THE NATURE OF SPONTANEOUS CURE OF SCHISTOSOMA MANSONI INFECTION IN THE RAT, RATTUS NORVEGICUS

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DECLARATIONS

This thesis is my original work and has not been presented for a degree in any other University.

Signed W. MUNGETI Date 27 February 1985

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This thesis has been submitted for examination with my approval as University Supervisor.

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The albino rat is an unusual host for the trematode parasite, Schistosoma mansoni. Development and migration of the worms proceed normally up to the fourth week of infection when maximum numbers can be recovered by perfusion of the liver. After this period, the number of worms which can be recovered declines sharply in the next 10 to 15 days. This rapid decline in worm population has been called spontaneous cure. Little is known about the mechanism of spontaneous cure and this work seeks to throw some light on its nature.

Previous studies have indicated that the immune response is involved in spontaneous cure. In the present work, attempts were made to explore this possibility further. The specific aims of the study were, firstly, to find out if the immune system is primarily responsible for spontaneous cure. For this part of the study, the course of infection was followed in rats which had been treated with (a) hydrocortisone, which suppresses cell-mediated immunity; and (b) indomethacin, an anti-inflammatory
drug. Secondly, attempts were made to study the immune effector mechanisms involved in spontaneous cure. The approach used was depletion of suspected effector cells by treatment of infected rats with selected killing agents, specifically, (i) silica particles, for killing macrophages; (ii) cyclophosphamide, for depleting B-cells; and (iii) an anti-rat eosinophil serum for destroying eosinophils.

The work showed that treatment of rats with a single dose of hydrocortisone before exposure to infection caused a pronounced inhibition of spontaneous cure in all three experiments conducted with the drug. Indomethacin treatment caused a small inhibition of spontaneous cure and consistently increased the susceptibility of rats to infection. In addition to these effects, indomethacin treatment appeared to increase the rate of growth of the worms. The results of the experiments with these two drugs show that worm growth and spontaneous cure are due to immunologically mediated processes.

In an attempt to find out whether macrophages played any role in spontaneous cure, rats were injected intravenously with a suspension of silica particles before exposure to or during infection with S. mansoni. In rats treated in this way, the decline
in numbers of worms between week 4 and week 6 after infection was slower than in normal rats. Rats treated with silica also had higher worm recoveries at the fourth week of infection, indicating that susceptibility to infection was increased.

In rats maintained under treatment with anti-eosinophil serum from the third week of infection, spontaneous cure was inhibited to a marked degree. In one experiment, only 18% of the worm population was lost between weeks 4 and 6 in rats treated with anti-eosinophil serum while in control rats treated with normal rabbit serum, a loss of over 50% occurred within the same period.

The results of the present work show that spontaneous cure is due to a specific cell-mediated immune response. They also suggest that eosinophils are major effector cells of the immune process responsible for spontaneous cure. A possible role for macrophages in processes that increase susceptibility to infection and in spontaneous cure has also been indicated. From the evidence presented here and observations from other workers, it may be concluded that both non-permissiveness and spontaneous cure in rats infected with S. mansoni are immunological processes involving different effector mechanisms.