



IMMUNOLOGICAL RESPONSES TO ASCARIS LUMBRICOIDES

LINNAEUS, 1758 IN MAN AND EXPERIMENTAL

STATEMENT OF WORK ON WHICH THE THESIS IS BASED

ANIMALS

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This thesis is based entirely on my own work except for the assistance of those mentioned in the Acknowledgement.

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ABSTRACT

This study was undertaken with the objective of identifying the effector mechanism of the immune response effective in resistance, observed with repeated exposure to the nematode Ascaris lumbricoides and furthermore to elucidate the participation of immunological mechanisms in clinical and pathological manifestations of ascariasis. In order to achieve this in the first instance the pattern of immune response to oral infection of A lumbricoides was studied in both rabbits and Macaca sinica monkeys. From these experimental infections, it was clearly evident, that resistance to reinfection developed in the host to infestation with A lumbricoides as immune rabbits were able to withstand a dose otherwise lethal to the non immunes. This was further confirmed with parasitological studies, which showed inhibition of larval migration, and retardation of larval development, as manifestations of immunity in the immune animal. The effective immune response as well as the pathological manifestations, were seen to differ clearly with the type of exposure. With occasional re-exposure effective immune mechanism was seen to operate at the pulmonary level. Both the humoral immune response, and the histopathological studies, correlated well with the development of immunity in the lungs. The extensive exudation and haemorrhagic damage by the migrating larvae in the non immune animals, was contained by the cellular reaction in the immune, with a concomitant

appearance of serum ascaris specific precipitating and complement fixing antibodies. The precipitating reaction was active early during this period, particularly against the metabolic products of the larvae as seen by the positive circum larval precipitin test. Furthermore the participation of non lymphoid cells particularly the eosinophils was prominent in the lungs during larval migration in the immune animals. Hence it is highly probable that these pathological changes are immunologically initiated. Although the lung was an important site of immunity, the liver was not seen to play an active role in immunity to this nematode, as evidence of larval trapping and cellular reaction in this organ was minimal. With repeated exposure however, the infective larvae were seen to be shunted off at the intestine itself as very few larvae were recovered from the liver and lungs and further the pathological changes in these organs were also minimal. The antibody response too showed a change in nature, with a gradual waning off of precipitating antibodies, and the potentiation of complement fixing and homocytotropic antibodies. Analysis of the immune response in clinical presentations of ascariasis using this information, was found to correlate well with the experimental situation. Precipitins were helpful only in evaluating pulmonary ascariasis, where the circum larval precipitin reaction using L₃ larvae was found to be very promising. The complement fixing antibodies as detected by the conglutinating complement

to expel and prevent establishment of new worms, as a spontaneous absorption test, was informative only in intestinal ascariasis. Although the precipitin reaction was given by the IgM class of antibodies in macac monkeys, in the human sera this reaction was found to reside in the IgG class.

The most striking feature however was the greatly elevated serum IgE levels met with, in children with ascariasis. Significantly raised IgE levels were also seen in children exposed to A lumbricoides as opposed to low levels in control groups. Serum IgG antibodies were found to be within normal limits, whilst serum IgM levels were low, in ascariasis. Peripheral eosinophilia was not a regular feature in intestinal ascariasis, and the median level was within the upper limit of the normal value. Furthermore no correlation was seen between the eosinophil response and the serum IgE levels.

Ascariasis with pulmonary symptoms was seen to be an uncommon clinical presentation, as was acute surgical conditions associated with heavy worm loads. Both these situations could be expected with development of concomitant immunity with small worm loads as a manifestation of resistance under our climatic conditions where exposure to ascaris is continuous. The common clinical presentation of abdominal pain, could well be a clinical manifestation of the gut

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to expel and prevent establishment of new worms, as a spontaneous cure mechanism which is seen in many nematode infestations. This is probably mediated via the enhanced IgE response.

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