CYTOKINES MEDIATED KILLING OF SEXUAL STAGES OF MALARIA PARASITES DURING INFECTIONS

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During a blood infection of Plasmodium cynomolgi in its natural host, the toque monkey, Macaca sinica, peak parasitaemia is often accompanied by a "crisis" in the infection; this is most pronounced in splenectomized animals. Crisis is characterized by the appearance of morphologically abnormal intra-erythrocytic parasites. At crisis there is also a sudden loss of infectivity of the parasites to mosquitoes which persists for 4 to 6 days. Neither of these phenomena has been explainted. Loss of infectivity at crisis was found to be due to death of circulating gametocytes; healthy infectious gametocytes pre-incubated for 3 hours in crisis serum lost infectivity to mosquitoes compared to controls in normal monkey serum. Removal of Tumour Necrosis Factor (TNF) and Interferon-gamma (γ -IFN) from crisis serum by the addition of anti-TNF and anti- γ IFN antibodies reversed the gametocytocidal effects of the crisis serum although removal of either TNF or γ -IFN alone had no effect indicating that gametocyte killing effects in crisis serum result from the combined action of cytokines, among them TNF and γ -IFN.

Cytokines induced in vitro from toque monkey peripheral blood mononuclear cells stimulated with lipopolysaccharide (LPS) also had a similar killing effect on gametocytes. These gametocytocidal effects of LPS stimulated PMBC supernatants were also removed by the addition of anti-TNF antibodies but not by anti- γ IFN antibodies. Recombinant TNF when added to TNF depleted LPS stimulated PBMC culture supernatants restored the gametocytocidal effects of the supernatants. However, recombinant TNF on its own had no killing effects on gametocytes indicating that factors in addition to TNF were involved in the gametocyte killing. These results are the first report of parasiticidal effects of cytokines against blood stage parasites during malarial infection.

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