

'Dengue: Australia's other pandemic'



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Pandemic dengue arrived in Australia in 2008-09. A large epidemic of Dengue Virus 3 (DENV-3) affected much of north Queensland, with over 900 cases and one death, in Cairns. This was accompanied by 18 imported viremic dengue cases into north Queensland from January to May 2009 and outbreaks of DENV-1, -2 and -4 in Townsville, Cairns and Innisfail, respectively. The virus was unique, with apparently shorter incubation periods, resulting in rapid transmission that exceeded the capacity of Queensland Health's five-man dengue control team. Furthermore, potential pesticide resistance reduced the efficacy of some control measures. This unprecedented level of dengue activity has highlighted problems with the Dengue Fever Management Plan (DFMP), forcing the implementation of new interventions to control the epidemic. These included adoption of the Emergency Management Framework that allowed access to resources beyond those budgeted. New emergency teams conducted interior residual spraying and treating of containers in yards with methoprene and this was supplemented by SES volunteers, who delivered cans of surface spray to residents. This wide-ranging approach rapidly reduced transmission. Nonetheless, the presence of high populations of *Ae. aegypti*, that sustained epidemic transmission in much of north Queensland, highlights the need for the expansion of the DFMP to fund a comprehensive source reduction campaign. The incursion and establishment of the vectors *Ae. aegypti* and *Ae. albopictus* into eastern urban areas could dramatically increase the range of dengue transmission in Australia. Novel vector control measures, such as the use of life-shortening *Wolbachia*, offer the potential to eliminate dengue transmission in the future.

Dengue, the other pandemic

For most Australians, the word pandemic conjures up images of flu clinics, surgical masks and luxury cruises. However, a

virus carried by a mosquito has been in pandemic mode for many years and that pandemic truly arrived in Australia in 2008. The dengue viruses comprise four serotypes that do not cross-protect and, indeed, can enhance pathology for secondary cases. Classical dengue fever can evolve into the life-threatening Dengue haemorrhagic fever (DHF) via immune enhancement. A dengue global pandemic has emerged in the tropics of SE Asia and the Americas in the last half of the 20th century¹, causing an estimated 50 to 100 million cases occurring annually². Australia has increasingly been subject to outbreaks of dengue, with 17 outbreaks consisting of 1,240 confirmed cases, including two deaths³, from 2000 to 2008 (Figure 1). Dengue in Australia is limited to urban areas of north Queensland, the only region in Australia that has the vector *Aedes aegypti* (Figure 2). This mosquito is highly urbanised, feeding almost exclusively on man and breeding in water-holding artificial containers in yards and houses⁴.

The DENV-3 epidemic redefines dengue control in north Queensland

A virulent DENV-3 strain reached Australia in November 2008 via a Cairns resident returning from Kalimantan, Indonesia. The individual became sick shortly after arrival in Cairns, but did not seek medical attention. It was only after several dengue cases had been confirmed in the area that the original imported case (patient zero) was discovered through creative contact tracing by a public health nurse. The outbreak of DENV-3 soon grew to epidemic proportions, with nearly 100 cases contracted by 1 January 2009, only 57 days since the virus was imported into Cairns. As of writing (June 2009), this epidemic would cause 906 cases in Cairns alone and also cause outbreaks in Townsville, Port Douglas, Cape York and several beach communities near Cairns.

What was special about this virus that resulted in epidemic transmission? First, a potted history of dengue control in north Queensland. Queensland Health's (QH) Dengue Fever Management Plan for north Queensland (DFMP) is a responsive plan that conducts aggressive vector control in response to recognised imported or locally acquired dengue cases⁵. Vector control consists of treating water-holding containers to kill larvae and spraying synthetic pyrethroid insecticides inside premises (interior residual spraying, IRS) to kill adult *Ae. aegypti*, hopefully before they can transmit dengue virus (typically 10 days after feeding on blood). Since 2003, lethal ovitraps⁶ (LOs) that kill egg-laying mosquitoes have largely replaced IRS, greatly reducing pesticide use and increasing the speed and coverage of treatment. These strategies have been successful (Figure 1), although occasional large outbreaks still occur. In the 2003 DENV-2 epidemic, centred in Parramatta Park, very high vector populations, coupled with a delay of 42 days in notification of

