Induction of resistance to filarial infections

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Filarial infections may be due to a variety of nematodes, of which seven species use man as a definitive host. The infections are transmitted to the host by arthropod vectors of great diversity. Of these species, two lymphatic-dwelling parasites, *Wuchereria bancrofti* and *Brugia malayi*, and two cutaneous and tissue-migrating ones, *Onchocerca volvulus* and *Loa loa*, cause considerable pathology, often leading to elephantiasis of genitals and extremities, blindness, inflammation and eosinophilia.

According to the World Health Organization, about 300 million people in Asia, Africa and South America are infected with the lymphatic-dwelling parasites (largely with *W. bancrofti*), and another 50 million or so in Africa and South America are infected by *O. volvulus* and *L. loa* infections.

The increasing resistance seen in the vector to the conventional insecticides and the lack of safe and effective chemotherapy/prophylactic agents particularly active against invading larvae and adult forms contribute to the gravity of the problem. Therefore additional approaches are clearly warranted to develop methods for the control of this disease. For this purpose adequate knowledge of the biochemical pathways operating in the parasite and on the host–parasite interactions, particularly on the nature of immune responses of the host to the infection, is essential.

Owing to paucity of the human filarial parasite material, the biochemical studies have been largely concentrated on animal parasite species. There are several host–parasite models that have contributed to the meagre and rather scattered information available on the biochemistry of a few of these parasites. The parasite itself occurs in three developmental stages, namely microfilaria, infective larva and adult forms, and each may differ from the other in certain aspects of its metabolism. The adult worm *Litomosoides carinii*, which infects rodents, is known to be aerobic, whereas the other parasites *Dipetalonema viteae* and *Brugia pahangi*, which also infect rodents, can survive under anaerobic conditions. The larval forms of all these species depend on aerobic metabolism for motility. The last-mentioned two species are homolactate ferments and are deficient in pyruvate dehydrogenase (Middleton & Szaj, 1979). As in several helminths, compounds that inhibit phosphofructokinase threaten the survival of the parasites (Szaj & Dunbar, 1975).

Chen & Howell (1979) observed a transcuticular uptake and utilization of nutrients by infective larvae and adult stages of *B. pahangi*.

Jaffe & Chrin (1980) compared the properties of some enzymes of folate metabolism of *B. pahangi* and of mammalian sources, and reported several notable differences in their properties. Prasad *et al.* (1980) found that pyridoxine deficiency of the host was detrimental for the development of infective larve to the adult stage.

On the immunological front, a spectrum of responses is seen in the population to the filarial infections, ranging from marked resistance to total susceptibility. There was a depressed response to mitogens in the lymphocytes of infected animals and human patients, as revealed by a study of [3H]thymidine uptake. Detailed immunological investigations in rodent and human filariasis revealed that in immune subjects certain immunoglobulins (*Subrahmanyam et al.*, 1976; Mehta *et al.*, 1980, 1981) promote adherence of macrophages and neutrophils to the larval stages of the parasites, which results in their death. Furthermore, mitogens such as concanavalin A or soluble mediator(s) from lymphocytes that stimulate antibody–dependent cell-mediated adhesion. Addition of cytochalasin B or neutrophils pretreated with trypsin to the reaction medium abrogated the adhesion phenomenon. Several agents that inhibit glycolysis, the production or action of superoxide or peroxide, protein synthesis and pinocytosis had no effect on this phenomenon.

The cytotoxicity caused to the parasites subsequent to antibody-dependent cellular adhesion strongly suggests the presence of functional antigens on the parasite surface. Identification and isolation of these antigens seem to be essential for inducing resistance against filarial infections.

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Surface chemistry of nematodes

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