A-23 The immunological mechanisms underlying a malarial paroxysm and associated parasite killing

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A phenomenon of intra-erythrocytic parasite inactivation which occurs in the circulation of *P.vivax* malaria patients coinciding with the event of a clinical paroxysm was previously described. Factors essential for this parasite inactivation are transferable by plasma taken during a paroxysm and they include TNF-alpha and a parasite toxin among other unidentified mediators. This was demonstrated in an *ex-vivo* assay in which intra-erythrocytic gametocytes were rendered non-infective to mosquitoes following incubation for 3h in paroxysm plasma by depletion and reconstitution experiments.

The other essential mediator for parasite inactivation is IL-2, and the phenomenon is dependent on the presence of T lymphocytes and monocytes. Parasite inactivating properties found in paroxysm plasma, can be conferred on normal plasma by the addition of a combination of rTNF-alpha, a freeze-thawed schizont extract and r-IL-2, but not by the exclusion of any one of these. The selective removal of monocytes from this cell and plasma mixture, but not of T-lymphocytes, abolishes the parasite inactivation, indicating that monocytes are essential for this sequence of events. T-cells are also essential and for the sole purpose of producing IL-2,because infectivity can be restored to gametocyte infected blood taken from a patient during or close to a paroxysm by removal of T lymphocytes but not in the presence of added rIL-2. Parasite inactivating effects of paroxysm plasma can be abolished by the addition of an anti-IL-2 antibody as well as by the removal of monocytes (but not lymphocytes) from the cell mixture. We postulate from these results, that parasite antigens liberated during schizont rupture acting as superantigens are recognized by and activate T-lymphocytes to produce IL-2. IL-2 stimulates monocytes to produce TNF-alpha and acts in conjunction with it and a parasite product acting

as an endotoxin, to produce the final mediators of parasite inactivation such as reactive nitrogen intermediates.