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NEW APPROACHES FOR THE CONTROL AND ERADICATION OF SCHISTOSOMIASIS IN VENEZUELA

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Schistosomiasis in America with the exception of Brazil, behaves as a chronic mild disease with few clinical manifestations due to low parasite burden. These features restrict the clinical and parasitological diagnosis. The most commonly used stool examination method, Kato-Katz, becomes insensitive when the majority of individuals excrete less than 100 eggs/g of feces. In view that antigen-detecting techniques have hot been able to reveal light infections, the antibody detecting assays remain as a very valuable diagnostic tool for epidemiological surveillance. The Venezuelan Schistosomiasis Research Group (CECOICE) has designed a mass chemotheraphy strategy based on sero-diagnosis. Since blood sampling is one of the important limitating factors for large seroepidemiological trials we developed a simple capillary technique that successfully overcomed most of the limitations of blood drawing. In this sense, ELISA seems to be the most adecuate test for epidemiological studies. Soluble egg Schistosoma mansoni *antigen (SEA) has been largely used in Venezuela. The sensitivity of ELISA-SEA in our hands is 90%, moreover its specificity reach 92% when populations from non-endemic areas but heavily infected with other intestinal parasites are analyzed.*

The Schistosomiasis Control Program is currently carrying out the surveillance of endemic areas using ELISA-SEA as the first screening method, followed by the Circumoval Precipitin test for validation assay. The results with these two serological techniques allowed us to defined the criteria of chemotherapy in populations of the endemic areas. On the search of better diagnostic technique, Alkaline Phosphatase Immunoenzyme Assay (APIA) is being evaluated in field surveys.

Key words: schistosomiasis – control

With the exception of Brazil, schistosomiasis in America behaves as a mild disease with few clinical manifestations due to low parasite burden. This is the case for Puerto Rico (Hiatt et al., 1980), Guadeloupe (Tribouly et al., 1975; INSERM, 1980), Santa Lucia (Doumenge et al., 1987), Dominican Republic (Doumenge et al., 1987) and Venezuela (Alarcón de Noya et al., 1987).

A low parasite load has probably been one of the reasons why schistosomiasis have not been eradicated from these countries. *Schistosoma mansoni* infected populations are often not aware of the occurrence of the disease, mainly because its symptoms are vague or non-specific. Clinical detection and parasitological diagnosis are hampered by the low excretion of eggs in the stools.

Since the beginings of the anti-Bilharzian campaing in Venezuela, the Control Program has relied on the traditional stool examination method of Kato as the only diagnostic method (Kato & Miura, 1954). On the other hand, control measures were mainly based on the chemical elimination of snails, sanitary education, improvement of sanitation and water supplies. These measures considerably reduced the infection in our country. However, during the last years several studies in the endemic area indicate that transmission continues to occur in Venezuela (Balzan, 1988). At the present time, there exists an increased risk of disease transmission, due to the adaptation of

