MECHANISM OF RESISTANCE TO SCHISTOSOMIASIS INDUCED BY NORMAL AND IRRADIATED CERCARIAE

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A variety of nuclear techniques were utilized to analyze resistance to Schistosoma mansoni in inbred rats, previously exposed to normal and highly irradiated (30 k rads - ^{60}Co) cercariae.

A number of observations are germaine:

1. The initial migratory kinetics of the parasite appear to be highly analogous to those in the mouse. Irradiation alters the initial aspects of that migratory pattern less than it affects later aspects.

2. The inbred rat develops a strong resistance following exposure to irradiated cercariae. Indeed, resistance is actually superior when the irradiated cercariae are utilized as opposed to normal cercariae. As such, these findings are wholly compatible with observations in the mouse.

3. The rat apparently manifests increased resistance in several anatomic sites: skin, perhaps lung, and liver. As such, the pattern of augmented resistance may differ from that usually described in the mouse wherein irradiated cercariae may lead preferentially to an augmentation of resistance at an earlier stage of development in comparison with that induced by normal cercariae.

4. A reason for the augmented immunological resistance may be that the irradiated cercariae deliver significantly greater quantities of biologically relevant schistosome antigens over more prolonged periods of time and more effectively stimulate T-dependent resistance mechanisms. Antigens disappear less rapidly from the parasite and can be detected for longer periods of time in the thoracic duct and the blood of the exposed recipient. T-cell activation is greater with irradiated cercariae. In addition, the parasite itself demonstrates an altered migratory pattern, reaching the lung later and residing longer there. Since the first site of immunologically mediated resistance occurs in the lung, this anatomic site may be extremely important in the production of protective immunity. In situ release of antigens may lead to a more prolonged effective stimulation.

5. Finally, radiation may alter the qualitative nature of antigenic presentation as well. Preliminary evidence would indicate that although total antigenic mass may be less in irradiated parasites, the salience of unique epitopes related to resistance may be greater. With specific reference to this issue, an epitope specifically recognized by a protecting monoclonal antibody is especially prominant in the membrane antigenic array of irradiated schistosomula.

These studies suggest that it is feasible to use combined radiobiologic and immunological techniques to ascertain the nature of resistance mechanisms.

STIMULATION OF PROTECTIVE IgA RESPONSES IN THE INTESTINE

Nathaniel F. Pierce

Secretory IgA (sIgA) antibodies, produced by plasma cells in the intestinal lamina propria, are a major means of protection against bacterial and viral infections of the gut. Such antibodies arise after naturally occurring enteric infections and may mediate lasting immunity. It is likely that vaccines designed to prevent enteric infections must evoke intestinal sIgA antibodies if lasting protection is to be achieved. An understanding of how protective sIgA responses are best stimulated may guide the development of such vaccines.

The route of antigen delivery, the form in which antigen is delivered, and the variety of antigens used, each determine the effectiveness of enteric immunization. The mucosal sIgA response is best stimulated by locally applied antigen, which is transferred from the gut lumen to mucosal lymphoid follicles, e.g. Peyer's patches, where IgA B cells arise; parenteral immunization stimulates mucosal sIgA responses inefficiently, if at all, and may actually suppress such responses. Most nonliving antigens evoke enteric sIgA responses inefficiently when given orally, numerous doses being required. However, some antigens, such as cholera toxin, are highly efficient; and adjuvants may be devised that improve the immunogenicity of other antigens. In contrast to nonliving antigens, viable organisms are very efficient mucosal immunogens. This may be because intact organisms are efficiently transported to mucosal lymphoid tissue for stimulation of IgA responses. Finally, sIgA-mediated antibacterial immunity is most efficient when antibodies directed against several bacterial virulence antigens are evoked. Such antibodies can act synergistically by interfering with separate events in the pathogenesis of mucosal infection.

Although few oral vaccines are presently available which safely reproduce the immunizing effect of naturally occurring enteric infections, present experimental evidence suggests that effective oral vaccines can be developed. These will likely involve either selected combinations of nonliving antigens, possibly delivered with adjuvants, or viable avirulent mutant organisms that retain antigens capable of evoking protective sIgA responses.

ECOLOGICAL CHARACTERIZATION OF HOST SNAILS HABITATS IN ENDEMIC AREAS OF SCHISTOSOMIASIS IN NORTH-EAST BRAZIL

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An account is given of an ecological investigation of freshwater habitats in N.E. Brazil, which was designed to identify and evaluate key environmental factors which might serve as indicators for the presence of the host-snails of schistosomiasis as well as those which might be manipulated to exclude or control them. The two areas selected for study, namely Pontezinha in Pernambuco State, and Alhandra in Paraiba State, provide good examples of urban and rural transmission sites respectively.

The studies, which were carried out at the begining and end of the rainy season, in both cases, involved the measurements of key physiochemical parameters, the recording of plant species, and relative estimates of the population densities of snail species (catch per unit time) in 42 and 15 predominantly lotic sites at Pontezinha and Alhandra respectively. Contiguous quadrat sampling was also carried out in selected sites.

