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SCHISTOSOMIASIS IN THE AMERICAS

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SCHISTOSOMIASIS IN THE AMERICAS*

INTRODUCTION

In the preparation of this document, devoted to the problems of schistosomiasis in the Americas, an effort has been made to avoid repeating the description of the work done by four study groups of the World Health Organization reported in the following publications:

1) Scientific Group on Research in Bilharziasis: Molluscicides, February, 1959.
2) Scientific Group on Research in Bilharziasis: Chemotherapy, October, 1959.
3) Scientific Group on Research in Bilharziasis: Assessment of Medical and Public Health Importance, July, 1960.
4) Scientific Group on Research in Bilharziasis: Immuno-Biological Diagnosis of Bilharziasis, August, 1961.

The Pan American Health Organization, mainly interested in the past in the development of control and preventive measures, has nevertheless been aware of the major research needs in the field of schistosomiasis and has taken part in some of the fundamental research studies, such as:

1) Field trials of new and potential molluscicides, and the development of application techniques for one of them (i.e. sodium pentachlorophenate - NaPCP - Brazil, 1950-1955. These were conducted in collaboration with the United States Public Health Service (NIAID, NIH) and the National Ministry of Health of Brazil.

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* Prepared for the first meeting of the PAHO Advisory Committee on Medical Research 18-22 June, 1962.

2) Snail ecology studies conducted in Brazil during 1952-1954 with the same collaboration as the above.

3) Research planning in the field of malacology as included in the activities of the PASB/WHO Working Group for the Development of Guidance for Identification of American Planorbidae Involved in Schistosomiasis, November, 1961.

Any plans to extend the Organization's role in such research should depend upon an appraisal of the present situation of schistosomiasis in the Americas, and this calls for evaluation of the research needs which this appraisal reveals. As a first step in this direction, this document gathers and summarizes the data available in the technical literature and in the reports of the Organization. This has been achieved through the help of a group comprised of Dr. N. Ansari, Dr. Ernest Carroll Faust, Dr. Emile A. Malek, Dr. Rafael Rodriguez-Molina, Dr. Harry Most and Dr. Willard H. Wright, with the secretariat services of Dr. E.C.Chamberlayne.

The text contains information on the distribution, the prevalence, the control programs, and the problems of schistosomiasis in the Americas, with an indication of research needs, plus outlines of a few research projects to meet these needs.

PREVALENCE, DISTRIBUTION AND CONTROL OF SCHISTOSOMIASIS IN THE AMERICAS

I. DEFINITION OF SCHISTOSOMIASIS

1. Schistosomiasis is a disease of man and domestic animals, primarily affecting the visceral organs of the victim, especially the intestines, liver, bladder and lungs. The infection is produced by blood flukes, trematodes belonging to the genus Schistosoma. Three of these species are important human parasites having extensive geographical distribution. Schistosoma japonicum is endemic in Japan, China, Celebes, Thailand and the Philippines, and involves an estimated 100,000,000 persons.[1/] The infection is found in certain domestic animals in Taiwan (Formosa) but autochthonous cases in man have not been recognized. Schistosoma haematobium occurs in a small focus in Maharashtra State in India and has been reported in Southwest Asia from Aden, Saudi Arabia, Yemen, Israel, Lebanon, Syria, Turkey, Iraq and Iran. In North Africa, the parasite is endemic in Morocco, Spanish Morocco, Algeria, Tunisia and Egypt. The species is widely distributed throughout the rest of Africa and occurs in Mauritius. A small focus exists in southern Portugal. It has been estimated that 40 million persons are infected.[1/] Schistosoma mansoni occurs in Israel, Yemen, Aden and Saudi Arabia and is widely distributed throughout Africa, although not to same extent as S. haematobium. In the Western Hemisphere, S. mansoni is endemic in the Dominican Republic, Puerto Rico, Vieques,

Antigua, Guadeloupe, Martinique and St. Lucia. It also occurs in Venezuela and Surinam and is extensively distributed in Brazil. This species is said to infect approximately 30 million individuals.[1]

2. For a clear conception of the epidemiology of schistosomiasis it is necessary to know that the agents of this disease require two hosts, viz., man or other susceptible mammals, in which the worms mature and discharge their eggs, and certain groups of aquatic molluscs (snails) in which the invading larva (miracidium), hatched from the egg in feces-contaminated water, undergoes development and multiplication; then the fork-tailed larval progeny (cercariae) erupt into the water and on contact with the skin of the definitive mammalian host penetrate and undertake migration through the blood stream and mature as they become localized in the mesenteric venules (*Schistosoma mansoni*, *Schistosoma japonicum*) or vesical plexus (*Schistosoma haematobium*); here they mate and the females discharge eggs over a period of many years. Thus, in all three types of schistosomiasis man on the one hand and the appropriate species of snails on the other must be reckoned with in any public health control program.

II. SCHISTOSOMIASIS MANSONI IN THE AMERICAS

Manson's schistosomiasis was probably introduced into the Americas with slaves brought from endemic foci in East, Central and West Africa in the 16th, 17th and 18th centuries (Scott[2]), and became established in those areas in the West Indies and South America where appropriate fresh water snails existed in water contaminated by infected human excreta. In this way, the disease became established in the New World. Although large numbers of infected African slaves were imported into other regions of the Americas (viz., Continental U.S.A., Mexico, Central American countries, Cuba, etc.), the absence or lack of abundance of susceptible snails prevented development of Manson's schistosomiasis in those countries, just as failure of vesical schistosomiasis in imported Africans failed to become established anywhere in the Americas, due to lack of snails utilized by *Schistosoma haematobium*.

1. Distribution and intensity of the infection. In the West Indies schistosomiasis mansoni occurs in only two small foci in the Dominican Republic,[3,4] i.e., Las Palmillas and Hato Mayor, both near the south coast east of Santo Domingo City. In St. Kitts in 1932 approximately 25% of the 56,000 inhabitants were infected in highly endemic coastal areas,[5] but by 1945 infection in man had practically abated and by 1959 was no longer present in the human population[6]. In Guadeloupe (with 275,000 inhabitants) and Martinique (with 277,000 inhabitants) somewhat less than 10% incidence is reported,[7,8] but nearly 25% of the 86,000 individuals in St. Lucia are infected, in the many endemic foci, including mountain streams.[9] An approximate estimate of the total infection of these islands is 100,000 persons.

In the Commonwealth of Puerto Rico the most recent survey of school children (White, Pimental and Garcia)[10/] indicates that the infection is widely established throughout the island, including all of the coastal areas except the northwest, likewise some upland centers, with incidence figures varying from 0.6 to 29.9% and an overall average of 10.0%, hence affecting nearly 235,000 persons. According to Maldonado and Oliver-González[11/] in 6 endemic foci investigated there was a decline from 22.2% to 11.3% between 1953 and 1955, but with continued high soil pollution.

