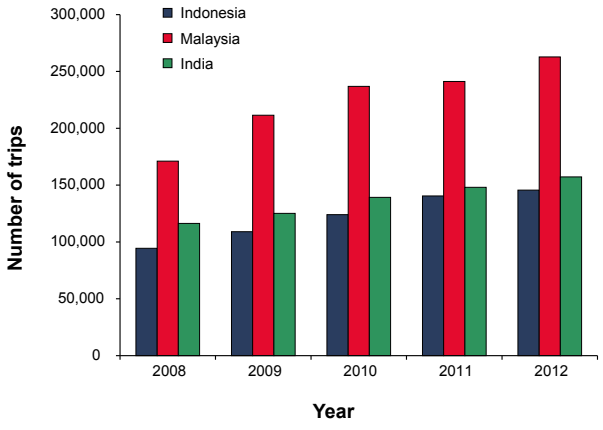


Table 1: Number of reported cases of CHIKV infection by country of acquisition and state or territory, 2008 to 2012

Country of acquisition	State/Territory							
	NSW	NT	QLD	SA	TAS	VIC	WA	Total
Indonesia	11	8	5	0	1	11	11	47
India	9	0	2	0	0	15	4	30
Malaysia	5	0	3	0	1	4	4	17
East Timor	0	4	0	0	0	4	1	9
Sri Lanka	0	0	0	1	0	3	0	4
Thailand	0	0	1	1	0	4	0	6
Vietnam	1	0	0	0	0	1	1	3
Bangladesh	3	0	0	0	0	0	0	3
Other countries*	5	1	2	1	0	6	2	17
Unknown/inadequately described	5	0	2	6	0	4	7	24
Total	39	13	15	9	2	52	30	160

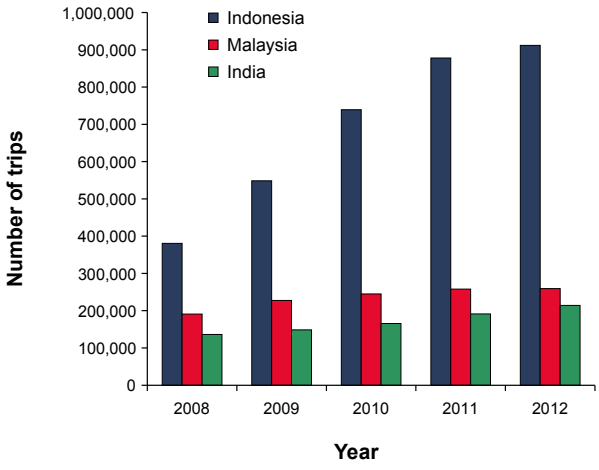
* 12 countries constituting 'Other countries' were known sources of chikungunya infection.

Figure 3: Total number of STRD from Australia, visiting Indonesia, Malaysia and India, 2008 to 2012



Data sourced from ABS

Figure 4: Total number of STVA, visiting Indonesia, Malaysia and India, 2008 to 2012



Data sourced from ABS

Table 2: CHIKV importation rates per 100,000 passengers, 2008 to 2012, by country

	Indonesia	Malaysia	India
n imported cases*	47	17	30
Total Passengers (STRD†)	3,458,100	1,180,600	855,600
CHIKV Import. Rates§	1.35	1.43	3.50
Total Passengers (STRD + STVA‡)	4,071,500	2,304,000	1,541,500
CHIKV Import. Rates§	1.15	0.73	1.94

* n imported cases: number of CHIKV imported cases

† STRD: Short-Term Resident Departures

§ CHIKV Import. Rates: Importation rates of chikungunya per 100,000 persons

‡ STVA: Short-Term Visitor Arrivals

suggests that, although Indonesia was the greatest source of infection acquisition, risk for CHIKV acquisition was highest for India (Table 2).

Discussion

Australia is at risk of local CHIKV transmission. Factors that determine Australia's risk include an immunologically naïve population (unless cross-protection with other alphaviruses occurs), regular introductions of the virus, presence of competent mosquito vectors, and an appropriate climate for exotic vectors. Climate change has the potential to increase vector range, as increased temperature and humidity could increase the areas in Australia receptive to vectors. The movement of workers and human behaviour might have an important role in emergence of CHIKV, as well as the introduction and establishment of *Ae. albopictus*. Indeed in Malaysia, migrant workers coming from endemic neighbouring countries are suspected to be the major source for CHIKV re-emergence.[30] Moreover, a recent study has shown that an increasing number of chikungunya cases have been reported to the Ministry of Health of Malaysia and the country may become endemic for CHIKV.[44] Due to the presence of *Ae. aegypti* and *Ae. albopictus* in the north of Australia, a local outbreak is likely to occur. Knowledge of vector competence of local mosquitoes is a starting point for understanding the risk of autochthonous transmission.[18] It is important to predict population health response requirements on the basis of knowledge of epidemic risk relative to number and timing of viraemic imports and relevant vector biology.

