A-24: Tumor necrosis factor(TNF) mediated parasite killing during malarial paroxysms

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The peak of fever in malarial paroxysms, which are prominent clinical manifestations of this disease, coincide with the appearance in the patient's plasma of factors that inactivate the parasite (gametocytes). This phenomenon of parasite inactivation can be demonstrated in an *in vitro* system as follows:

incubating gamatocytes from infected patients in paroxysm plasma for 3 h renders them non-infective to mosquitoes well fed through an artificial membrane. It was previously shown that this gametocyte inactivating effect was mediated by TNF alpha acting in conjuction with other essential plasma factor(s). The effect is transient and it is absent from the patient's plasma 4 h after a paroxysm (i.e. in post-paroxysm plasma). In the present study we have elucidated the gametocyte inactivating mechanism further and defined yet another plasma factor essential for this phenomenon. *P. vivax* gametocytes incubated in paroxysm plasma of a non-immune *P. vivax* patient lost up to 75% of their infectivity to mosquitoes. This suppression of infectivity was reversed by the addition of a rabbit anti-serum raised against a *P. vivax* schizont extract as well as by an immune human serum taken from an endemic *P. vivax* patient during convalescence, suggesting that a parasite product(s) was essential for gametocyte inactivation. This was confirmed by the fact that the gametocyte inactivating effects which were absent from post-paroxysm plasma could be induced in it by the addition of a combination of rTNF and a freeze-thawed *P. vivax* schizont extract. However, the addition of rTNF and parasite extract to normal plasma did not induce gametocyte inactivation implying that other as yet unidentified factor(s) are involved; these additional factor(s) must be present in both paroxysm and post-paroxysm plasma, although the presence of both TNF and the parasite component in paroxysm plasma is much more transient. Understanding this phenomenon which correlates with clinical disease may lead to the basis of malarial pathogenesis.