A-07: Acquisition of an anti-disease, clinical immunity to malaria in an endemic area of Sri Lanka

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Repeated infections of malaria give rise to a partial degree of protection against the disease, as manifested by a reduction in both parasite densities in peripheral blood (anti-parasite immunity), and the intensity of clinical disease; this appears as a clinical tolerance to parasites i.e an anti-disease immunity. The objective of this study was to ascertain the degree to which clinical immunity is acquired by a community living in a malaria endemic region, as a result of repeated malaria infections, and whether this immunity is species specific, and age-acquired.

A population of 1942, resident in Kataragama, in southern Sri Lanka where both *P.falciparum* and *P.vivax* are endemic, was chosen for this study. For a period of 18 months commencing from January 1992, the malaria infections that occurred in this population were monitored with respect to age of patient, tensity of clinical disease and parasite density.

Malaria was monitored by (1) passive case detection at 2 diagnosis and treatment centres in the area, and (2) an active case detection mechanism whereby 6 mass blood surveys of the entire population were conducted at approximately 3 monthly intervals. In every malaria patient thus detected the parasiteamia and the severity of the disease was measured using a questionnaire, in which 11 clinical symptoms were scored for their degree of severity according to the patients perception using a numerical scoring system. A clinical score was thus obtained for each patient, the higher the score the greater the intensity of disease. In a sample of patients, plasma levels of C-reactive Proteins (CRP) were assayed as an indicator of the degree of underlying pathology.

Records from 947 patients (547 due to *P.vivax* and the rest *P.falciparum*) were analysed for this study. The median clinical scores for primary infections of both *P.vivax* and *P.falciparum* infections were similar, the values being 13.0 and 13.3 respectively. When *P.vivax* infections were preceded by a single *P.vivax* infection the score was reduced to 11.0 and by multiple homologous infections, still further, to 9.2. When the parasite density of the patients was accounted for, the clinical score per parasite decreased 3-fold from a primary to multiple infections, suggesting the development of a clinical immunity.

When *P.vivax* infections were preceded by *P.falciparum* there was little effect on the clinical score of the *P.vivax* infection. Multiple infections with *P.falciparum* led, in contrast,to only a slight drop in the clinical score of a subsequent *P.falciparum* infection, from 13.3 to 11.0. When *P.falciparum* infections were preceded by *P.vivax* infections however, the clinical score decreased from 11.75 to 9.3 and the clinical score per parasite reduced two fold.

When the age of the whole population of patients was considered, both the clinical scores and the plasma C-reactive protein levels during an infection increased with increasing age.

These results indicate that over the short-term, repeated infections with *P.vivax* malaria confers a clinical immunity to subsequent infections of both *P.vivax* and *P.falciparum*. *P.falciparum* however, is less effective in inducing clinical tolerance; previous *P.falciparum* infections only conferred a mild degree of immunity to subsequent homologous infections and none to the heterologous species *P.vivax*.

Although clinical immunity is acquired and boosted in the short-term, it decreased with age of patients in this population. Clinical immunity thus appears not to be age-acquired. This loss of clinical tolerance in older age groups, in whom the incidence rate of malaria is low, is likely to be due to the lack of boosting by frequent infections, as a result of the acquisition of an anti-parasite immunity.