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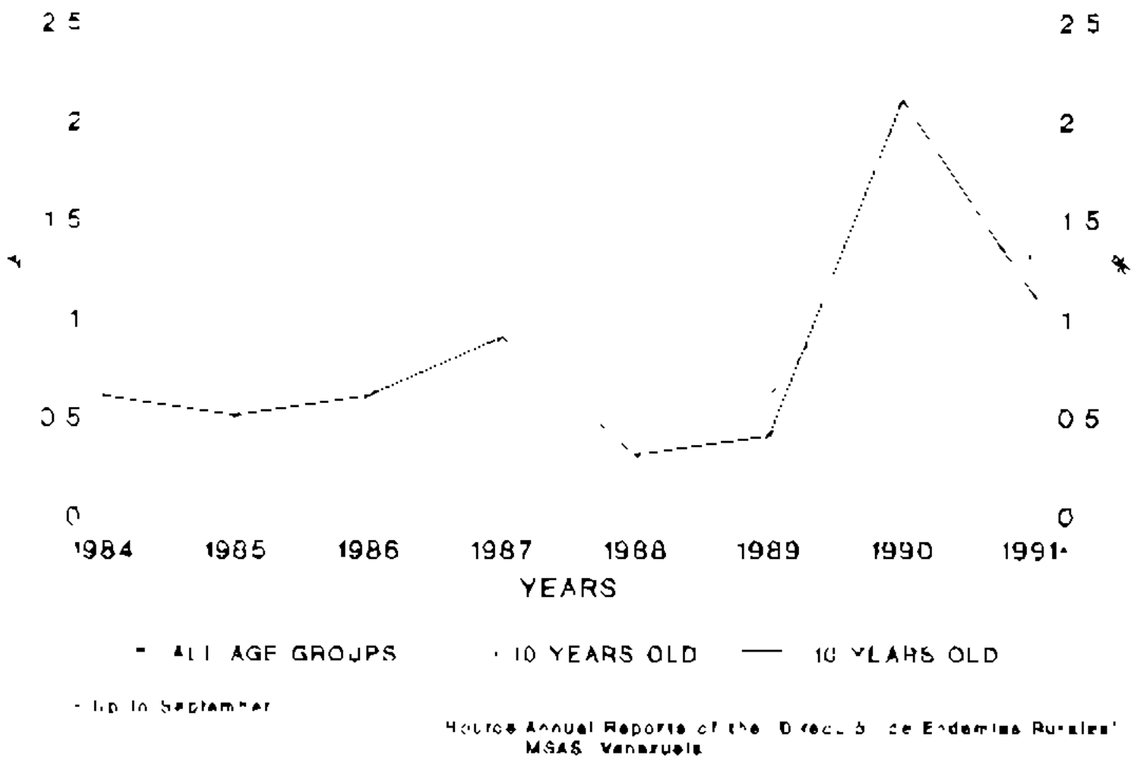
Biomphalaria glabrata to sub-urban areas (Alarcón de Noya et al., 1987) and its detection out of the traditional endemic area (Balzan, 1988).

Since 1984, important and deleterious social, economic and sanitary changes have occurred in the country. Of relevance is the fact that most of the growing nation factories are sited in the endemic area and have attracted a large number of people of low economic, cultural and sanitary conditions, who have invaded large sub-urban areas with water bodies and streams harbouring *B. glabrata*. This situation is particularly critical in suburbs of Valencia, Maracay and La Victoria, where it has being observed the infection of large wards for instance, Barrio Bicentenario in Valencia. High prevalence with low parasite burden characterizes now the general schistosomiasis situation in the endemic area. It is important to notice the steady increase of prevalence in children since 1989, suggesting an active schistosomiasis transmission (Fig. 1).



SCHISTOSOMIASIS RESEARCH GROUP

Since 1983, the members of the Venezuelan Schistosomiasis Research Group (SRG) (Incani, 1987) join the Control Program in a collaborative effort to eradicate schistosomiasis. Thereafter, the authorities of the Venezuelan Ministry of Health proposed them to the President of the country as Advisors of the Control Program.

Eradication of schistosomiasis in Venezuela appears feasible since the endemic area is relatively small and far away of the schistosomiasis foci of the neighboring countries (Noya, 1991). In order to assess the impact of the Program, the SRG advised that alongside to the classical stool examination, additionally use serologic techniques for this ambitious aim, since coprological methods alone underestimate the prevalence of infection.

From that time on, a change in the strategy of control was initiated, giving a new emphasis to systematic diagnosis and mass chemotherapy. Some teaching and training activities were however, required before starting the joint effort.

At this time, it is convenient to point out the activities currently carried out by the SRG: (1) Training of laboratory technicians from the Ministry of Health as specialized personnel of the diagnostic centers in each state of the endemic area. This training has been oriented to: (a) Maintenance of the parasite life cycle in the laboratory to obtain parasites for antigen production; (b) Processing and analysis of serum samples by ELISA. (2) Training of official rural visitors and sanitary inspectors in blood drawing using a new capillary technique (Noya et al., 1989) and venipuncture. This personnel is responsable for surveillance of vector molluscs in water bodies and streams, as well as for feces and blood sample collection. (3) Joint field-work. In some occasions, members of the SRG and Control Program personnel work together in specific transmission sites that have been previously screened as indicated later in this article. Complete journeys for sample collection, clinical examination and treatment are usually carried out. (4) Continuous re-evaluation of the clinical characteristics of *S. mansoni*-infected patients from the endemic area (Alarcón de Noya et al., 1987; Noya & Alarcón de Noya, 1988). (5) Validation of *S. mansoni* adult worm Alkaline Phosphatase Immunoassay (APIA) (Pujol et al., 1989) in the diagnostic centers. (6) Biological measures for snail control. Research in this area has been oriented mainly toward the use of competitors snails like *Thiara granifera* (Pointier et al., 1992) and more recently, the use of plant molluscicides (*Phytolaca octandra*). (7) Adquisition of laboratory equipment for the diagnostic centers including computers for complete informatization of the data. All the information regarding water bodies, streams and localities, as well as the forms used by the Control Program, are currently being codified.

