The Complement Activation in Dengue Hemorrhagic Fever

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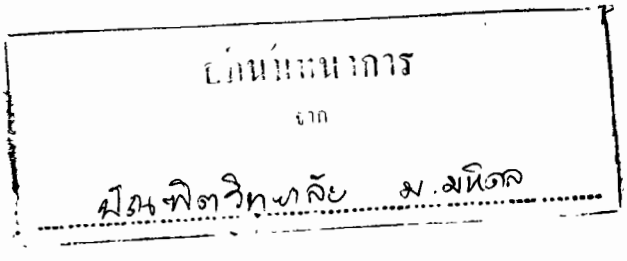

Summary

The findings from these experiments can be summarized as following:

1. With ICEP test, precipitating antibody to dengue viral antigen were titrated. The antibody titers increased rapidly in patients and were not found in normal healthy popolation. So, this test is very useful for quick diagnostic and detection of precipitating antibody. This precipitating antibody titers were low or absence in sera collected during the acute stage of the severe cases. An absence of precipitating antibody may be one of important factor in pathogenesis of this disease.

2. C_3 activation was found in correlation with shock, in DHF grade III and IV only. The activation was at maximum in the grade IV patients in which the circulating immune complex was reported to be lower. This test may be useful to identify potential shock victims and to guide the therapy of shock once it develops. It is also useful as a test to determine the ability of certain substance to activate complement.

3. Enzyme Immunoassay for the detection of dengue viral antigen was sensitive with only the direct method,

especially in control system (dengue antigen from infected suckling mouse brain). The sensitivity was high since it could detect dengue type 2 antigen at HA unit of 0.0128. In NHS, few cases had titer of 0.2 to 0.44 HA unit, but in patients' sera collected at acute phase this titer was much higher with the range from 0.5 to more than 128 HA units. The presence of dengue antigen in sera of grade III and IV patients collected at acute stage was significantly higher than its presence in the grade I and II ($P < .001$) suggesting the involvement of circulating antigen and the severity of disease.

4. Conglutinin binding test for the detection of immune complex indicated that the presence of immune complex did not correlate with the severity of the disease especially when studied in the same patient during the acute, recovery, and convalescent phase.

5. First trial to search for the cause of Complement activation was done by using dengue type 2 antigen from different sources. The results suggesting that this antigen alone can activate the complement system via the alternative pathway. In <u>in vivo</u> situation, dengue viral antigen may be released into the circulation in suitable quantity and many of the biological consequences of complement activation would follow. This experiment provided

evidence that dengue viral antigen alone may lead to complement activation and this complement splitting property of dengue type-2 antigen(s) may be used to explain the complement consumption in primary DHF cases. In secondary DHF where soluble complex of dengue antigen-antibody may be formed, the combine effect of these 2 complement splitting agents may lead to massive C_3 activation as observed in clinical cases.