

MODELOS EXPERIMENTAIS

EXPERIMENTAL MODELS

PATOLOGIA

PATHOLOGY

DIVERSOS

MISCELLANEOUS

MP

CONTRIBUTIONS AT IMMUNOPATHOLOGIC STUDY IN *HOLOCHILUS BRASILIENSIS NANUS*
THOMAS, 1987

MP-1

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Wild rodents *Holochilus brasiliensis nanus* were infected with *Schistosoma mansoni* isolated from a human patient from the lower land region of the State of Maranhão-Brazil. Sera were taken weekly for anti-schistosoma antibodies and immunoglobulins dosage. The rodents were sacrificed and perfused 60 days after infection. The principal parasitized organs (liver and intestines) were fixed in 10% formalin and processed for histopathological study. High titers of IgG, IgM and IgA specific antibodies were detected by indirect immunofluorescence tests. High levels of IgG2a, IgM and IgA were also detected by radial immunodiffusion method. These data indicate that the *Holochilus* respond to *Schistosoma* infection with high levels of the three principal classes of antibodies. The histopathological study showed periovular granulomatous reactions of exudative and fibrous type in liver and intestine. In the mucous membrane of intestine the periovular lesions were predominantly of the exudative type with large number of eosinophils (micro abscess). In the muscular and in the serous membrane of the intestine the granulomas were of the proliferative and fibrous type suggesting a sequestration mechanism.

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EXPERIMENTAL SCHISTOSOMIASIS IN *CALLITHRIX JACCHUS*. A
HISTOPATHOLOGIC STUDY

MP-2

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Four common marmosets (*Callithrix jacchus*) were infected with a local strain (SLM) of *S. mansoni* isolated from pigmented *B. glabrata*. The animals were exposed, two subcutaneously and two percutaneously to 150 cercariae. Independently of the route used, worms were found within the portal system. Sixty days after the infection, many hepatic periovular granulomas were detected. On the 80th day, fibrosis surrounding the hepatic granulomas was observed. We consider these to be promising results and intend to more fully study the host-parasite relationship in this experimental model.

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MP-3

THE BABOON AS A MODEL FOR ACUTE SCHISTOSOMIASIS

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Acute schistosomiasis (AS) is a syndrome that may follow exposure to the cercariae of human schistosomes. Many questions about AS remain unanswered, including etiology, factors governing its occurrence and severity, and treatment. The lack of well-defined animal models has hampered progress on AS. We have, during years of experience with experimental schistosomiasis mansoni in baboons, gathered data that supports the conclusion that this species develops AS after exposure to *S. mansoni* cercariae. Among the symptoms observed are diarrhea, hematochezia, anorexia, and cachexia. We have also lost several baboons during the acute phase. Among the signs of AS which we have recorded are cercarial dermatitis, transient eosinophilia, elevated SGOT during both preoviposition and postoviposition times, and hypergammaglobulinemia. In addition, there is close correspondence between human and baboon in many other immunological correlates of AS, including antibody production, antigen specific lymphocyte transformation, and granulomas, both *in vivo* and *in vitro*. We therefore suggest that the baboon is a good model for the study of human AS.

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MP-4

BEHAVIOUR OF ISOLATES OF *SCHISTOSOMA MANSONI* IN MICE
OBTAINED FROM PATIENTS WITH DIFFERENT CLINICAL FORMS

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Twenty isolates of *Schistosoma mansoni* were obtained from 6 patients with Schistosome -infections (type I), 6 with the hepato-intestinal (type II), and 8 with the hepatoesplenic (type III) forms. Each isolate was inoculated in mice divided in three groups of 16, exposed to 25, 50 and 100 cercariae, respectively. Controls were 12 uninfected mice. Mice were studied on the 90th and the 180th according to the following parameters: 1) weight of liver, spleen, lung and intestine; 2) histopathological study; 3) egg count in the small intestine (proximal and medial) and large intestine (distal); 4) classification, counting and measuring the diameters of granulomas in liver and counting in lung, spleen and intestine. There was no correlation between the clinical forms of schistosomiasis and the behaviour of the isolates of *S. mansoni* in mice, the parasitological and histopathological alterations being only proportional to the inoculum used and the duration of the infection.

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ULTRASTRUCTURAL CYTOCHEMISTRY IN THE LIVER OF MICE FED THE REGIONAL BASIC DIET OF ENDEMIC AREAS OF SCHISTOSOMIASIS MANSONI IN NORTHEASTERN BRAZIL

MP-5

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The effects of the Regional Basic Diet (RBD) on the liver of albino mice was studied in a previous paper, using the transmission electron microscopy. An ultrastructural cytochemical investigation has been pursued on the lipid inclusions, glycogen content and peroxisomes morphology and distribution in the liver of RBD-mice, which were compared with those fed a 23% casein diet (controls). Animals were killed at 30, 42, 66, 86 and 120 days of dietary intake. Lipid inclusions, stained by the imidazol technique, were abundant in RBD mice, reaching its peak around 66 days of dietary intake, and decreasing in number late on. Small vesicles of smooth endoplasmic reticulum (SER) could be seen near lipid droplets. The glycogen, stained by the Thiéry's technique, presented mainly as collections of particles forming rosettes (alpha particles) with a diffuse cytoplasmic distribution and a higher concentration around lipid droplets. Glycogen concentration was unchanged throughout the experiment. Peroxisomal catalase was detected after incubation in a diaminobenzidine (DAB) containing medium. The overall percentage of these organelles increased from 42 days of dietary intake on, and in the control group, after 86 days of diet consumption. These data suggest the importance of these organelles in the lipid synthesis and fatty acid degradation in the liver.