The three countries in South America in which Manson's schistosomiasis is known to be indigenous are Venezuela, Surinam and Brazil. The very few infections diagnosed in French Guiana were no doubt imported and there is no good evidence that the disease is endemic in that country.[12/] A single fecal specimen of an individual from a relatively inacessible mountain village in western Antioquia, Colombia,[13/] requires careful epidemiological study of the region to determine if the infection was locally acquired or was imported. In Venezuela, endemic areas exist in the States of Aragua, Carabobo, Miranda, Maracay, and the Federal District. The disease has been reported also from the State of Guarico. All the endemic areas are in the northcentral part of the country, with prevalence figures of 9.9 to 31.6%. The number of cases in Venezuela is estimated to be approximately 30,000.[14/] In Surinam there is intensive prevalence on the coastal strip. Of 100,000 individuals living in the endemic area, about 9,300 are infected, although more detailed surveys may disclose a larger number.[15/]

The most widely distributed region of Manson's schistosomiasis in the Americas is Brazil. Beginning in the State of Para, two centers of endemicity have been discovered, one on the coast east around Belem, and one inland at Forlandia; there are possibly two or three other minor foci. There is no report of this infection in the State of Ampara, northeast of Pará. Only one small northern coastal area is known for the State of Maranhão. Reported infection in the State of Piaui is relatively insignificant. However, higher prevalence rates occur in the coastal and adjacent forested areas of the northeastern group of states, beginning with Ceará (0.93% incidence), with increasing intensity through Rio Grande do Norte (2.31%) and Paraiba (7.53%), to attain a maximum in Pernambuco (25.17%), Alagôas (20.48%) and Sergipe (30%), and in some foci reaching 60% intensity. The disease is widely disseminated throughout the coastal two-fifths of the large State of Bahia (16.55%), and is also reported as indigenous in the mid-San Francisco Valley and even in the western plateau. Minas Gerais, although an inland state, has rather widely disseminated infection throughout all but the western section, and has a moderately high overall percentage incidence (4.41) which in some localities reaches near saturation (93.9%). Proceeding down the coast the disease exists to a much lesser extent in isolated foci in the States of Espirito Santo (1.63%), Guanabara (0.10%), São Paulo (both on the coast and inland next to Paraná, in the north and in the central plateau), and in the north of Paraná (0.12%). Endemic foci occur in the State of Rio de Janeiro. The infection has not been reported as indigenous for the southermost states of Sta. Catarina and Rio Grande do Sul. Only one center of doubtful endemicity has been reported for the State of Goiás, and it is questionable whether or not infection is locally propagated in the State of Mato Grosso. The total cases in Brazil amount to an estimated 4 to 6 million.[16,17]

Thus, the amount of indigenous schistosomiasis presently known or estimated for South America is between 4,150,000 and 6,170,000 cases. Adding to this figure the 100,000 cases in the West Indies, one arrives at the total of 4,250,000 to 6,270,000 or 6.7 to 8% of the population of about 80 million persons in these endemic countries.

In continental United States of America there are no autochthonous foci. The infection rate among the many tens of thousands of persons of Puerto Rican birth living in New York City is about 10%.[18] In Philadelphia a small sampling of Puerto Rican school children, based on a single fecal examination each, showed an incidence percentage of 3.0.[19]

2. Planorbid snails involved.

Australorbis glabratus is the well-known and highly susceptible intermediate host of *Schistosoma mansoni* in several extensive areas of the West Indies and South America. A second species, *A. tenagophilus* (syn. *A. nigricans*), is widely distributed in central and Southern Brazil. Although it is usually regarded as a poor host, hence of secondary importance, in areas of heavy fecal pollution of the water the infection rates in this snail may reach levels as high as those of *A. glabratus* under comparable conditions.[20]

Tropicorbis stramineus (syn. *T. centimetralis*) has extensive distribution in Brazil, from the Amazon region to the Central States, while in certain areas of the northeastern part of the country it is the only known intermediate host.

Several species of Tropicorbis have been found experimentally to be potential hosts for S. mansoni. T. havanensis from Baton Rouge, Louisiana, has been shown to be moderately susceptible (17% with normal shedding of cercariae, compared with 95 to 100% for A. glabratus),[21,22] whereas a different strain of the same species from lagoons in a New Orleans park was completely refractory.[23] T. rüsei (probably = T. peregrinus) from a limestone sink pond in Puerto Rico (Richards),[24] and T. albicans, also from Puerto Rico (Richards, unpubl. data); T. chilensis from Rio Mapucho near Santiago, Chile (Barbosa and Barbosa, 1958),[25] and T. phillipianus (Barbosa and Barbosa, 1958)[26] from Guayaquil, Ecuador, have all been demonstrated to be good experimental hosts. (Both T. chilensis and T. phillipianus occur in habitats west of the Andes, where schistosomiasis has not known to have become established up to the present time.)

The aquatic snail hosts of the schistosomes can live for long periods out of the water. Many observations have been made in tropical and subtropical areas in Africa and in the Western Hemisphere on the ability of these snails to withstand drought for several months (Greany, 1952 in the Sudan;[27] Barlow, 1933 in Egypt;[28] Olivier and Barbosa, 1955[29] Barbosa and Olivier, 1958 in Brazil[30] and Malek, 1958 in the Sudan).[31]

The snails that survive the dry period are not actually exposed to severe desiccation or to high temperatures but are usually covered and protected in the shade of vegetation and in a microhabitat which preserves a certain degree of humidity. The humidity of this microhabitat determines whether the snail will survive until the end of the dry period. The surviving snails are also protected in mud cracks. If they are found in the mud this does not mean that they have actively burrowed into the mud but had accidentally been buried.

The ability of these snails to survive drought periods makes clearance of canals of mud and vegetation an inefficient method of eradicating these watercourses of their snail fauna. A large number of the snail hosts in Egypt withstand a 40-day dry period in irrigation canals after these canals have been cleared of their mud and vegetation. A number of snails survive in the mud and among the vegetation dumped on the banks of these canals. This is an important aspect to be considered in molluscicciding programs. The few survivors on the banks are out of reach of the chemical and can repopulate the canal, if the mud is put back in the canal purposely or accidentally.

The most extensive studies on the ability of the snail vectors to withstand desiccation were carried out by Olivier and Barbosa[29/] to northeastern Brazil. Australorbis glabratus and Tropicorbis stramineus survived in pools that remain dried up for 5-7 months every year. The reproductive potentials of snails that survive the dry season is apparently very pronounced, as these survivors can repopulate the habitat to maximum density in about 50 days after the flooding of the area. In northeastern Brazil it has been observed that a certain species of snail in several localities exhibits various degrees of tolerance to desiccation. Moreover, snails from permanent bodies of water are less tolerant of drying than those from temporary pools.

Of epidemiological significance is the finding that partially developed infections of Schistosoma mansoni are arrested when the snail is out of the water but its development is resumed when the snail is put back in the water in the laboratory, or when the water returns to the habitat in the field. These immature infections are thus carried from one season to the other and thus are able to maintain endemicity in the area.

Infection, however, dies in the snails exposed to drought, if it is mature. Such an observation has been reported by workers in Brazil and others in Africa.

3. Molluscan habitats.

The planorbid hosts of Schistosoma mansoni usually live in shallow waters of streams or pools that are more or less permanent, with a moderate amount of organic pollution, moderate penetration of light, little turbidity, a muddy substratum rich in organic matter supporting growth of aquatic weeds and microflora, and further characterized by being stagnant or slow-flowing. However, these snails are able to accomodate themselves to a wide range of ecological conditions. For example, they also breed in large bodies of water such as lakes or reservoirs, in small ponds, and in the sheltered backwaters of torrential rivers; likewise in irrigation and drainage ditches, swamps and burrow pits.