EVALUATION OF SEROLOGICAL METHODS

The SRG has studied some communities in order to validate the sensitivity and specificity of the COPT, ELISA and APIA.

The evaluation of 138 *S. mansoni*-infected persons from Caraballeda, D. F., with eggs in the stools (88% of them with less than 100 eggs/gr of feces) revealed that the mean sensitivity of COPT was 95.6% for all age groups, while the sensitivity by ELISA-SEA was 86% (Alarcón de Noya, 1988). In parallel, studying 81 persons from a Valencia ward (Bicentenario), the prevalence by stool examination (three Kato per person) was 10%, by ELISA-SEA 62% and by COPT 42%. These results evidence the discrepancy of sensitivity between the stool examination and the serological tests in populations with low parasitic burden. The COPT is usually taken to reflect active schistosome infection (Romero, 1962; Hillier et al., 1979; Mott & Dixon, 1982). On the other hand, ELISA-SEA is probably overestimating the prevalence because it includes active cases, cases that were cured but still show antibodies detected by ELISA (Alarcón de Noya, 1988) and false positives by cross reactivity with other intestinal parasites (Correa-Oliveira et al., 1988).

To validate the specificity of COPT as well as that of ELISA-SEA and APIA, we analyzed 407 sera from an isolated community far away from the endemic area. Stools samples were all negative for *S. mansoni* but the frequency of intestinal poliparasitism was very high. ELISA-SEA was negative in all but in 42 persons (10.3%) strengthening previous results on cross-reactivity with other intestinal parasites in ELISA-SEA. However, COPT and APIA were negative in this latter group, demonstrating the high specificity of these two test (manuscript in preparation).

Although ELISA-SEA overestimated the number of active infection prevalence, it is the most useful test for mass surveillance. The COPT is an excellent test but it is time consuming, cumbersome and can only be carried out when biological material is available, preferably fresh. As for APIA, it should continue to be tested in the field to assess how it behaves in different communities.

NEW APPROACHES TO ERADICATION STRATEGY

Chemotherapy in Venezuela had been aplied only to infected persons who were detected by stool examination. The new strategy of control based on mass chemotherapy necessarily have to depend on reliable diagnosis tests. The guidelines of control established by the WHO, rest upon the prevalence of schistosomiasis determined by stool examination (WHO, 1985).

In Venezuela, contrary to other latitudes, coprological methods alone are no more suitable to our specific epidemiological conditions. Therefore, the SRG has proposed to the Ministry of Health the following strategy (Fig. 2):