The results make it possible to draw the following conclusions: (i) There were no significant differences in the estimates of relative snail densities made at the begining and end of the rainy season in either of the two study areas. (ii) Calcium hardness showed a positive statistically significant linear relationship with the relative estimates of snail densities. However, none of the following physiochemical factors showed any statistically significant relationship with the estimates of relative snail densities: alkalinity, carbon dioxide, total iron, ammonia, silica, sulphate, specific conductance, magnesium hardness, percentage oxygen saturation, pH and turbidity. (iii)There was a statistically significant tendency for snails to be found on depositing rather than on eroding type substrates. (iv) There were statistically significant tendencies for host snails to be positively associated with Cyperus spp. and to be negatively associated with Amaranthus spp., but no significant positive or negative associations were found between the occurence of snails and the other 30 genera or species of macrophytes found in the sampling sites.

The ecological significance of the results and their implications to biological and environmental control strategies will be discussed.

BANCROFTIAN FILARIASIS IN MAYOTTE: ASSESSMENT OF SURVEY AND CONTROL METHODS

Gaston Pichon.
Jean Mouchet

1) Detection rate :

Negative Binomial fits much better the pattern of microfilarial (mf) counts than Log-normal distribution does. This allows a nomogram relating different epidemetrons to be constructed. For a given focus, the detection rate and the optimal volume of the blood sample can be easily derived from the Dmf-50.

2) D.E.C. provocation test (D.P.T.) :

On village-scale, the classical nocturnal blood-sampling was compared to the D.P.T. The mf counts from both methods were highly correlated, but the D.P.T. was poorly sensitive, and was not representative of the real pattern of the parasitic reservoir.

3) Delayed treatment strategy :

In Polynesia, Laigret (1978) showed that a yearly D.E.C. dose was enough to reach a 50-percent reduction of the mf index. Trials in several Mahorese villages resulted in a complete failure of this method : ten months after the mass drug administration, neither the mf index nor the Dmf-50 were modified. This discrepancy is explained by the long history of intensive filariasis control in Polynesia. This strategy does not seem to be appropriate to a "virgin" focus.

EVALUATION OF MUTANT V. CHOLERAE AS LIVE ORAL VACCINES IN ADULT RABBITS

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Mutant strains of V. cholerae have been developed in several laboratories for possible use as live oral cholera vaccines. Both chemical mutagenesis and recombinant DNA techniques have been used to create strains that are either A^-B^- or A^-B^+ with regard to synthesis of cholera toxin subunits. To evaluate the effectiveness of these strains as live enteric vaccines, we have studied their relative ability to colonize and immunize the small intestine of adult rabbits. Mutant strains and their virulent parents were studied quantitatively for their ability to colonize unobstructed intestine, evoke resistance to recolonization with virulent strains, immunize against cholera-like diarrhea caused by virulent challenge using the RITARD technique, and evoke mucosal antitoxin responses. The results show that, 1) the efficiency of intestinal colonization was: virulent strains > A^-B^- or A^-B^+ gene-deletion mutants >> a chemically induced mutant, 2) a single small inoculum (i.e. < 100 cfu) of virulent V. cholerae or a gene deletion mutant evoked marked resistance to attempted recolonization, 3) A^-B^+ gene deletion mutants evoked mucosal antitoxin responses much less efficiently than did a virulent A^+B^+ strain, and 4) a virulent A^+B^+ strain more efficiently protected rabbits against RITARD challenge than did an A^-B^- gene-deletion mutant. These results show that V. cholerae, specifically deleted of genes which regulate toxin synthesis, colonize and immunize rabbit intestine less efficiently than do their fully virulent parental strains; a chemically induced mutant was even less effective. The rabbit models used in these studies appear well suited for detailed evaluation of mutant V. cholerae or oral vaccines.

PROSPECTS FOR PRACTICAL APPLICATION OF BIOLOGICAL CONTROL

J. S. Pillai

From the earliest days effective vector control depended upon the successful intergration of insecticides, environmental sanitation, methods to reduce vector/man contact and where possible the use of larvivorous fish. In the 1950's with the introduction of DDT and other toxic chemicals, insecticides assumed the dominant role. However, the development of vector resistance, the dislocations to the environment coupled with an escalation of the costs of the chemicals themselves created serious difficulties to IVC strategies which relied heavily on the use of insecticides. This has brought about a new appreciation of the role of biocontrol agents even though the number available for operational use is limited. However, recent progress in developing the spore-forming bacterium Bacillus thuringiensis serotype 14 (B.t. H-14) as a biolarvicide constitute an important advance. B.t. H-14 produces a crystalline delta endotoxin which is specifically toxic to mosquito and blackfly larvae. It is now used very extensively in the West African Onchocerciasis Control Programme where the Simulid vector has developed resistance to the chemical Temephos(R) Insecticidal formulations of the bacterium are now being produced for vector control programmes by commercial and governmental organizations in many parts of the world.

Some strains of another spore-forming bacterium Bacillus sphaericus have also been found to be toxic to mosquito larvae especially to Culex quinquefasciatus which breeds in polluted waters and is a vector of human filariasis world wide. There are high hopes that suitable formulations of the pesticide will soon be available for operational use.

Other potential microbial agents include representatives of Fungi, Protozoa and Nematodes. Macrobial agents are also important e.g. larvivorous fish and the predatory Toxorhynchites, or competitive snail for the replacement of the snail hosts of Schistosomaisis. Insect parasitoids could play a significant role against vectors of Sleeping Sickness in Africa, Chagas' Disease in S.America or Leishmaniasis in Asia. Selected examples of biocontrol agents and their potential for vector control will be discussed.

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