In Puerto Rico the alluvial areas have many locales favorable to A. glabratus and constitute the major foci for the transmission of the disease. Although this species also occurs in limestone sink ponds on the North Coast, this area is relatively free of the disease, possibly because of infrequent use by the population (Harry and Aldrich).[32/]

The physico-chemical composition of the water probably plays an important role in the distribution of these snail hosts. For A. glabratus the maximum tolerated concentration of chlorides as NaCl was found experimentally to be 3641 ppm (Deschiens),[33/] while in natural planorbid habitats in Brazil de Andrade[34/] found that the maximum chloride content is 2562 ppm. Lime is essential for the formation of the snail's shell; the calcium ion is also important in the animal's metabolism and helps to regulate the permeability of the tissues. Although these snail hosts tolerate a wide range of water hardness, in very soft water they are scarce and their shells become relatively thin.

Harry and Aldrich[32/] observed the absence of A. glabratus from most Puerto Rican waters containing only small amount of inorganic ions. Optimum snail habitats in this area usually have 150 to 500 ppm., but snails have been found in concentrations up to 3,000 ppm; only rarely are they found in Puerto Rican waters which have concentrations consistently lower than 150 ppm. It seems likely that other factors are responsible for the rarity of the snails in such waters, since these snails can be reared experimentally in distilled water.

Development cycle of susceptible snails. In most endemic areas of schistosomiasis in the Americas the temperature and other environmental factors are very favorable for reproduction and growth, so that in permanent bodies of fresh water reproduction continues almost throughout the year unless interrupted by heavy rains. In temporary bodies of water reproduction is interrupted by the dry season but is resumed by the few survivors as soon as the water is replenished. In northeastern Brazil the snails may attain saturation density within 50 days if there are a few mature snails in the habitat (Barbosa and Olivier.[30/]

In addition to the seasonal fluctuation in the population density of the snails there is also fluctuation in their infection with the schistosomes. Some techniques have been in use to estimate the snail population for ecological field studies, for studies on the transmission potentials of these snails, and for evaluation of mollusciciding operations. Choice of the sampling method depends on the objective of the study and on the area, since a method applicable for one area may not be suitable for another. These techniques reviewed and evaluated by Hairston et al.[35/] and in World Health Organization Tech. Rep. Ser. 214 (1961).[36/] By the use of standard sieves, scoops, dredges and the like, the population density is estimated by recording the average number of snails collected in each dip. Counts per unit of time from measured and marked areas in the habitat have been recommended by Olivier and Schneiderman.[37/] The quadrat method used in many ecological surveys has been adapted to amphibious snails (Pesigan et al.,[38/] and can also be used in dried-up habitats of the aquatic hosts. Palm leaf traps placed in the water at regular intervals along both banks of canals are very effective in survey work. The snails collect on these leaves to feed on the thin algal film.

4. Technics for determining the prevalence of schistosomiasis mansoni in man. (a) The usual method employed in an epidemiological survey is to make a fecal examination of the respective population groups. For convenience, the population sampling usually consists of school-age children, who represent a relatively uniform group and provide

opportunity to assess changes which may occur in prevalence of the disease in a relatively short span of years. Clean cylinders of waxed cardboard with a close-fitting lid, such as half-pint ice cream containers, are particularly suited for distribution to the children the day before the fecal samples are to be obtained. For each pupil a record is made of sex, age, and residence in the area, whether urban or rural. On delivery of the specimens next morning the containers are taken to the diagnostic laboratory and if not examined immediately are refrigerated until they are to be processed. Since relatively few eggs are laid per female Schistosoma mansoni per day (only about one-sixth the number produced by S. japonicum), direct fecal films frequently fail to reveal the characteristic eggs unless the infection has just matured or the number of worms is considerable. Concentration by approved sedimentation techniques is therefore indicated, utilizing a few grams of the feces thoroughly comminuted in tap water, poured through two layers of wetted cheesecloth and allowed to sediment in a 500 ml. urinalysis jar, with 2 or 3 decantations of the supernatant water to reduce the amount of sediment in which the eggs will be found. Adding 0.5% glycerine to the water will improve the technique (Faust and Hoffman),[39/] while sodium sulfate-Triton detergent in the water will speed up the process (Faust and Ingalls;[40/] Maldonade and Acosta-Matienzo).[41/] Care must be taken not to pour off any of the bottom sediment during decantations. In case gross inspection of the feces shows that there is considerably fatty material, the formalin-ether technique of Ritchie[42/] may be employed.

(b). In the clinic these same concentration techniques are recommended, but with older patients having more chronic infection the chances of recovering the eggs are fewer. Hence snipping a small sample of intestinal tissue from the level of the valve of Houston and pressing it between 2 microscope slides, often reveals characteristic eggs lodged in the tissues when the fecal sediment is negative.[43,44]

(c). Various immunological tests have been employed for the diagnosis of schistosomiasis. A critical evaluation of these tests has been provided by Kagan and Pellegrino.[45] The intradermal test is of value in adults but is less effective in children. It has a relatively high efficacy in disclosing chronic infections but is of less value in determining recent acute infections. Positive reactions, however, do not necessarily indicate a current infection, since skin sensitivity may persist for years after the termination of infection, either spontaneously or by chemotherapy. Results vary somewhat with the type of antigen, the dilution employed and the method of reading the reaction.

Numerous serological methods have been utilized for the diagnosis of the disease. The complement fixation has proved to be very reliable, since it provides a high percentage of positives and few non-specific reactions. The precipitin test is not as effective as the CF and some other serological tests and tends to give a considerable percentage of non-specific reactions with crude antigens. The circumoval precipitin test is a sensitive method for detecting chronic schistosome infections. The "cercarien-hüllen reaktion" (CHR) of Vogel and Minning has proved to be useful in endemic areas where it is not difficult to secure large numbers of cercariae. The cercarial agglutination test is promising but needs further evaluation. The miracidial immobilization method of diagnosis has given good initial results but has not been applied on a practical scale. The flocculation and hemagglutination tests have both been employed in the diagnosis of schistosomiasis and offer considerable promise; further evaluation needs to be made. A more recent development in serological technique concerns the fluorescent antibody reaction of Sadun et al.[46,47] and Anderson et al.[48] This test shows great promise and apparently is highly specific. It can be carried out with finger blood dried on filter paper and therefore would be valuable in epidemiological surveys.[48]

At the time of fecal examination, rectal biopsy or serological test, it is highly important to ascertain whether a positive person has been resident for some years in the examination area or has recently immigrated into the area, in order to determine if he lives in a known endemic focus of the area or has come from another endemic region.

5. Epidemiological determinants of infection. (a). The most likely first evidence of an infection consists in the discovery of human cases. As indicated above, it is essential to determine if the discovery represents a previously undiagnosed endemic focus, or provides evidence of an immigrant from another focus who conceivably might initiate a new area of infection where the appropriate molluscan host is present.

A possible, as-yet undetermined source of S. mansoni eggs for infecting the snail is the non-human reservoir. A considerable number of mammals have been found naturally infected in schistosomiasis territory in the Americas, including opossums, rats, native mice and cavies in Brazil,[49/] the rabbit in Venezuela[50/] and the African green monkey in St. Kitts.[51/] Even though these animals may be infected, it is necessary to determine which ones, if any, excrete viable S. mansoni eggs directly into the snail's habitats frequented by human beings.

