

Rethinking the antibody-dependent enhancement dengue hemorrhagic fever model

October 26 2009

Research published this week in *PLoS Medicine* challenges the dogma of the antibody-dependent enhancement model (ADE) for the development of dengue hemorrhagic fever (DHF).

Dengue virus infection usually causes a severe 'flu like illness, although symptoms may be mild in young children. DHF, however, is a severe and sometimes fatal complication of dengue virus infection that affects about half a million people every year. DHF patients usually fall into two groups; children and adults who become infected with a second dengue virus serotype after an initial "primary" dengue virus infection with a different serotype, and infants with primary dengue virus infections born to mothers who have some dengue virus immunity. The current model for development of DHF in infants around 6 months old is that antidengue virus antibodies transferred from a dengue-immune mother to her child somehow enhance dengue virus infection, resulting in more severe symptoms (the 'antibody-dependent enhancement' model).

A prospective nested case-control study of infant dengue carried out by Daniel Libraty (of the University of Massachusetts Medical School, Worcester, MA) and colleagues reveals that <u>maternal antibodies</u> against dengue protect infants from the full spectrum of dengue disease. They also found that all infants with symptomatic dengue <u>virus infection</u> had antibodies with measurable ADE activity, but that there was no link between the amount of ADE activity and the development of DHF. They



failed to find evidence supporting a role for the ADE model of development of DHF but did find that a higher weight-for-age was a risk factor for DHF.

The authors conclude that 'the results should encourage a rethinking or refinement of the currently promulgated ADE model for infant DHF, promote prospective studies of infant dengue and stimulate new directions of research into novel potential mechanisms for infant DHF'.

More information: Libraty DH, Acosta LP, Tallo V, Segubre-Mercado E, Bautista A, et al. (2009) A Prospective Nested Case-Control Study of Dengue in Infants: Rethinking and Refining the Antibody-Dependent Enhancement Dengue Hemorrhagic Fever Model. PLoS Med 6(10): e1000171. doi:10.1371/journal.pmed.1000171

Source: Public Library of Science (<u>news</u>: <u>web</u>)

Citation: Rethinking the antibody-dependent enhancement dengue hemorrhagic fever model (2009, October 26) retrieved 27 April 2024 from https://medicalxpress.com/news/2009-10-rethinking-antibody-dependent-dengue-hemorrhagic-fever.html

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