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LIVER INJURY IN MICE FED THE REGIONAL BASIC DIET OF ENDEMIC AREAS OF SCHISTOSOMIASIS MANSONI IN NORTHEASTERN BRAZIL: AN ELECTRON MICROSCOPIC STUDY

MP-6

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Previous papers demonstrated that the Regional Basic Diet (RBD), a food association (beans, manioc flour, sun-dried meat and sweet potatoes) ingested usually by human populations of endemic areas of Schistosomiasis mansoni in Northeast Brazil, has negative effects on the growth, food intake and protein utilization of mice infected with *S. mansoni*, liver lesions being detected by light microscopy. The present experimental model reproduces the marasmatic form of protein-energy malnutrition. The transmission electron microscopy was used to study the hepatic lesions which were compared to those in mice fed a 23% casein diet. Animals were sacrificed at 30, 42, 66 and 86 days of RBD intake. Numerous lipid inclusions in the cytoplasm of the hepatocytes, abundant mitochondria with lamellar and/or tubular cristae, eventual pyknotic mitochondrial forms, curved profiles of RER encircling mitochondria and focal areas of hyperplasia of the SER in the neighbourhood of areas of higher lipid droplets concentration were detected in the RBD-fed mice. Based upon present results one could speculate about some of the liver alterations occurring in *S. mansoni* infected patients as being ascribed to malnutrition.

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MP-7

INFLUENCE OF COLCHICINE ON SCHISTOSOMAL GRANULOMA FIBROSIS.

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Amorphous material and altered collagen fragments within dilated secretory vesicles and cisternae of fibroblast cytoplasm were the main ultrastructural changes seen in hepatic periovular granulomas formed in mice infected with *Schistosoma mansoni* and treated with colchicine. Despite promoting ultrastructural changes in the fibroblasts found in hepatic periovular granulomas colchicine administration of infected mice did not significantly change the light microscopic appearance of the hepatic schistosomal lesions, did not diminish the amount of total hepatic collagen, and did not change the collagen isotypes in the granulomas, as observed after a comparative study with non-colchicine treated infected control mice. When administered to mice two weeks after curative treatment of schistosomiasis with Praziquantel, colchicine did not seem to increase extra-cellular collagen degradation or to induce a more rapid resorption of hepatic periovular granulomas, although still producing the ultrastructural alterations in fibroblasts.

MP-8

**THE LUNG PHASE IS NOT NECESSARY FOR THE DEVELOPMENT OF
SCHISTOSOMA MANSONI IN AKR/J MICE**

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The life-cycle of *Schistosoma mansoni* in the vertebrate host presents a lung phase, which has been questioned for its real importance to the parasite development. In this study, 0,5 ml of well water containing about 200 *S. mansoni* cercariae were inoculated into the peritoneal cavity of AKR/J albino mice. Adult worms were recovered from that site 60 days after. The degree of development of the parasite was evaluated through microscopical observations. The recovered worms reached sexual maturity, females presenting eggs in their uterus and mature and viable eggs were found in the peritoneal fluid. The results show that lung phase is not necessary for the development of the parasite. Migration of inoculated larvae from the lungs to the peritoneal cavity is most unlikely to occur, since this worm is only found in the peritoneal cavity when larvae are previously injected into that site.

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VIABILITY OF *SCHISTOSOMA MANSONI* EGGS PRODUCED BY WORMS
FROM THE PERITONEAL CAVITY OF AKR/J MICE.

MP-9

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The development of *S. mansoni* may be obtained in the peritoneal cavity of vertebrate host by injecting cercariae directly into that site. In most animals this development is limited to a few days or may be prolonged enough to produce adult worms, usually smaller, laying few or no eggs at all. Inversely, the worms in the peritoneal cavity of AKR/J mice are more likely those from the portal system, eggs being produced in larger numbers, some of them surrounded by a granuloma that remains unattached to the tissues, freely floating in the peritoneal fluid. The viability of miracidia from eggs contained in these granulomas was verified through experimental infection of *Biomphalaria glabrata*. Thirty days after infection, the snails shed cercariae of normal appearance, able to infect both mice and hamsters. These rodents passed viable eggs through the faeces. The main conclusion is that eggs from free floating granulomas from worms developed in the peritoneal cavity of AKR/J mice are fertile and able to lead the subsequent life cycle in snails and afterwards in vertebrate hosts.

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SCHISTOSOMA MANSONI - N.Z. RABBIT: MIGRATION TRACKED BY
AUTORADIOGRAPHIC ANALYSIS

MP-10

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26 naive rabbits infected simultaneously route with L-(⁷⁵Se) Selenomethionine-labelled cercariae were sacrificed (2 animals day) 1, 2, 4, 6, 8, 10, 15, 20, 25, 30, 40 and 50 days after infection for obtention of skin lung liver and mesentery. Autoradiographic foci were detected from the 1st day in the skin up to the 15th day in the liver. Adult worms were recovered at the 60th day post infection by perfusion of hepatic and mesenteric veins. The results clearly demonstrated the peak of parasites in the skin and lungs as the post liver phase of *S. mansoni* life cycle in rabbits.