One hundred and sixty imported CHIKV cases were reported between 2008 and 2012. Under-reporting, due either to misdiagnosis or asymptomatic infection, is highly probable. Even for RRV, which is endemic, under-reporting is considerable.[26] These data give an overview of viraemic importations over the last 5 years and enable assessment of the most important source countries. Fifty seven per cent of reported cases come from Indonesia, India and Malaysia, countries where CHIKV has recently re-emerged. There was no strict importation seasonality during the study period. The inclusion of 15% of cases with unknown or inadequately described source represents significant missing data in the NNDSS.

We utilised travel data, along with the sources of CHIKV notifications in Australia to identify the highest risk source countries. Although Indonesia accounted for the majority of CHIKV notifications in Australia, India had the highest CHIKV importation rate. Travel to India has been steadily increasing in recent years, although not as rapidly as travel to other countries and CHIKV cases in Australia may increase in the future if this trend continues. It is also noteworthy that rates of CHIKV infection in returning travellers from East Timor could be higher than rates for India, Malaysia and Indonesia, given the relatively small number of total arrivals from that country. However, the total infections acquired in East Timor accounted for a small percentage of cases (<6% of cases between 2008 and 2012).

Notwithstanding the efforts of state and territory health departments (notably the Northern Territory Health Department and Queensland Health) to successfully manage exotic mosquito-borne diseases and their vectors, [45,46] the introduction of exotic vectors cannot be wholly prevented. It is likely that *Ae. albopictus* will become established on the Australian mainland.[23] Although numerous detections of *Ae. albopictus* have been successfully managed without the establishment of this species as yet, incursions continue to occur. In recent times *Ae. albopictus* was detected near Melbourne (December 2012) and is the subject of an on-going surveillance and control program (S. Lynch, Victorian Department of Primary Industries, *pers. comm.* 20 Dec 2012). The mosquitoes entered via a consignment of lucky bamboo (*Dracaena*). In Australia, other mosquito species such as *Ae. vigilax, Ae. procax, Ae. notoscriptus* and *Cq. linealis*,[47-49] could potentially transmit CHIKV,[18] although this is highly unlikely because of their behavior and ecology.

CHIKV has re-emerged after two to four decades, in some countries e.g. after 39 years in the Democratic Republic of Congo, 32 years in India, and 20 years in Indonesia.[51] In Southeast Asian endemic regions, where the original Asian genotype circulated for several decades, new strains belonging to the Indian Ocean Lineages (IOL) have emerged,[52,53] and caused major outbreaks especially in Malaysia.[53-57] The shift in viral genotypes is a major threat not only for the Asian region but also for the Western Pacific and Australia, where *Ae. aegypti* and *Ae. albopictus* are present in Queensland.

If local CHIKV transmission were to occur in Australia, this virus might cause considerable problems for public health authorities and impact on the nation's blood supply. CHIKV presents a risk to transfusion safety. During an outbreak in La Réunion Island in 2005 in which 30% of the population were infected, local blood donation was suspended and pathogen reduction of platelet components was implemented as an additional safety measure.[16] Dengue is episodic in north Queensland. A recent study has demonstrated that local outbreaks pose a relatively high risk to the safety of Australia's blood supply, with the large 2009 epidemic costing the Australian Red Cross Blood Service in excess of one million Australian dollars.[17] If CHIKV were to become established here with similar seasonal outbreaks in the north, it is likely to cause similar impacts on blood safety.

There are neither specific treatments for CHIKV nor a licensed vaccine. However, some treatments exist to relieve symptoms, for example non-steroidal anti-inflammatory drugs, as well as ribavirin and chloroquine.[13,58,59] A candidate live-attenuated virus vaccine (LAV) based on the wild-type Thai CHIKV strain has shown promising results,[60] provoking a good immune response in humans. In addition, a novel CHIK vaccine candidate, called CHIKV/IRES, has been developed and also shows promising results.[61]

Conclusion

This study highlights the main source of CHIKV viraemic reported cases and assists risk determination which could facilitate the formulation of public health policy and ensure the maintenance of the safety of the blood supply. The re-emergence of chikungunya in Asia and Indian Ocean islands and the emergence in the South Pacific regions, with several chikungunya outbreaks in Papua New Guinea, emphasise the potential of the virus to cause large outbreaks in susceptible populations. Overseas-travel, particularly for holidays, is probably the primary mechanism for CHIKV introduction to Australia. Therefore, epidemiology, human movements, vector biology and ecology are all crucial to population health planning for potential CHIKV importation into Australia.[62]

The Australian population is increasingly at risk for CHIKV establishment as the number of visitors coming from countries endemic for CHIKV and the numbers of residents going to visit these countries have increased in recent years. This risk will continue to increase if these countries remain attractive and affordable visitor destinations, and if in-country control efforts or Australian surveillance and traveller education programs are ineffective. In addition to direct morbidity costs, a CHIKV outbreak could significantly impact blood supply and tourism.

It would be useful to determine how long people stay in the endemic country, for what purpose (work, family visit, travel) and obtain information about the host (age, sex, income, level of education) and virus (strains). Australian authorities must continue to implement vector surveillance and control programs for the major vectors, *Ae. aegypti* and *Ae. albopictus* and ensure that the ongoing biosecurity measures are maintained in order to keep the country free of *Ae. albopictus*. Media and stakeholders should be kept well informed. Greater knowledge of the characteristics of each imported case is needed. Modeling of transmission risk is also important in order to predict future vector distribution and disease risk.

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