SECTION A

CYTOKINES MEDIATE KILLING OF SEXUAL STAGE MALARIA PARASITES DURING INFECTIONS

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During a blood infection of lasmodium cynomolgi in its natural host Macaca sinica, peak parasitaemia is often accompanied by a "crisis" in the infection; this is most pronounced in splenectomized animals. Crisis is characterized by appearance of morphologically abnormal intra-erythrocytic parasites. At crisis there is also a sudden loss of infectivity of parasites to mosquitoes which persists for 4-6 days. These phenomena haven't been explained. Healthy infectious gametocytes pre-incubated for 3 hours in crisis serum lost infectivity to mosquitoes. Pre-incubation with anti-Tumour necrosis factor and anti-Interferon-gamma antibodies reversed the gametocytocidal effects of crisis-serum although pre-incubation with either anti-TNF or anti-IFN-gamma alone had no effect indicating that gametocyte killing effects in crisis serum are mediated by cytokines TNF and IFN-gamma.

Cytokines induced in vitro from toque monkey peripheral blood mononuclear cells stimulated with lipopolysaccharide (LPS) also had similar killing effects on gametocytes. These effects were also removed by the addition of anti-TNF antibodies but not by anti-IFN-gama antibodies. Recombinant TNF, when added to TNF-depleted LPS-stimulated PBMC culture supernatants, restored the gametocytocidal effects of the supernatants. TNF on its own had no killing effects on gametocytes indicating that factors in addition to TNF were involved in the gametocyte killing.