

during a course of DHF. A prospective study of hospitalized patients suspected of having dengue infection has demonstrated that several immunological parameters were up-regulated in DHF compared to DF (dengue fever) patients. These include a cell surface activation marker; CD69 on CD8+T cells and NK cells, cytokines such as IL-10, IFN- $\gamma$ , and soluble cytokine receptors. A recent study has shown that patients who sub-sequently developed severe dengue infection have more tumor necrosis factor secreting, dengue-specific CD8+ T cells in their peripheral blood than individuals who developed DF. Expansion of cross reactive CD8+ T cells during a secondary dengue infection has been demonstrated in a recent study. These observations suggest that stimulation of dengue specific T cells during a secondary infection may lead to the activation of various immune cells and cytokine cascades, resulting in inflammation and release of vasoactive substances which cause plasma leakage and coagulopathy.

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## **SPATIAL COHERENCE AND ASSOCIATION OF TEMPERATURE, RAINFALL AND THE INCIDENCE OF DENGUE HEMORRHAGIC FEVER IN THAILAND**

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The seasonal increase in dengue hemorrhagic fever in Thailand is often cited as occurring concomitantly with the warm, rainy season. We have investigated this relationship in detail to determine if the seasonal variance in incidence is associated with seasonal variance in temperature and rainfall across Thailand. Using a time-series decomposition technique, the empirical mode decomposition, we examine the seasonal variance of DHF, rainfall and temperature in a large dataset describing monthly DHF incidence, mean monthly temperature and monthly rainfall in 41 provinces for 14 years. The empirical mode decomposition sifts time-series data into modes of different periodicities. Using the non-parametric spline covariance function, we find that temperature is synchronized across the country while DHF incidence and rainfall vary markedly in phase in different parts of the country. Phase coherence analysis of DHF incidence and rainfall suggests that the timing of the dengue season is linked to the timing of rainfall across Thailand. Additionally, we have found that annual DHF incidence rates are associated with higher mean annual temperatures. This relationship is modified by the distance from Bangkok, with provinces close to Bangkok varying little with varying temperature, while those furthest from Bangkok are more strongly associated with temperature. This modification of the effect of temperature suggests that several processes at different temporal and spatial scales affect incidence across the country.

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