(b). The second epidemiological determinant is the snail host, its prevalence and local abundance. Australorbis glabratus is the most prevalent susceptible snail in the general area, but it may not be in the locale where it can be readily infected from human sources. Thus it is essential to discover what opportunities there are, if any, for the snail to be exposed. Moreover, different strains or races of the same species of snail exhibit different degrees of susceptibility to the same strain of the schistosome; and likewise different strains or races of S. mansoni have different degrees of infectiousness for the same species of snail. Hence the parasite can become established and maintain itself in a certain locality only if snail and parasite are mutually adaptable.

High prevalence rates in man may be associated with low rates in the snail hosts. This is especially the case when Tropicorbis stramineus is involved. In one endemic area in Pernambuco State, Brazil, where the incidence in man was 30.9%, that in T. stramineus was only 0.1%, while in another area in the same State human infection was 30.1% and 8.8% of Australorbis glabratus were infected.[52,53/]

(c). The third determinant consists of the types of human activities favoring propagation of the disease. Among the determining factors are, on the one hand, the insanitary disposal of human excreta which directly or indirectly contaminates the water close to the snail's breeding grounds. Is egg-infested urban sewerage discharged into the water, or is the night pot (comode) rinsed out in the water? Is a latrine placed over the bank of the water so that the feces fall directly into the water? Again, are the feces evacuated directly onto the ground above the water, so that they are washed down by the first rain? All of these human customs provide potential opportunity for infection of the snail host. Finally, to complete the cycle between the infected snail and the human host there must be human contact with the infested water containing the infective-stage schistosome larvae which have emerged from the snail and which during their infective period of several hours are in the top level of the water (in the case of S. mansoni). The opportunities for human exposure are multiple, although they vary somewhat in different endemic areas. Agricultural pursuits such as irrigation, rice- and sugar-cane cultivation and irrigated vegetable gardening constitute the principal hazards for adult males. Domestic use of infested water for laundry, bathing and drinking purposes provide another major source of infection. For children, walking barefooted through the water, swimming and fishing in the streams are frequent means of acquiring repeated infections. In perhaps a minority of instances reservoirs of unfiltered urban water supplies are inhabited by the snail host which has become infected.

III. CLINICAL ASPECTS OF SCHISTOSOMIASIS MANSONI

1. Introduction In discussing the clinical aspects or clinical patterns in schistosomiasis mansoni, the following considerations must be borne in mind:

When the physician examines a patient suffering from this condition, (diagnosis having been established by finding of ova in the stools, by serologic tests or by finding of ova in a small piece of tissue removed from the rectal valves ("rectal biopsy"), he wants to know the following : What organs and to what extent are they involved by the disease? The tools that make this information available to the physician include the history offered by the patient, such as the number of exposures and duration of symptoms; analysis and evaluation of symptomatology; and a complete physical examination including recto-sigmoidoscopic examination. Does the patient have a large liver, a large spleen? Is he suffering from dysentery? Has he ever vomited blood or passed blood in the stools? Are the lungs and the heart in a normal condition? Are anemia, leukocytosis and eosinophilia present? Are the cephalin flocculation and excretion of bromsulphalein tests abnormal? Are there clinical evidences of pulmonary and portal hypertension?

The patient may appear to be asymptomatic in spite of the fact that schistosome ova are present in the stools and the circumoval preciptin reaction is 4+. After studying the case the physician cannot visualize the amount of disease in terms of number of living worms, and the number of ova in the host, because unlike bacteria, fungi, or viruses, schistosomes do not multiply in the human host. So many cercariae penetrate the skin at a given exposure; so many attain maturity to (X) numbers of adult male and female worms, which after copulation produce large numbers of ova daily, of which an unknown number is carried by the circulating blood to the liver, lungs, and other organs of the body; and finally, (X) numbers of eggs are passed daily in the stools. The physician's armamentarium offers no method by which he may quantitate the number of worms harbored by his patient, nor can he estimate the number of cercariae that penetrated the skin during any single exposure.

Value of the egg count as an index of intensity of infection: When a sample of stool contains 500 ova per gram, the finding does not necessarily mean that the infection is a heavy one, since egg counts vary considerably and the number of eggs on the following day might be considerably less.

In disease caused by schistosomes, tissue changes depend on the number of worms present in the host, and these vary according to the number of larvae (cercariae) that penetrated the skin. This characteristic of infections gives rise to variability and differences in the clinical response to the disease in different patients. To illustrate: Two individuals of the same sex and age are exposed at the same time to polluted water. One develops a severe, acute type of infection associated with involvement of the liver and spleen, while the other does not show any clinical evidence of the disease though they both have schistosomiasis, as demonstrated by ova in the stools. Presumably, they were exposed to the same number of cercariae in the water. It is logical to assume that one patient became heavily infected while the other acquired but a light infection with the parasite.

Patients suffering from schistosomiasis frequently harbor intestinal helminths such as hookworm, Ascaris, Strongyloides, and Trichuris. The presence of these worms may add further confusion to evaluation of symptomatology in terms of S. mansoni infection.

Longevity of infection in man. The writer has observed living ova in the stools of an adult who has resided in New York City over 25 years, where re-infection is not possible.

Pathogenesis of the disease in man. According to E. Koppisch [54/] schistosomiasis mansoni may be classified into three stages:

(a) An early stage of migration during which the cercariae are being carried by the blood to the liver, maturing into adult parasites within intrahepatic portal veins.

(b) An intermediate stage during which ova are accumulating in various organs: and

(c) A late stage characterized by serious, irreversible and permanent damage to organs mainly through fibrosis.

The organs most frequently affected as a result of infection with the parasite are the colon, liver, spleen, rectum, and lungs.

The greatest damage to the tissues is caused by the ova. Histologically the predominant lesion is the pseudotubercle, a lesion incited by the ova retained in the tissues.

CLINICAL MANIFESTATIONS

1. Incubation period. (Time elapsing from first exposure to clinical onset).

Mild itching and uticaria lasting from a few minutes to several hours when present are immediate manifestations following exposure. Mild pyrexia may accompany urticaria. Anorexia, headaches, generalized aches and pains, mild diarrhea accompanied by abdominal discomfort may follow and last one to two weeks. These symptoms occur after invasion of the parasites and during the period of intravascular migration of the cercariae, as well as prior to the maturation of the worms in the portal circulation.

2. Acute stage. Estimated incidence in Puerto Rico: 1 to 5 per cent.

This stage is rarely observed by the physician or is diagnosed as something else. In the majority of cases the type of reaction is mild and the clinical picture may amount merely to disturbances in general health. Loss of weight, lack of appetite, headache, abdominal and limb pains, mild pyrexial attacks, associated with possible transient urticarial eruption, may then be the only clinical indications of schistosome infection. Occasionally, however, sudden and severe clinical manifestations may occur.

Diaz-Rivera et al. [55/] reported 12 cases occurring in young males who were studied over a period of 6 years, following initial and consecutive exposures and infection. It was assumed that the individuals became infected in heavily contaminated streams in bright daylight and mid-afternoon in Puerto Rico. The clinical picture was characterized by a sudden onset and by the explosiveness and severity of the constitutional manifestations, which comprised shaking chills, spiking temperature up to 104° and 105°F, profuse diaphoresis, non-productive cough, generalized body aches, pain in the extremities, weekness, lassitude,, nausea and womiting and watery and bloody diarrhea accompanied by tenesmus associated with generalized crampy abdominal pain. Along with these manifestations there occurred moist rales over the lungs, hepatosplenomegaly, high eosinophilic leukocytosis, anemia, and a high serum globulin with an increase of the gamma globulin fraction, as shown by electrophoretic analysis. A clinical manifestation rarely mentioned in the literature but present in all cases was generalized lymphadenopathy.