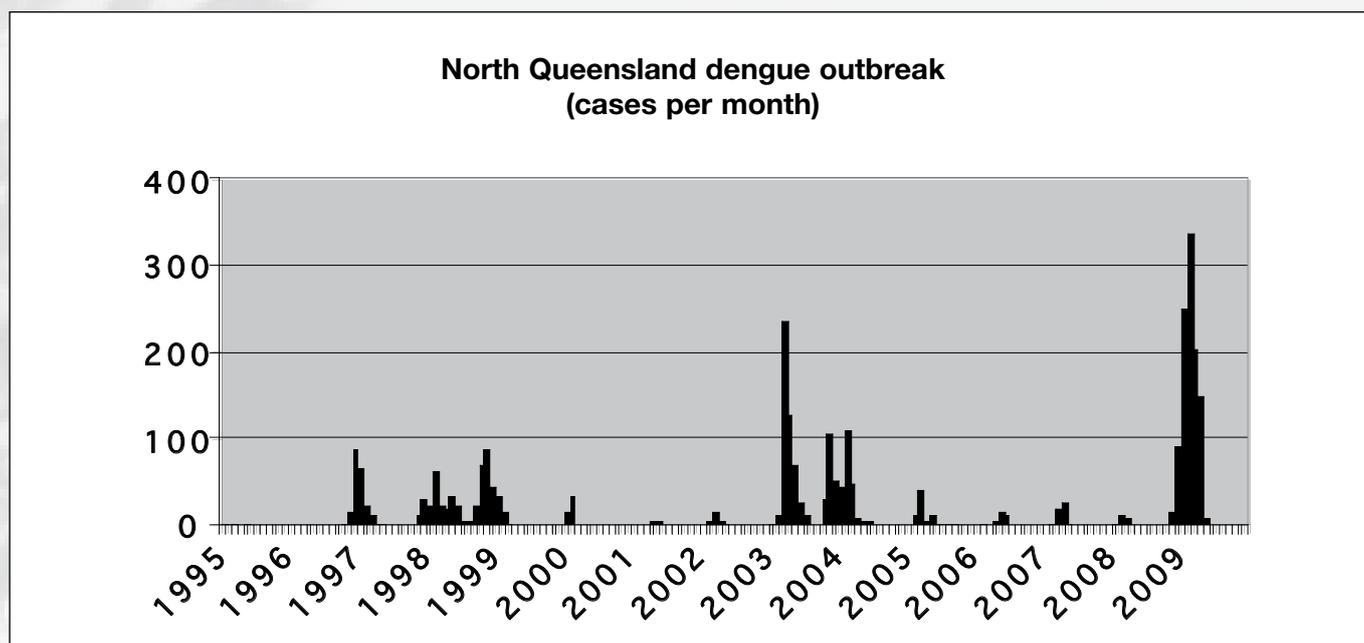


Figure 1. Outbreaks of confirmed dengue, by month, in north Queensland 1995-2009.

the imported case, allowed epidemic transmission to initiate and spread unchecked for several weeks before control began^{7,8}. A similar scenario occurred during the 2008-09 DENV-3 epidemic, with a notification delay of 25 days in an area with high populations of *Ae. aegypti*. Clearly, long notification delays for imported cases, in areas with high populations of the vector, risk epidemic transmission. However, transmission persisted during the 2008 outbreak despite vector control. Survival of field-collected female *Ae. aegypti* exposed to a diagnostic dose of bifenthrin, the synthetic pyrethroid used in LOs, suggested that mosquitoes were becoming resistant to the pesticide.

We also have strong circumstantial evidence that the virus was transmitted abnormally fast. In three instances in the current outbreak, we were able to identify a successive round of transmission from a patient who introduced the virus into an isolated area that had no evidence of previous dengue transmission. In each case the total incubation period (TIP), the sum of the extrinsic incubation period (EIP) within the mosquito and then subsequent intrinsic incubation period (IIP) in man, ranged from 9 to 11 days. Generally the TIP is 2-3 weeks, consisting of an EIP of 10-12 days⁹ and IIP of 4-6 days¹⁰. For example, the TIP of the initiation of the DENV-2 outbreak in 2003



Figure 2. Female *Aedes aegypti* emerging from pupal skin (photo courtesy of Paul Zborowski).

was 17 days. The relatively fast transmission of the 2008 DENV-3 meant that mosquitoes were infected and secondary transmission was initiated, by the time QH was notified of a dengue case. Thus, as people moved, especially during the Christmas holidays, they spread dengue throughout the region, creating numerous new foci of transmission.

An official epidemic was declared on 20 January, activating QH's Disaster Plan. An Incident Management Framework to manage the situation was initiated on 22 January. Both of these are unprecedented actions by QH and allowed us access to extra resources to fight the epidemic. Indeed, up to 50 emergency staff members were in the field at one time. Due to potential pesticide resistance and the fast transmission of the virus, LOs were abandoned in favour of the effective, but laborious, IRS of houses. Several new initiatives were also developed as the large number of active cases forced us to expand our response from case chasing to blanket treatment over a wide area. Dengue warning letters were posted to residents identified by a database as living within 100 metres of active transmission. A special search and destroy team swept across residential areas, treating all containers with the insect growth regulator methoprene. Teams from the State Emergency Service (SES) supported by rapidly delivering brochures and cans of surface spray in affected suburbs. Insect repellent was delivered to all primary schools in north Queensland. And a new 'dengue defence' health education campaign was developed. Cases peaked at 102/week in mid-February, with a single death later that month. Cases then declined precipitously: as of June only one to two cases a week are being reported.

