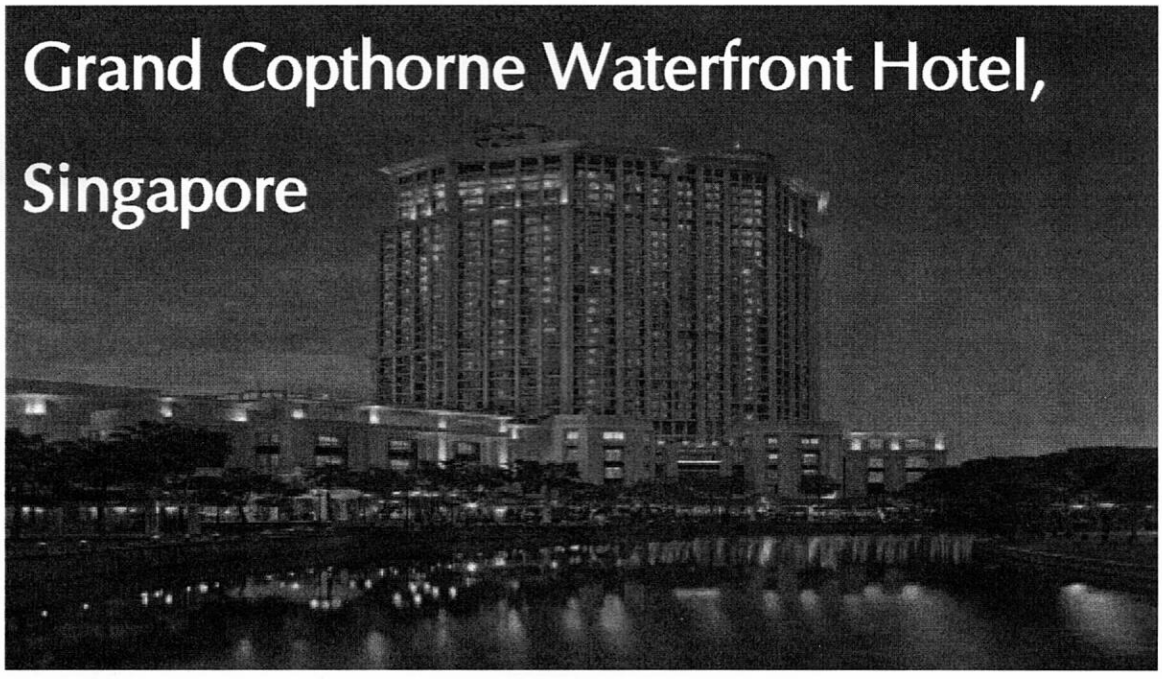
Program Outline

22 - 26 January 2017

(Sunday - Thursday)

Venue:

Grand Copthorne Waterfront Hotel, Singapore



Riverfront Ballroom, Level 2

Dulharie WIJERATNE (A-15)

Role of Dengue Virus Specific T cell Responses in the Pathogenesis of Acute Dengue Infection

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The role of dengue virus (DENV) specific T cell responses in the pathogenesis of dengue hemorrhagic fever (DHF) is not clear. Although it is debated whether cross reactive T cell are protective or result in immunopathology, more recent studies in naturally infected individuals, have suggested that DENV-specific T cell responses are likely to be protective. Previous studies have not fully addressed the role of T cells in acute dengue, partly due to small sample sizes, the time of sample collection and evaluation of T cell responses to only limited DENV proteins. Therefore we sought to investigate the role of DENV NS1, NS3, NS5 and pooled peptide specific T cell responses in the disease outcome and viraemia in a relatively larger cohort.

83 adult patients, with acute dengue were recruited between day 4 and day 8 of illness. All clinical and laboratory data were serially recorded and fluid leakage was confirmed by ultra sound scans. The clinical disease severity was classified according to the WHO 2011 guidelines. *Ex vivo* IFN-γ Elispot assays were carried out to identify DENV specific T cell responses to DENV NS1, NS3, NS5 and pooled. DENV infection was confirmed by quantitative real time PCR, which was also used to measure the viral load.

In our cohort 49 patients had DHF and 34 dengue fever (DF). The overall DENV specific T cell responses were significantly higher (p=0.02) in patients with DF (median 42.5, IQR 8.7 to 217.5) compared to those with DHF (median=15, IQR 0 to 75). DENV NS3, NS5 and the overall T cell responses inversely correlated with the degree of viraemia, which was most significant for DENV-NS3 specific T cell responses (Spearman's r = -0.45, p=0.0002), especially in those with DF (Spearmans r=-0.73, p=0.0001). DENV-NS1 specific responses did not show any correlation with viral loads in either patients with DF or DHF.

The median duration of illness when the patients were recruited to the study was 5.2 (IQR 4 to 6) days. The frequency of DENV NS3 specific T cell responses did not correlate with the day of recruitment, whereas DENV-NS1 specific T cell responses significantly increased from patients who were recruited from day 4 to day 6 (Spearmans r=0.37, p=0.0005). The overall DENV-specific T cell response (median 30, IQR 10 to 135) and DENV-NS3 responses (median 90, IQR 17.5 to 582.5) were higher in those with DF recruited on day 4, when compared to those who proceeded to develop DHF (overall specific responses: median= 5, IQR 0 to 15 and NS3: median=15, IQR =0 to 260). There was no significant difference in DENV specific T cell responses in primary and secondary dengue infection (P >0.05).

In conclusion, a higher frequency of DENV-specific T cell responses, and especially in early illness appears to contribute to better clinical outcome. As DENV NS3 specific T cell response, was most strongly associated with the degree of viraemia and also was highest in those with DF, T cell responses to this protein could be associated with better clinical outcome.