After a variable period of pyrexia that lasted over 74 days in one case, the symtomatology gradually sibsided and improvement followed defervescence, which abated by lysis. No deaths occurred. Delayed signs of allergy were observed in some cases, including transitory puffiness of eyelids and face, urticaria and purpura.

This severe though self-limited reaction associated with predominating constitutional manifestations maybe indistinguishable from an acute infectious disease, such as typhoid fever. When observed in young adults recently returned from endemic areas, it may resemble collagen disease or lymphoma and is conditioned by the intensity of infection, degree of immunity and by individual susceptibility. The severity of the symptomatology is dependent in part upon a state of tissue and organ hypersensitivity, the adult worms and the ova being the source of allergens.

The cases of acute schistosomiasis reported above received anthelmintic therapy (Stibophen). Transitory improvement particularly in appetite and disappearance of weakness was observed and gains in weight were registered within 2 to 7 weeks following treatment. However, three to five years following the acute stage and after repeated therapy most of the patients still have ova in the stools, associated with enlargement of the liver and spleen. A few patients who were clinically well at this time still showed evidence of schistosomiasis such as liver fibrosis (needle biopsy), ova in the stools and positive biopsy specimens removed from the rectal mucosa.

3. <u>Asymptomatic stage.</u> Estimated incidence in Puerto Rico: 50 to 60 per cent.

manifestation rarely mentioned in the literature but present in all cases was generalized lymphadenopathy.

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3. Asymptomatic stage. Estimated incidence in Puerto Rico: 50 to 60 per cent.

In our experience, in many patients who are hospitalized for disease other than schistosomiasis a diagnosis of that infection is established as a result of routine fecal examination, particularly when stool concentration techniques are employed. These infections with S. mansoni are considered incidental findings not related to the primary disease responsible for the patient's admission to the hospital. The finding of S. mansoni ova in individuals who do not complain of or show clinical manifestations of the disease is more commonly observed in well-nourished and well-developed persons belonging to the higher socio-economic strata of society, such as many United States war veterans and other individuals who can afford the services of private practitioners. In charity hospitals, however, the indigent patient, more often than not, presents clinical and laboratory evidence of severe schistosomiasis. In addition he is frequently under-nourished, anemic, and harbors several helminths or protozoan parasites. Other aggravating factors as pulmonary tuberculosis or other intercurrent infectious disease may be present.

Fortunately individuals classified in the group of asymptomatic schistosomiasis comprise the largest number of cases encountered in Puerto Rico.

If not treated with anti-schistosomal drugs, asymptomatic infections may persist for several years without obvious or demonstrable evidence of progression of the disease. Some patients, when becoming aware that they harbor the parasite, begin to complain of mild to severe gastrointestinal symptoms such as pain and recurrent diarrhea. Whether these manifestations are of psychic or organic origin is at times impossible to decide. Should the patient become debilitated from the stress of another intercurrent disease or from surgery, re-activation of symptomatology consistent with S. mansoni infection may occur.

4. Symptomatic stage - chronic. Estimated incidence in Puerto Rico: 25 to 35 per cent.

Usually, patients presenting symptoms, physical signs, and laboratory evidence of the disease are cases of chronic infections where symptoms have been present for six months to several years at the time the patients are seen by the physician. The majority of these cases do not recall having had an illness that can be identified as the acute stage of the disease. Many individuals present a history of repeated exposures prior to the appearance of symptoms. This is common in endemic areas. Some, a smaller group, give a history of a single accidental exposure followed at an indefinite time after exposure, not by the acute stage, but by episodes of abdominal pain associated with mild diarrhea or dysentery (blood in the stools associated with mucous and tenesmus).

Symptomatic cases of the disease may be divided into two groups:

(a) one in which the clinical manifestations are mainly gastrointestinal and metabolic, (15 to 20 per cent); and

(b) the other, where there are evidences of involvement mainly to liver and lungs (10 to 15 per cent).

Gastrointestinal manifestations include frequent generalized abdominal pain, associated with diarrhea, intermittent with constipation. Stools may be liquid, soft, or solid and are mixed with streaks of red blood or with mucus. Tenesmus may be present and severe. Loss of weight and anorexia occur. The colonic and rectal mucosa is congested and may show punctate hemorrhages that can be seen on proctoscopic examination. Small circumscribed yellowish spots that are made up of conglomerate of eggs may be seen also on the surface of the mucosa by proctoscopic examination. There is thickening of the intestinal wall due to edema and fibrosis of the sub-mucosa. Occasionally pedunculated or sessile polpi are found in the rectum. Numerous ova may be present in sections of these polypi.

A piece of the rectal valves of Houston (size of a grain of rice) may be obtained thru the proctoscope by means of a Jackson's laryngoscopic forceps. When the unstained tissue is compressed between two glass slides, the ova can be readily recognized under the low power lens of the microscope. A very small piece of tissue may contain up to several hundred ova. In many cases when repeated stool examinations have been negative, rectal biopsy has shown living or dead ova. Occasionally, however, stools contain ova when the biopsy is negative. The number of ova in the rectal tissue may be used as a rough index of intensity of infection.

When hepatosplenomegaly appears, the late manifestations of the disease frequently give rise to a new and ominous clinical picture. The clinical manifestations are emaciation, hepatosplenomegaly, ascitis, evidence of cirrhosis of the liver, and of portal hypertension. Some cases develop hypersplenism associated with leukopenia, thrombocytopenia, and macrocytic anemia. However, the bone marrow is not megaloblastic. Bilirubinemia and jaundice are seen rarely even in the presence of advanced cirrhosis. Uncontrollable massive hematemesis from ruptured gastro-esophageal varices is a frequent cause of death. Ascites and hepatic insufficiency may occur. In Egypt, rectal and colonic papilomata may produce prolapse of the rectum and intestinal obstruction late in the course of the disease.

When the above manifestations appear, certain alterations have taken place in the liver. Ova transported from the rectum and colon by venous blood are retained in the portal spaces producing embolization. Pseudotubercles form around the eggs accompanied by eosinophils. The organ becomes enlarged, but later it may contract as scarring ensues. On section of the liver the characteristic picture is a periportal fibrosis. The larger portal veins are surrounded by collars of fibrous tissue constituting the characteristic pipe-stem cirrhosis of Symmers. The spleen frequently becomes enlarged sometimes weighing more than 1,500 gms. It presents chronic passive congestion but schistosomal pseudotubercles are seldom seen in Puerto Rico. Ova and pseudotubercles are more commonly encountered in Egypt than in America.

Rodrígues and associates[56] have reported a comparative study of portal (Laennec's) and bilharzial cirrhosis. A summary of their work is given:

"One hundred and twelve cases of cirrhosis of the liver have been analyzed. The series included 69 cases of portal cirrhosis, 22 cases of bilharzial cirrhosis, 11 patients with concurrent Schistosoma mansoni and alcoholism, 7 cases of posthepatic cirrhosis, two of biliary cirrhosis and one of transfusion hemosiderosis.

