

in Rhesus macaques. Flavivirus-naïve macaques were inoculated with D2 virus and randomized in the first study to receive a single dose of Roferon[®]-A (10 MU/m²) or placebo, and in the second study to receive PEGASYS[®] (6 µg/kg) or placebo, one day after the onset of viremia. Serial daily viremia levels were measured, and convalescent D2 virus neutralizing antibody titers were determined. Compared to placebo, Roferon[®]-A temporarily suppressed D2 virus replication and delayed the time to peak viremia by a median of 2 days. Mean peak serum viremia levels and area under the curve (AUC) virus concentrations were not different between the two groups. This finding led to a study of pegylated rIFN-α. PEGASYS[®] produced a 1-log drop in mean daily viremia levels over 4 days when compared to placebo. Peak viremia levels were not significantly affected, but D2 virus AUC and elimination t_{1/2} trended lower in the PEGASYS[®] group. There were no significant differences in D2 virus PRNT₅₀ between two groups at 30 and 90 days post-infection. Rapid identification of dengue viremic patients early in illness may provide an opportunity to suppress viremia and ameliorate subsequent disease severity. A single injection of PEGASYS[®], or a combination of PEGASYS[®] and Roferon[®]-A, early in dengue illness should be further investigated.

**53rd Annual Meeting of the American Society Tropical Medicine and Hygiene (ASTMH).
Miami, Florida, USA. 7-11 November 2004.**

Am J Trop Med Hyg. 2004; 70(4 suppl):293.

RELATIONSHIP OF PREEXISTING DENGUE VIRUS (DV) NEUTRALIZING ANTIBODY LEVELS TO VIREMIA AND SEVERITY OF DISEASE IN A PROSPECTIVE COHORT STUDY OF DV INFECTION IN THAILAND

**Endy TP, Nisalak A, Chunsuttitwat S, Vaughn DW, Green S, Ennis FA, Rothman AL
and Libraty DH**

Background: Infection with any 1 of the 4 dengue viruses (DVs) can produce several illnesses, ranging from a mild febrile illness to classic dengue fever (DF) to dengue hemorrhagic fever (DHF), a potentially life-threatening disease. Most DHF cases occur after sequential heterotypic DV infections. The role of preexisting humoral immunity in modifying severity of dengue disease is not well understood.

Methods: We conducted a prospective cohort study of children in a region where dengue disease is hyperendemic and examined the role of preexisting neutralizing anti-DV anti-bodies (Abs) in modifying secondary dengue-3 virus (D3V), dengue-2 virus (D2V), and dengue-1 virus (D1V) infections.

Results: In secondary D3V infection, higher levels of preexisting neutralizing Ab directed against D3V (reference virus strain and patient's virus isolate) were associated with lower viremia levels and milder disease. Preexisting neutralizing Ab levels against D2V were not associated with severity of secondary D2V infection. The levels of preexisting neutralizing Ab against the infecting virus isolates were not associated with viremia levels in secondary D2V or D1V infections.

Conclusions: Cross-reactive memory humoral immune responses appear to be beneficial in symptomatic secondary D3V infection, but not in secondary D2V or D1V infection. These results may have important implications for the development of live attenuated tetravalent dengue vaccines.

J Infect Dis. 2004; 189(6): 990-1000.

THE RELATIONSHIP OF PREEXISTING DENGUE VIRUS NEUTRALIZING ANTIBODY LEVELS TO VIREMIA AND DISEASE SEVERITY IN SECONDARY DENGUE INFECTIONS

**Gibbons RV, Endy TP, Nisalak A, Chunsutthiwat S, Vaughn DW, Green S, Ennis FA,
Rothman A and Libraty DH**

Neutralizing antibody is a common marker of protective immunity for most of the existing vaccines and has been the surrogate marker for protection in the development of an effective tetravalent dengue vaccine. The host's humoral immune response following natural dengue virus infection results in a diverse antibody response, including a variety of combinations of protective and non-protective, neutralizing and non-neutralizing, and heterotypic and serotype-specific antibodies.

Antibodies can be protective in dengue virus infection. In this presentation we will discuss the recently published results from a prospective cohort in Thailand (Endy TP, et al. JID 189: 990-1000;2004) showing that in secondary DEN3 infection levels of neutralizing anti-body against DEN3 were associated with lower viremia and milder disease. However, in secondary DEN2 infection levels of neutralizing antibody against DEN2 were not associated with the severity of secondary DEN2 infection; and that levels of neutralizing antibody against the infecting virus isolates were not associated with viremia levels in secondary DEN1 or DEN2 infections.

This data suggests that cross-reactive humoral immune responses are beneficial in symptomatic secondary DEN3, but not secondary DEN2 or DEN1 infection. Implications for vaccine development will be discussed.

**1st Regional Meeting of Pediatric Dengue Virus Initiative (PDVI). Bangkok, Thailand.
18-20 October 2004.**

**WHO/TDR and PDVI Joint Workshop on Dengue Diagnostics and Dengue Classification/
Case Management. Geneva, Switzerland. 4-6 October 2004.**