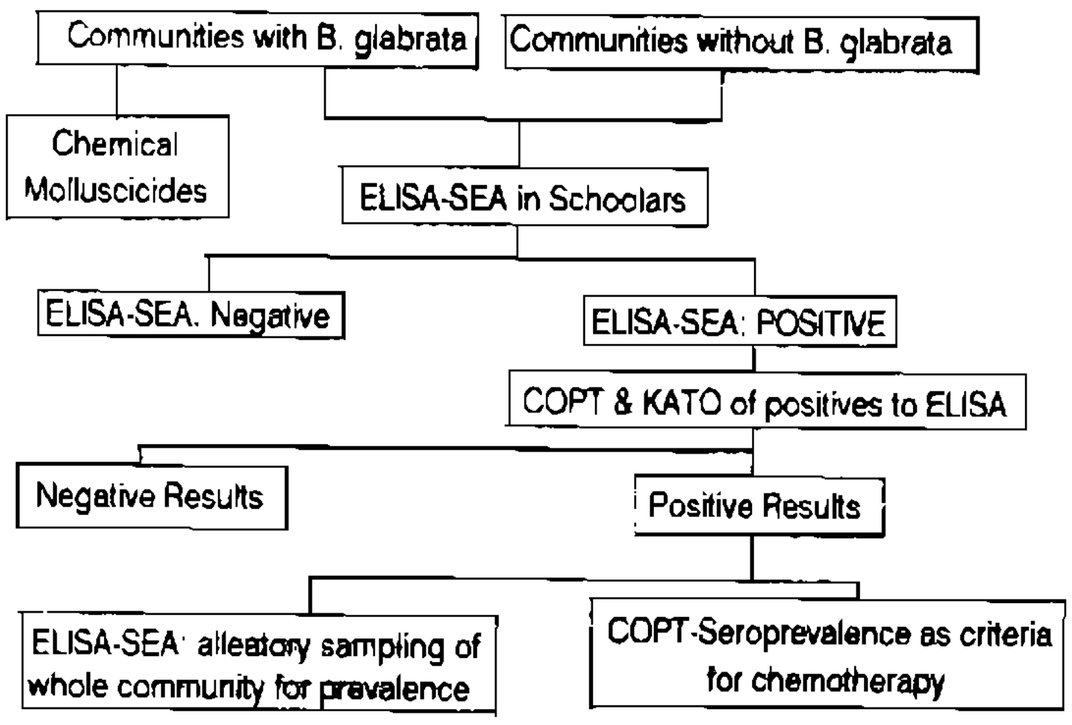


Fig. 2: algorithm in the diagnosis and control of schistosomiasis in Venezuela.

1. Activities to be performed in communities with water bodies and streams with *B. glabrata.*

1.1. Focal application of chemical molluscicides.

1.2. Capillary sampling to children at 1st, 3rd and 6th elementary school grades, and ELISA analysis with Soluble Egg Antigen (ELISA-SEA) (Spencer et al., 1991).

1.2.1. If ELISA-SEA results are negative, do not continue evaluation.

1.2.2. If ELISA-SEA is positive:

1.2.2.1. Validation of active *S. mansoni* infection with Kato-Katz (Katz et al., 1972) and Circumoval Precipitin Test (COPT) (Oliver-Gonzalez, 1954) with sera obtain by venipuncture of those children positive by ELISA-SEA.

1.2.2.2. In case of COPT positive results, perform aleatory capillary sampling to the whole village and analysis by ELISA-SEA, for establishment of sero-prevalence of each area of prevalence.

1.2.2.3. Under special circunstances, when the impact of chemotherapy want to be assessed, aleatory venous blood samples must be taken in order to compare later on with COPT.

2. Activities to be perform in communities of the endemic areas with water bodies and streams without *B. glabrata.*

2.1. Sampling to school children as in 1.2.

With this information, we should establish the criteria of mass chemotherapy according to the guidelines recommended by WHO but using serology as the diagnostic method (Fig. 3).

Developing criteria for mass-chemotherapy based on serology in Venezuela

All treatments will be done with Praziquantel at 40 mg/kg body weight and the guideline would be the following (Fig. 3):