"Bilharzial cirrhosis occurred in younger patients and portal hypertension and hypersplenism were more frequent. Anemia, when present, was due to bleeding esophageal varices or to hypersplenism. Liver function tests were characterized by a high incidence of abnormality in Bromsulphalein dye retention and tests dependent on alterations in plasma protein constituents.

"The cases of portal cirrhosis disclosed a higher incidence of edema and ascites. Jaundice and signs and symptoms attributed to endrocrine disturbances were more frequently observed. Leukocytosis was encountered more often in portal cirrhosis, suggesting a more extensive hepatic necrosis. Anemia was of three types: of blood loss, associated with hypersplenism and macrocytic anemia.

"Bleeding esophageal varices and hepatic insufficiency were the immediate causes of death in the cases of portal cirrhosis. Bleeding varices and postoperative complications following an esophagogastrostomy were the main causes in bilharzial cirrhosis.

"This study has shown that patients infected with Schistosoma mansoni may present a clinical picture which differs in many respects from the usual one in liver cirrhosis of other etiologies. The exact role that the parasite plays in the production of this clinical picture remains to be elucidated by future experimental and pathological studies."

In the lungs small grayish nodules averaging 1 mm. in diameter are visible or palpable through the pulmonary tissue. These are made up of pseudotubercles around the eggs that have been carried by the blood. In some cases the gross appearance of the lung resembles miliary tuberculosis. Microscopically, there are pseudotubercles, patches of eosinophilic infiltration and occasional hemorrhages. The eggs arriving in the lungs as emboli obstruct the small arteries, and the intima becomes thickened by fibrosis. In time, the right side of the heart undergoes hypertrophy and failure ensues.

Other pathologic findings in the lungs are those of an obliterative endarteritis, the pathophysiologic abnormalities being increased pulmonary vascular resistance with subsequent pulmonary hypertension. The most important pathologic factor is egg embolization of the terminal arterioles and inflammation surrounding the ova. The mechanisms by which ova reach the lungs is not clear. As oviposition is known to occur in the portal system, the way by which the ova can reach the vena cava are, either, through portocaval anastomotic vessels or through venous shunts in the damaged liver. Egg embolization from the hemorrhoidal plexus of veins seems a more logical explanation of migration of eggs to the lungs.

As a rule patients who develop marked pulmonary impairment leading to chronic cor pulmonale, heart failure and death, also present extensive portal (liver) fibrosis associated with congestive splenomegaly. Hypertrophy of the right ventricle and pulmonary artery dilation are part of the postmortem findings in these cases.

Summary. Various clinical aspects or patterns of schistosomiasis mansoni encountered by the physician in endemic areas have been discussed. In a general way, anatomical alterations are in agreement with clinical manifestations, (symptomatology; physical examination; stool examination; rectal biopsy; complete blood count; serologic tests; liver function tests; liver biopsy).[57/]

About 50% of individuals in Puerto Rico showing ova in the stools are asymptomatic, particularly those well nourished individuals belonging to higher socio-economic strata.

The disease is most commonly encountered among the rural indigent and the poorly nourished. The factors of poverty and malnutrition may influence the course of the disease; and anemia, other parasitosis, surgery and tuberculosis may complicate or aggravate the clinical picture.

The massively infected previously unexposed individual frequently

presents severe clinical manifestations from the onset of the disease (acute stage), the severity of symptomatology being conditioned by organ hypersensitivity. Symptoms when present are referred to the gastrointestinal tract (colon and rectum), liver, spleen, and lungs. The degree of severity of the allergic state is indicated by the marked eosinophilic response in the peripheral circulation during the acute stage. In some cases the persistence of marked eosinophilia seems to point to a prolonged allergic response, the adult parasites and ova being the source of allergens. Enlargement of the liver and spleen with generalized lymphadenopathy also may appear during the acute phase of the disease, probably associated with an allergic and hypersensitive state in which the cercariae, the adult worms, and the ova are the allergens. If no further exposure occurs, the size of the liver and spleen may revert to normal, particularly if anthelmintic therapy is administered early, and if the general nutrition of the patient is improved.

In Puerto Rico, schistosomiasis is more commonly is an intestinal disorder (symptomatic, chronic stage) and although liver and lungs are frequently involved, severe hepatic and pulmonary manifestations are rare. Gastrointestinal symptoms and signs are more commonly observed in chronic, long standing infections. These are referred to the colon and rectum and comprise bouts of diarrhea alternating with constipation. Diarrhea may be accompanied by blood, mucous or tenesmus, and is associated with congestion and edema of the colonic and rectal mucosa.

The late stage of the disease is associated with fibrosis (cirrhosis) of the liver, portal hypertension and marked splenic enlargement, resulting from intrahepatic vascular obstruction, and is more freqmently observed in highly endemic areas. Repeated exposures to the parasite appears to be a common factor in this stage.

Pulmonary insufficiency leading to pulmonary hypertension associated with chronic cor pulmonale and heart failure generally develop in individuals also presenting hepatoplenomegaly and portal hypertension. The pathogenesis of the pulmonary alterations is dependent on an extensive arteriolitis as a result of multiple and persistent egg embolization and subsequent proliferation of connective tissue leading to a reduction in the pulmonary vascular bed.

The late stages of the disease may give rise to chronic invalidism which may lead to death, caused either by massive and repeated hemorrhages, (hematemesis) resulting from ruptured gastro-esophageal varices, or from cardiac failure secondary to pulmonary hypertension and insufficiency.

IV. THE ECONOMIC ASPECTS OF SCHISTOSOMIASIS

It is difficult, if not impossible, to measure the cost of schistosomiasis to the individual and to the community. This is indeed true for many, if not all, tropical diseases. Epidemiological services in many parts of the tropics have not been developed to the point where the reporting of vital statistics can be regarded as satisfactory. Even for the Americas, where disease reporting is on a more efficient basis than in many other parts of the tropical world, it is only possible to estimate rather crudely the number of schistosomiasis cases in the endemic areas. In 1957, five countries in the Americas reported cases of schistosomiasis to the World Health Organization. In 1959 and 1960, only three countries reported cases to PAHO. The morbidity rates per 100,000 population in these countries in the latter year were as follows: Dominican Republic 1.4, Venezuela 24.7 and Virgin Islands (U.S.A.) 15.6.[58] Since schistosomiasis is not endemic in the Virgin Islands, the cases no doubt represented imported ones.

Even if reliable evidence were available concerning the number of infected individuals, the task of delineating the economic loss from the disease would be an imponderable one. There is little evidence concerning the overall incapacitation invoked by the disease. It is possible to evaluate total disability but much more difficult to estimate the extent of partial disability. Marked differences are noted in the degree of clinical involvement and such differences exist on an individual and on a community basis. Even in a community with high endemicity, certain persons will be less severely affected than others. Certain areas are marked by a high percentage of severe infections while in other areas clinical involvement appears to be at a minimum. It is this latter situation which apparently has given rise to the concept that schistosomiasis for the most part is a disease of little public health significance and for this reason merits little attention on the part of health authorities. In Africa, especially, there are two schools of thought concerning the gravity of the disease. One view is that the condition in most of Africa is so mild that it can be discounted in contradistinction to the situation in Egypt where marked clinical manifestations are evident. The other view is that schistosomiasis in most of Africa is a serious condition which warrants concern on the part of health authorities. It is the opinion of Gelfand[59] that those who minimize the importance of the disease have had little autopsy experience and lack the benefit of adequate clinical observation. Gelfand's opinion concerned urinary schistosomiasis and is therefore more significant when considered in connection with schistosomiasis mansoni which generally produces more severe manifestations, because of greater egg output.

