A-24 Regulation of adherence of *Plasmodium falciparum*-infected erythrocytes to ICAM-1 by plasma from cerebral malaria patients

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The adherence of *P.falciparum*-infected erythrocytes (IE) to endothelial cells has been implicated in malarial pathogenesis. This property, and the expression of endothelial cell receptors such as ICAM-1 are known to be regulated by certain host and parasite factors. In this study, the intrinsic adherence of parasite isolates from natural *P.falciparum* infections and the ability of patients' plasma factors to induce the expression of ICAM-1 were compared between severe and complicated (SC) and uncomplicated infections which were classified based on clinical and biochemical criteria. The SC group comprised cerebral malaria (CM) and multiple organ failure syndrome (MOFS) patients. Parasite isolates from 7 SC and 39 uncomplicated patients were cultured and percentage rosetting and intrinsic adherence was assessed using CHO-ICAM-1 and CHO-CD36 cells. Plasma was collected from 21 SC and 22 uncomplicated *P.falciparum* patients and regulation of expression of receptors was assessed by "cell-ELISA" using live CHO cells following stimulation with 20% plasma.

Adherence of IE to CHO-ICAM-1 cells was significantly higher in the SC group compared to that in the uncomplicated group ($p=0.006;z=2.74$), whereas adherence to CHO-CD36 cells and rosetting of these two groups were comparable. Plasma from CM patients ($p=0.064;t=1.93$) but not from MOFS patients ($p=0.804;t=0.025$) upregulated the expression of ICAM-1 to a greater extent than did plasma from uncomplicated patients. This data strongly implicates the binding of IE to ICAM-1 in the pathogenesis of severe and complicated malaria.

Moreover, the upregulation of ICAM-1 expression by plasma from CM patients alone and not from MOPS patients suggests that binding to ICAM-1 may be

specifically involved in the pathogenesis of cerebral malaria and that the pathological mechanisms underlying these syndromes may be different.