INTRODUCTION

Dengue virus has caused extensive epidemics resulting in mass suffering in India, South-East Asia and some other parts of the world. It produces a benign febrile illness or haemorrhagic illness with shock. It is considered to be an immunopathological disease but the pathogenesis is not fully understood. The mechanisms which have been considered in the causation of the disease are formation of virus-antibody immune complexes (Russell, 1981); enhanced replication of the virus in presence of subneutralizing concentrations of antibody (Halstead et al., 1977); production of factors by mononuclear cells which activate complement and clotting systems resulting in increased vascular permeability and shock (Russell & Brandt, 1973). It has been suggested that the severity of dengue virus infection is related to the number of infected cells (Ruangjirachuporn et al., 1979).

Macrophages have been shown to play a critical role in host defence mechanisms against a number of viral infections (reviewed by Mogensen, 1979). During these processes macrophages get
damaged and may develop functional defects. Such functional defects in macrophages can be produced directly by the virus replication or are induced by indirect mechanisms. Macrophage functions are influenced by the action of lymphokines, including interferon (reviewed by Unanue, 1981).

Macrophages have receptors to which the Fc-portion of IgG gets attached, therefore, their receptors are known as Fc-receptors. The binding of IgG coated erythrocytes through Fc-receptor triggers the mechanism by which the bound erythrocyte is phagocytosed. Thus, such a macrophage shows both attached as well as ingested erythrocytes.

The pathogenic events of DV infection appear to be shared by man and monkey (Halstead et al., 1973, b, c). Due to the difficulties involved in maintaining large animals in the laboratory such studies on monkeys have been limited.

Evidences accumulated during recent years indicate that the cells of the macrophage-monocyte phagocytic system are the cells that principally support replication of dengue virus in man, monkey and mouse. In man it has been shown by isolation
of the virus (Scott et al., 1960); by electron microscopy (Boonpucknavig et al., 1979; Halstead, 1981a). Similar observations have been made in rhesus monkeys with respect to virus isolation and the distribution of virus antigen in macrophages of different organs (Marchette et al., 1976; Halstead et al., 1977; Halstead & O’Rourke, 1977; Halstead, 1981a). In the mouse, dengue virus has been demonstrated by electron microscopy (Nath et al., 1983), fluorescent antibody technique (Hotta et al., 1981a, b) and by replication in human (Brandt et al., 1981) and mouse macrophage cell lines (Halstead et al., 1982). On the other hand the phagocytic and migratory functions of macrophages are adversely affected in dengue virus-infected mice due to the production of a cytotoxic factor (CF) in the spleen (Gulati et al., 1982) which also suppresses the macrophage functions of human blood leucocytes in vitro (Chaturvedi et al., 1982a) and induces mouse macrophages to produce a cytotoxin (Gulati et al., 1983a, b, c). The role of macrophages in various immune phenomena in dengue virus infection have been described (Chaturvedi et al., 1981b, 1982b; Shukla & Chaturvedi, 1982, 1983). Due to the extensive
involvement of macrophages in dengue virus infection it has been termed 'Macrophagitis' (Halstead, 1981b).

Recently the mechanism of macrophage infection by dengue virus has been studied in some detail by Russell and co-workers. They have suggested that the virus can infect monocytes in one of two ways: through a trypsin-sensitive virus receptor or through a trypsin-insensitive Fc-receptor (Russell, 1981; Daughaday et al., 1981). Immune enhancement of dengue virus infection by a non-cytophilic antibody, as shown by Halstead (1981b), occurs through Fc-receptors of monocytes. The central role played by the macrophages in dengue virus infection prompted me to further explore those areas which were untouched. The present study was therefore, undertaken mainly to investigate the Fc-receptor mediated macrophage functions in dengue virus infection of mice.

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