A few studies have been made on Puerto Rican components of the U.S. Army in non-endemic areas in Continental U.S., following rejection of many male Puerto Ricans of military age because of Schistosoma mansoni. Among such persons without complaints, Lyons and Benson[60] found that treatment produced remarkable improvement in their appearance, with increased appetite, gain in weight, more capacity for hard work, and healthier outlook on life. Observations on civilians of Puerto Rican birth in New York City and in Puerto Rico indicate that infection acquired there is presently no less severe than it was two decades ago.[18,61] Pessôa[62] compiled data on severe infections in children of pre-school and school age in the highly endemic areas of Alagôas, Brazil, where 50 per cent of the severe hepatosplenic form of the disease was found in youths 15 years of age, and where 80 per cent of severely infected persons are in the age group 10-30 years. Similar data have been reported by Brener and Mouão[63/] for the State of Minas Gerais. In Venezuela there are higher death and morbidity rates in the four political subdivisions endemic for schistosomiasis compared to the non-endemic areas (Curiel, Guzman and Ochôa).[64/] The so-called inapparent infection has been demonstrated to represent a subnormal state of physical being. There is justification to conclude that "mild infections," even though moderately well tolerated, represent a medical and public health situation which needs to be controlled.

There are other factors which add difficulty to the task of evaluating the economic impact of schistosomiasis. In most endemic areas, concomitant conditions are prevalent and these conditions, such as malaria, filariasis, intestinal parasitic infections and malnutrition, contribute to the ill health of the population. It is not possible to determine with any degree of exactitude the relative contribution of each of these concomitant conditions to the lowered health standards of the community.

Schistosomiasis is an insidious disease. Only in exceptional cases does it preseht acute alarming clinical manifestations and these instances only arise for the most part after heavy exposure of previously unexposed individuals. Since there is no multiplication of the etiological agent in the body of the infected person, the lesions of the disease build up slowly and the damage to the host is compounded over a long period of time. If the body exerts a sufficient immunological response to the infection, the disease may be arrested in time; if not, and exposure is repetitious, the disease may reach the stage in which the individual is totally incapacitated. In any event, however, there is little doubt that the resistance of the infected person is lowered and that as a result he becomes more susceptible to intercurrent infections.

If schistosomiasis were an acutely fatal disease, some overall estimate might be made of the damage which it causes. However, few deaths are ever attributed to the disease and mortality figures are extremely low.

With the above facts in mind, it is not difficult to understand that the problem of evaluating the economic consequences of the disease is at present an unsolvable one. There are no accurate standards for measuring the extent of clinical involvement and consequently no precise method of estimating the amount of damage which the disease has caused to the individual or the community.

1. Estimated costs of physical incapacity from schistosomiasis. Certain data are available concerning the economic loss from the disease. Most of the data represent estimates which would fail to satisfy an economist but in a few cases the information is of a more precise nature.

In Japan the economic loss, plus the cost of treatment for an area of 90 square miles, was reckoned at $3 million per annum, and the loss for the Island of Kyushu at $2,500,000. In Egypt, where the disease is hyperendemic, the reduction in total economic productivity is estimated to be some 30 per cent and the financial loss $57 million annually. Medical treatment of some 1,700 American soldiers infected in Leyte during World War II was estimated to have cost $3 million, and it was calculated that 300,000 working days were lost.[65]

The economic cost of illness can be divided into three categories, viz: Resource use, resource transfer and resource loss.[66] These concern the nation as well as the individual.

Resource use includes the cost of public health and medical care programs. It also embraces the payments of the individual to the persons and the institutions ministering to him during his illness. In the countries which are highly developed economically, the ill person pays the physician, the nurse, the pharmacist, the hospital and the private laboratory. In many areas, sick persons cannot command all of these services. Regardless of the type of ministration, however, in most instances he still pays something for medical care even though such care may be woefully inadequate.

Resource transfer refers to the cash payments for the time loss occasioned by illness. In the highly developed countries it is convenient to measure the magnitude of this transaction by having recourse to the records of social security programs. However, in many tropical areas, there is little or no form of monetary recompensation for illness and it is therefore difficult to arrive at any valid figure of the magnitude of resource transfer.

Resource loss is also of importance and includes the economic consequences of work days lost and decrease in productivity. In countries with well developed social security and other systems of health insurance, factual data can be produced to indicate the extent of resource loss. In other countries with no such systems or only partially inclusive systems, the loss in terms of productivity cannot be calculated with any degree of accuracy.

There are, however, data to indicate that the percentage of economically active males is lower in some tropical areas than in the highly industrialized countries of North America and Western Europe. The working population may be roughly equated with that between the ages of 15 and 65. MacDonald 67/ has indicated that the expectation of life of the average male inhabitant of England and Wales at 15 years is 55.0 years, and for the similar inhabitant of the former Belgian Congo for example is 37.8 years, a difference of 17.2 years. If allowance is made for the probability of some persons surviving long past 65 and others dying earlier, the expectations of life in the age period 15 to 65 are reduced to 46.7 and 35.3. The difference between these two figures represents the cost of premature death to the Congo in comparison with England and Wales. It amounts to about 24 per cent of the potential annual wealth of the country, and is additional to loss due to ill-health, of which no account is taken in the life tables. The economic significance of either death or disablement varies with the age of the individual when it occurs. A Congolese aged 15 years has an expectation of about 35 working years, but this declines with advancing age to 25, 18, 11 and 4 years of expectation at 30, 40, 50, and 60 years of age, and his potential value to the community sinks accordingly.

This illustration concerns productivity in general and, as indicated, does not consider loss due to ill health. It is given as an example of the complexity of endeavoring to evaluate the economic cost of the disease in general. When one attempts to confine his estimation to a particular disease, such as schistosomiasis, the variables are even more imposing and the task more difficult.

2. <u>The economic burden of schistosomiasis on the community</u>. Data are available from at least one carefully planned and controlled study on the economic impact of schistosomiasis. This study was part of a WHO cooperative project on the Island of Leyte, Republic of the Philippines.[68,69]

The study involved a measurement of the disability due to schistosomiasis. After a preliminary sampling, a group of 278 individuals was selected for interviews, case histories, clinical gradient estimations, and follow-up for more than two years. As a result of the findings, it was estimated that approximately 38 per cent of a quarter million infected individuals in the Philippines manifested symptoms of schistosomiasis. Of the 100,000 cases, 57 per cent were classified as mild, 39 per cent as moderate and 4 per cent as severe and very severe. Careful inquiry was made into the amount of illness and the number of days lost from work. Four categories were established as a result of the survey. Class I involved non-disabling sickness in which there was no absence from work but with an assumed loss of working capacity of 25 per cent. Of the disabling illnesses, Class II concerning absence from work but no confinement with an assumed loss of working capacity of 50 per cent. Class III involved patients confined to the house with a loss of working capacity of 75 per cent and Class IV comprised individuals confined to bed by their schistosome infection with total loss of working capacity.

