

Circulating Lymphocytotoxic Factors in Malaria Patients

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OBJECTIVE : To assay for substances in malarious plasma which are toxic for lymphocytes.

BACKGROUND : There have been several reports in the literature of plasma borne antibodies which are cytotoxic for autologous lymphocytes. Terasaki et al. reported cytotoxic factors in the plasma of patients infected with either systemic lupus erythematosus or rheumatoid arthritis (1). These findings were confirmed by the work of Michlmayr et al. (2) who indicated that both T lymphocytes and B lymphocytes were target cells although primarily the former were killed. Dettoratius et al. (3) extended these findings with their report of lymphocytotoxicity in patients infected with hepatitis. Earlier work in this laboratory (4) indicated that there is a marked suppression in the proportion of circulating T lymphocytes during infection with malaria. It was reasoned that lymphocytotoxicity might be one mechanism underlying the observed phenomenon. We thus decided to screen patient plasma for cytotoxic activity under optimal conditions as reported by other workers.

METHODS : Cytotoxic assays were performed with the plasma of 42 patients infected with either *P. falciparum* and *P. vivax*. Methodology according to Terasaki (1) was employed with modification. Autologous control sera and target lymphocytes were obtained from normal volunteers. Lymphocytes isolated by ficoll gradient centrifugation were adjusted to a concentration of 4×10^3 cells in 0.02 ml SBSS pH 7.3. Target cells were incubated with sera for 1/2 hour at 15°C at which time .02 ml of 1:5 dilution of complement was added; the incubation was continued for another 2½ hours. Following incubation the percent of dead cells per 100 mononuclear cells were calculated by dye exclusion.

RESULTS : The results of these experiments indicated a general similarity in the percent of target cell death in the normal and test cultures of each series. In 5 test plasma cultures there was evidence of significant cell disruption. Cell death in these cultures ranged between 12% and 54% (mean 26%) as opposed to 7% in the single control culture. There was no evidence of cytotoxic activity in the plasma of 37 other malaria patients as compared with controls. Interpretation of the 5 positive plasma is difficult in that the target lymphocytes were provided by a donor who was later found infected with hepatitis. No activity was found in the plasma of these 5 patients when a follow-up assay was conducted against lymphocytes from the same donor or other donors. Due to the lack of firm evidence for cytotoxic activity in the plasma of these malaria

patients work in this area has been aborted. This is a final report.

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