However, the dengue pandemic still threatened north Queensland. An unprecedented number of imported cases have been reported in 2009, with 18 imported viraemic dengue cases up to June 2009. This is a huge increase on the yearly average of

9 (1999-2007) and the year is only halfway through! The DENV-3 epidemic spread to Townsville, causing 17 cases and outbreaks of DENV-1, DENV-2 and DENV-4 struck Townsville, Cairns and Innisfail, respectively. In total, 1016 dengue cases have been confirmed in north Queensland from November 2008 to June 2009, with unprecedented transmission of all four serotypes.

What lessons can we learn to prevent recurrent dengue epidemics in light of a continued onslaught of imported cases? First, we must eliminate the current DENV-3 strain. This virus has shown the propensity for rapid expansion, leading to explosive transmission and must not survive the dry season lest it re-emerge next wet season. Second, we must acknowledge that the DFMP failed to contain the outbreak and rebuild it to handle a scenario of increased imports of more virulent strains of dengue. The health education campaign failed to prevent significant mosquito breeding, as evidenced by the truly astounding populations of *Ae. aegypti* encountered in Cairns during the outbreak (Figure 3). Clearly, the vector control program of the DFMP must change direction from a reactive to a preventative program. There are currently only five dengue vector control staff permanently employed by QH in Cairns. In order to prevent scenes depicted in Figure 3, many more staff must be placed on the ground to police the region. Health education must target residents who have large numbers of containers on their property and instil the belief that you cannot have a yard festooned with containers and live in north Queensland. In addition, medical surveillance must adopt faster surveillance methods to minimise notification delays. The new NS1 dengue antigen assay shows great promise¹¹ and was successfully used by Cairns Base Hospital to diagnose cases during this outbreak.

The future of dengue in Australia

In the short term, the scale of dengue control in Cairns will likely significantly reduce vector populations, with a quiet year ahead. But *Ae. aegypti* populations will soon rebound, unless an expanded dengue prevention program is adopted in north Queensland. In addition, with a large number of imported cases and an increasingly large population that has contracted dengue, secondary dengue cases with attendant DHF and deaths will rise.

Efforts to find new adult control methods must be expanded to counter resistance to synthetic pyrethroids. Despite the failure of bifenthrin-treated LOs, new biodegradable models¹² offer promise of a fast, green solution to dengue control, especially if new pesticides can be employed. The synthetic pyrethroid metofluthrin is promising for rapid control of adult mosquitoes. Metofluthrin is released from a paper emanator as an odourless vapour that can kill *Ae. aegypti* within a household for several days¹³. The threat that *Ae. aegypti* could expand into Brisbane is real and, with the growth of water storage, potentially devastating outbreaks of dengue could occur in older suburbs dominated by unscreened Queensland housing. Finally, the Asian Tiger Mosquito (*Ae. albopictus*) may soon become established on the Australian mainland and expand down the east coast¹⁴. While this would introduce the risk of dengue transmission in areas that currently have none (e.g. Sydney), it may reduce the risk of epidemic in the north. This mosquito feeds on many mammals and thus is less likely to sustain epidemic transmission of dengue than the human-feeding *Ae. aegypti*¹⁵. Indeed, since its arrival in the Torres Strait in 2005, *Ae. aegypti* has largely disappeared from the outer islands and no dengue has been reported.



Figure 3. Some Cairns residents produced tremendous amounts of *Aedes aegypti*. This boat and the tyres within it were flooded and contained large numbers of *Ae. aegypti* larvae and pupae.

The long-term future holds great promise for novel vector control methods. Professor Scott O'Neill's Bill and Melinda Gates Foundation-funded project has shown that a strain of the bacteria *Wolbachia* significantly reduces the lifespan of *Ae. aegypti* and could be used to 'dengue-proof' natural populations of the mosquito¹⁶. Simulated field trials are currently under way at James Cook University's new Mosquito Research Facility in Cairns. And, hopefully, by the time *Wolbachia* is available for release, resident *Ae. aegypti* populations will be maintained below epidemic thresholds by a sustained source reduction program.

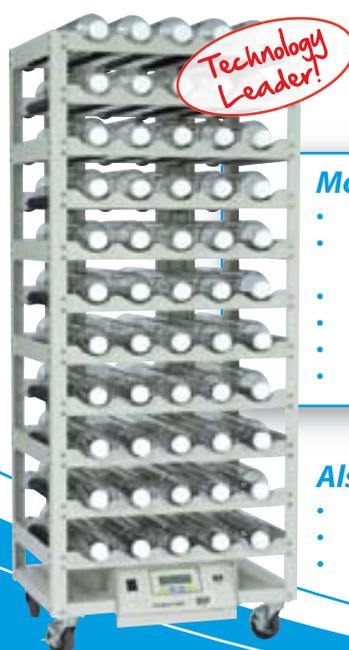
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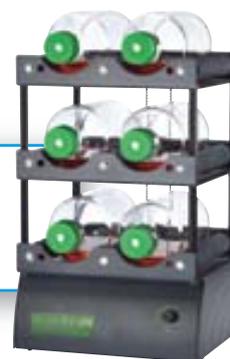
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