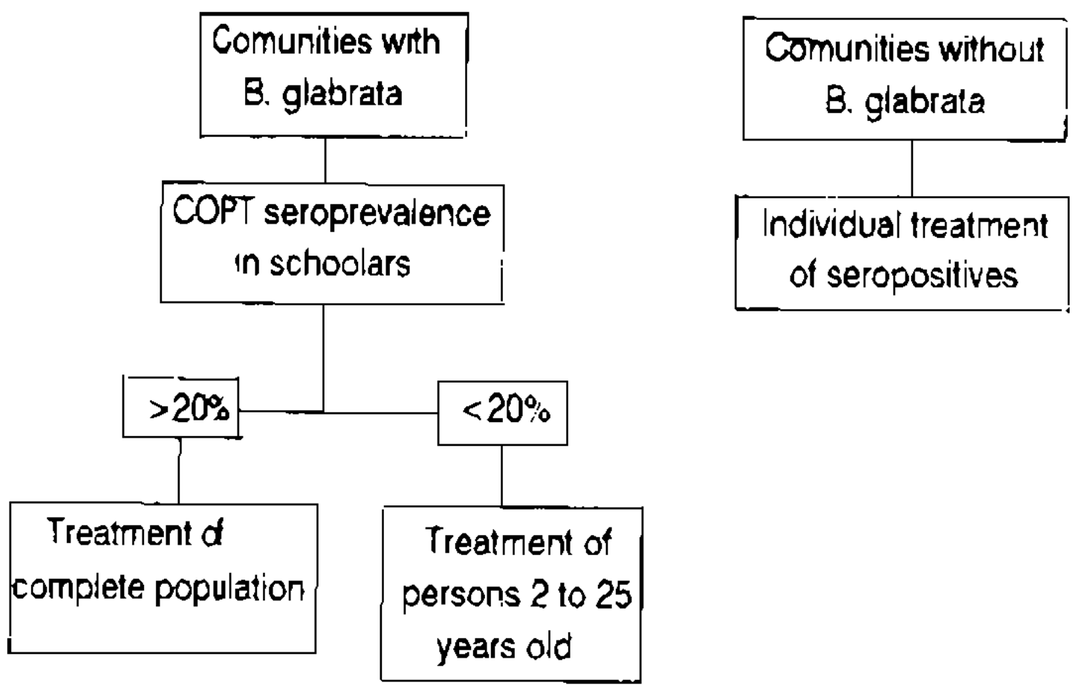


Fig. 3: criteria for chemotherapy as control measure, based on seroprevalence in Venezuela.

1. Communities with water bodies with *B. glabrata.*

1.1. When the sero-prevalence for COPT from the school children is higher than 20%, the whole community will be treated.

1.2. When the COPT sero-prevalence of schoolars is less than 20%, the treatment will be given to all people between 2 and 25 years old.

2. For endemic areas with water bodies and streams without *B. glabrata.*

Individual treatment to positive persons only.

FINAL REMARKS

There has been a great deal of discussion in relation to the sanitary structures that might be organized in developing countries for control of schistosomiasis and other widely distributed parasitic diseases.

In Venezuela, the proposition of incorporation of diagnosis and treatment for schistosomiasis to the primary healt care services (Gryseels, 1989; Tanner, 1989) has not been followed mainly because of the success of the Control Program in pursuing the eradication of this and other parasitic diseases. Furthermore, the primary health care services are conducted in our country by young physicians that stay for not longer than a year in rural schistosomiasis endemic areas. Although our medical rural network is adecuate, this structure has not played an important role in the clinical diagnosis of the disease, even in communities of high transmission as in Caraballeda, (Alarcón de Noya et al., 1987). Moreover, at the present time, it is not feasible to clinically diagnose the asymptomatic cases, which are the majority in Venezuela.

For countries with similar epidemiological situation, especially related to the low parasite burden, low prevalence and small area of transmission, an integrated vertical local strategy might give better results. That is: epidemiological surveillance, moluscicide application, sampling collection and mass chemotherapy, all depending on the Control Program; elaboration of antigens, diagnostic assays, quality control, training and adviser activities by a SRG.

We probably have the advantage that the Control Program is composed by various dependances such as vector control, engineering, sanitary education, water supplies, letrine construction, rural housing, so it is easy to understand that a well planified schedule may reach good results if bureaucratization is avoided.

The vertical program necessarely must pursue the progressive integration with the health services and the participation of the community for a more efficient economic and lasting control program. Therefore, social researchers and anthropologists must be incorporated to SRG with the objective of search the population attitudes to the disease and to the control program.

As it has been stated before, eradication or even reduction of transmission by chemotherapy alone, seems to be very difficult to achieve (Gryseels, 1989). If eradication is the objective, we suggest the application of moluscicides before mass chemotherapy, in order to prevent the

reinfection of children, who are the most important source of transmission, even in countries with low rate of infection.

Finally, only a multidisciplinary approach will be the most rational way to eradicate this complex parasitic disease.

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