

This study aimed at dissecting immune mechanisms of resistance/susceptibility in schistosomiasis in a well-characterized cohort of hyper exposed adults with a high prevalence of HIV-1. The impact schistosome infections may have on the HIV/AIDS pandemic was investigated.

First the general effect of HIV-1 co-infection on immune responses to schistosomes was examined. Schistosomiasis patients with HIV-1 co-infections had significantly lower interleukin (IL) -4 ( $P = 0.03$ ) and IL-10 ( $P = 0.005$ ) production than did HIV-1 negative individuals. In contrast, gamma interferon (IFN- $\gamma$ ) production levels were similar between the two groups. Furthermore, in patients with HIV-1, a decrease in CD4<sup>+</sup> T cells was correlated with an increased Th1/Th2 cytokine production ratio ( $r = -0.53$ ;  $P = 0.01$ ). The differences in the immune response profile of persons without liver fibrosis compared with persons that have schistosomiasis related pathology as detected by ultrasound, and how this may be affected by a patient's HIV-1 status was also investigated. The proportion of patients with fibrosis was lower in HIV-1 seropositive (4%) than in HIV-1 seronegative groups (20%) even though this was insignificant by Fisher's exact test ( $P = 0.1014$ , odds ratio = 3.067). Mean CD4<sup>+</sup> cell count levels were significantly lower ( $P > 0.01$ ) in the IP > A (pathology) group than in the IPA (normal liver) group after controlling for HIV-1 status but CD8<sup>+</sup> cell counts were similar in patients with or without fibrosis. Generally, all cytokine production by PBMC in response to phaeohaemagglutinin PHA, SEA (egg antigens) and SWAP (adult worm antigens) was higher in the IPA group in both the HIV-1 positive and negative patients than in the IP > A. However, following chemotherapeutic treatment of the hepatosplenic patients, responsiveness to both schistosome-derived antigens was elevated, with the SWAP driven responses being more dramatically increased. These immune response profiles were compared with susceptibility/resistance to schistosomiasis. IL-4 and IL-5 production were strongly correlated with susceptibility ( $P = 0.0010$ , and  $P = 0.0005$  respectively) while there was no relationship susceptibility and IL-10 and IFN- $\gamma$  production.

As a follow up of these immune response studies in schistosomiasis, their possible effect of on HIV-1 susceptibility was investigated. The *in vitro* susceptibility of CD4<sup>+</sup> T cells and monocytes from persons with schistosomiasis compared to cells from former patients and cells obtained from persons with no prior exposure to schistosomes was investigated using *in vitro* HIV-1 infection assays. Viral replication dynamics were monitored in the cell culture supernatants using a P24 (HIV core antigen protein) ELISA for determination of viral load. P24 mean levels were higher for cells from active infection patients. However, stimulated cells generally produced more virus than unstimulated cells and stimulated cells from former patients were more susceptible than antigen stimulated cells from active infection patients ( $P < 0.1$ ; Mann Whitney U). Levels of the chemokine HIV co-receptors CXCR-4 and CCR-5 as analyzed using FACS, were significantly higher on cells obtained from egg positive patients than on cells from egg negative patients ( $P < 0.03$ ; t-test).

Thus schistosomiasis and HIV-1 have deleterious effects on the host, both singly and co-infectionally. These findings suggest that parasitic diseases like schistosomiasis may be an important component in the natural history of HIV/AIDS and that control of parasitic diseases may have additional benefits with respect to the HIV/AIDS epidemic in Sub-Saharan Africa. Thus the control of parasitic diseases should be integrated in HIV/AIDS control strategies.