

Australian Paediatric Surveillance Unit STUDY INFORMATION SHEET Dengue



BACKGROUND

The dengue virus (DENV) is a mosquito-borne flavivirus transmitted from the bite of an infected female mosquito belonging to the *Aedes* genus. A restricted number of species acts as vectors for dengue virus transmission, however, the *Aedes aegypti* species is the principal species responsible for viral circulation of the serotypes known to cause human disease (DENV-1, DENV-2, DENV-3, and DENV-4).⁽¹⁾ In 2013, A fifth serotype was identified in Malaysia, however its impact on humans has not been established.⁽²⁾ *Aedes albopictus*, is a less efficient vector but its geographic expansion into tropical and temperate climates continues.⁽³⁾

Dengue occurs in many tropical and subtropical regions of the world (mainly Asia, the Western Pacific Islands, Latin America and Africa) but the disease has been spreading to new areas and has resulted in localised outbreaks in Europe and the southern parts of the United States.⁽³⁾ Dengue is the most common arboviral disease globally and the reported global burden of disease has increased 400% in the last two decades, at a higher rate than any other communicable disease.⁽³⁾ Global warming, population growth and density, degraded urban environments, increased international travel and inadequate mosquito control programmes have likely contributed to the broader geographic distribution of the Aedes mosquitoes and acceleration of disease, amplifying the potential for epidemic dengue in temperate regions.^(3, 4)

Although there has been a resurgence of dengue in Australia during the last three decades, outbreaks have been restricted to far North Queensland (Cairns and Townsville) and the Torres Strait Islands. (4, 5) However *Aedes aegypti* mosquitoes have historically been reported in most mainland Australian states and DENV outbreaks were occasionally documented in northern areas of Western Australia and New South Wales prior to 1955. (2, 4) *Aedes albopictus* is currently confined to the Torres Strait Islands, however this mosquito has the potential to colonise large areas of mainland Australia given its temperate tolerance. The most recent outbreak of DENV infection was reported in Rockhampton, Queensland in 2019. This was the first outbreak of locally acquired dengue in Central Queensland for 65 years and it was caused by the DENV-2 serotype. Overseas acquired cases of dengue are reported in most Australian jurisdictions each year due to the rise in regional tourism, especially to popular destinations such as Bali where dengue is endemic. The potential for importation of dengue into Australia and the risk of spread of vectors suggests that increased rates of disease will be seen throughout Australia. (6)

The spectrum of symptoms associated with DENV infection range from a mild febrile illness usually mistaken for the flu to severe dengue which is a life-threatening emergency and includes dengue haemorrhagic fever and dengue shock syndrome. The clinical presentation may be influenced by the host factors such as age, and immunological status, most fatal cases occurring in children and young adults. Despite this, little is known about dengue in children, including in Australia. Vertical transmission from mother to child in utero has been described but is thought to be uncommon and would be unlikely in Australia given the current level of dengue activity. Presently, there is no specific treatment for dengue and care is supportive. In 2015, the world's first dengue vaccine was developed by Sanofi Pasteur (CYD-TDV or Dengvaxia) and second-generation dengue vaccines are currently underway in phase 3 trials.

STUDY OBJECTIVES

- 1. To identify cases of dengue in Australian children aged < 16 years and to document the distribution of cases who are seen by paediatricians.
- 2. To describe dengue in children, including demographics, clinical features and severity, treatment; and short- term outcomes in children with dengue, prior to vaccination of this population group.
- 3. To document serotype trends of DENV paediatric infections in Australia.

CASE DEFINITION

Confirmed case: a confirmed case requires laboratory definitive evidence AND clinical evidence.

<u>Laboratory definitive evidence</u>: isolation of dengue virus or detection of dengue virus by nucleic acid testing, detection of dengue non-structural protein 1 (NS1) antigen in blood by EIA, IgG seroconversion or a significant increase in antibody level or a fourfold or greater rise in titre to dengue virus, proven by neutralisation or another specific test or detection of dengue virus-specific IgM in cerebrospinal fluid, in the absence of IgM to Murray Valley encephalitis, West Nile virus/Kunjin or Japanese encephalitis viruses.

<u>Clinical evidence</u>: a clinically compatible illness includes fever, headache, arthralgia, myalgia, rash, nausea, and vomiting, with possible progression to severe plasma leakage, severe haemorrhage, or severe organ impairment – CNS, liver, heart or other.

Probable case: requires laboratory suggestive evidence AND clinical evidence AND epidemiological evidence or clinical evidence and household epidemiological evidence.

<u>Laboratory suggestive evidence</u>: Detection of NS1 antigen in blood by a rapid antigen test (unless dengue NS1 antigen by EIA is negative) or detection of dengue virus-specific IgM in blood.

<u>Clinical evidence:</u> A clinically compatible illness (e.g. fever, headache, arthralgia, myalgia, rash, nausea/vomiting)

Please report any infant who, in the opinion of the notifying paediatrician, is a confirmed or a probable case.

REPORTING

Follow-up of notifications: A case report form requesting details will be sent to clinicians who notify a case.

PRINCIPAL INVESTIGATOR

FURTHER INFORMATION

For further information related to this study or assistance completing the Case Report Form, please contact the APSU by either:

• email: SCHN-APSU@health.nsw.gov.au or

• phone: (02) 9845 300

SELECTED REFERENCES

- 1. Tully D, Griffiths CL. Dengvaxia: the world's first vaccine for prevention of secondary dengue. Therapeutic Advances in Vaccines and Immunotherapy. 2021;9:25151355211015839.
- 2. The Series of National Guidelines (SoNGs). Dengue, Communicable Diseases Network Australia (CDNA) National Guidelines for Public Health Units 2015. Available from: https://www1.health.gov.au/internet/main/publishing.nsf/Content/FE1CB334E23F9DD4CA257BF0001C11FC/\$File/dengue-song.pdf [accessed September 14, 2021]
- 3. Wilder-Smith A, Ooi E-E, Horstick O, Wills B. Dengue. The Lancet. 2019;393(10169):350-63.
- 4. Russell RC, Currie BJ, Lindsay MD, Mackenzie JS, Ritchie SA, Whelan PI. Dengue and climate change in Australia: predictions for the future should incorporate knowledge from the past. Medical Journal of Australia. 2009;190(5):265-8.
- 5. Walker J, Pyke A, Florian P, Rodney Harris RM, Khandaker G. Re-defining the dengue-receptive area of Queensland after the 2019 dengue outbreak in Rockhampton. The Medical Journal of Australia. 2021;215(4):182-.
- 6. Wilder-Smith A. The expanding geographic range of dengue in Australia. The Medical Journal of Australia. 2021;215(4):171-2.
- 7. Zeng Z, Zhan J, Chen L, Chen H, Cheng S. Global, regional, and national dengue burden from 1990 to 2017: A systematic analysis based on the global burden of disease study 2017. EClinicalMedicine. 2021;32:100712.
- 8. Wakimoto MD, Camacho LAB, Guaraldo L, Damasceno LS, Brasil P. Dengue in children: a systematic review of clinical and laboratory factors associated with severity. Expert review of anti-infective therapy. 2015;13(12):1441-56.