The final calculations from the survey indicated for the Philippines as a whole an annual loss of working capacity from schistosomiasis amounting to $1,350,000 with an additional cost for medical expenditures of $5,282,500. It was calculated that the economic loss from schistosomiasis in the Philippines imposed a heavier economic burden than did malaria and was several times greater than the estimated cost of controlling the disease in that country.

With this in mind, it may be of interest to cite data concerning the economic benefits which followed malaria control programs in the same country. School absenteeism was reduced from 40 to 50 per cent daily to 3 per cent daily in 3 years from 1946 to 1949, in which intensive malaria control measures were in force. During the same time, daily time loss among workers in industrial enterprises was reduced from 35 per cent to 2 to 4 per cent. The same amount of output was possible in 1949 with only 75 to 80 per cent of the 1946 labor force.[69]

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V. METHODS OF CONTROL OF SCHISTOSOMIASIS MANSONI

In so far as is presently known, maintenance of this disease in the Americas involves only two alternate hosts, man and the susceptible snail. Interruption of the cycle can be effected theoretically by preventing human exposure, by sanitary disposal of human excreta, by measures directed against the snail host, by safeguarding against non-human reservoirs which may play a role in perpetuating the cycle, by chemotherapeutic treatment of human carriers, and by widespread educational propaganda concerning the dangers of the disease and how to avoid exposure. All of these methods are related in some measure to the aquatic habitants of the snails. From a practical viewpoint it is necessary to consider which of these procedures will be most effective in each country, considering the various endemic areas, the habits and cultural levels of the exposed population, the number of available trained personnel, the funds available for conducting the control program, and the probably effectiveness of each available procedure over short and long periods of operation. These several methods of control will be considered in this section and will be evaluated in Section VI.

1. Safe domestic water supply. This constitutes one of the cooperative projects which has been under way in Latin America for approximately two decades. Primary emphasis has been placed on urban centers to assure potable water for members of the community in their homes, for drinking, bathing, and washing of clothes. Safe laundry facilities have been installed for community use near the homes, to prevent use of infested water in nearby streams and canals. Turbidity in the urban water supply is eliminated by settling of water in reservoirs and by filtration; chlorination with 1-3 parts per million of

nascent chlorine for 30 minutes kills the viable infective-stage schistosome larvae present in water derived from contaminated sources. In addition, where a single urban water supply has not been practical, dug wells from safe underground sources, with concrete curbs, have been installed to provide uncontaminated water for domestic use.

If bath water is allowed to stand for 60 hours after being drawn from infested streams, it is safe for use. Copper sulphate at a concentration of 50 parts per million or more will destroy all or nearly all cercariae or infective larvae after exposures of 1 hour or more. Water for bathing purposes is also safe if heated at 50ºC. (122ºF.) for 3 minutes.

2. Sanitary disposal of human excreta. Hand-in-hand with the installation of safe domestic water supplies is the necessity for sanitary disposal of human excreta. For the urban centers community disposal plants are required, planned and constructed under the supervision of experienced sanitary engineers, and including sanitary flush toilets for each home. This type of facility requires that the sewerage discharged from the system be settled satisfactorily so that it will not contaminate the body of water into which it is emptied.

Not all sewage treatment processes are effedtive for the destruction of schistosome ova.[70/] At low temperatures of 44º to 65ºF. digestion or digestion and storage periods of 2 to 3 months are required to render schistosome ova non-viable. Higher temperatures facilitate destruction. In drying sludge a survival period of 3 weeks for the ova can be expected at temperatures of 60º to 75ºF. A reduction of the moisture content of the sludge apparently has no deleterious effect upon the ova until the moisture drops well below (less than 20 per cent) the spadeability content (60 to 70 per cent) commonly used as the criterion for disposal. In sludge dried at very warm temperatures, 85º to 90º F., the ova become non-viable within 9 to 10 days. Considerable attention must be paid to prevailing temperatures in determining the retention periods for drying sludge. Intermittent sand filtration is very effective for removing schistosome ova from sewage. Trickling filters are not effective for removing schistosome miracidia from sewage. Septic tank processing with moderate temperatures of 60º to 75º F. renders schistosome ova non-viable in 2 to 3 weeks. Care needs to be exercised to obviate incoming ova escaping with the effluent.

In villages and rural areas where community sewage disposal is not practical, sanitary latrines are required; they need to be placed so that the human excreta will not be discharged directly into bodies of water or indirectly through ground water so as to contaminate dug wells supplying water for domestic use.

3. Control of the snail intermediate host. Since the susceptible snail is a *sine qua non* for continuation of the life cycle of the parasite, it is logical to direct control efforts against this important facet of transmission. Various methods have been utilized toward this end. These measures include the application of molluscicidal chemicals, the physical clearing of vegetation in the aquatic habitats of the snail, the employment of engineering procedures to eliminate or assist in eliminating areas providing favorable harborage for the snail, and biological control.

(a) Molluscicides. For the molluscicide operation to be successful, it has to be well planned and preceded with at least a year of preliminary studies in the area to be treated. Objectives of these studies are to develop the best strategy in applying the molluscicide, to give a maximum decrease in transmission at a low cost. In this way, the choice of the molluscicide most suitable for the local conditions, the timing of the operation and base line data to be used in the post-control evaluation are among the important goals of the preliminary studies. Information should be gathered during this period as to the hydrography of the area, the molluscan fauna in general, and the species which are recognized hosts in other places. The latter species of snails should be accepted provisionally to act in this capacity until laboratory and field studies are conducted.

The distribution of all snails in the area, the seasonal fluctuation in their life cycle and in the trematode infection rates should be determined.

Preliminary studies should be carried out in the laboratory and in the field.

A study of the ecology of the snail hosts during the precontrol period is essential for the success of the mollusciciding program. The following data have to be gathered on those species that were proved to be hosts: Distribution throughout the scheme; the areas where they are abundant and others in which they are scarce or absent; the distribution of the vegetation in the water courses; the seasonal fluctuation in the population density of the snails throughout the area for at least one year before the application of the molluscicide; and the peak or peaks in egg laying.

Data on the seasonal fluctuation in the population density is important in the timing of the operation. It is usually beneficial to apply the molluscicide when reproduction is at its highest, as young snails are more susceptible to the molluscicide than adult snails.

Of importance also is the determination of infection rates among the snails and their seasonal fluctuation. Reduction in transmission is affected if the water is treated when it is most infective.

Water analyses have to be carried out periodically with emphasis on the hardness and hydrogen ion concentration. A knowledge of the chemistry of the water is essential in the choice of a molluscicide which would be effective in the particular type of water in the area to be treated.

Copper sulphate. Copper sulphate has been employed as a molluscicide for several decades with a certain amount of success in some areas.[71] It has been applied both periodically and by continuous application of low concentrations. The latter method has apparently been of value in controlling the molluscan intermediate hosts in the Gezira area of the Sudan. The chemical tends to be precipitated out of water with a high alkalinity. It combines with organic matter and its activity may be rapidly dissipated; for this reason, it is necessary to clear vegetation before its use, a requirement which adds greatly to the cost of control campaigns. The compound is slightly ovicidal but has little or no effect on cercariae. At usual rates of application, it is less toxic to fish than some other compounds. It has no practical toxicity to man or animals. However, it is highly corrosive to containers, pumps, etc. which must be rinsed thoroughly after use. In order to achieve molluscicidal effect in periodic applications concentrations of 20 to 30 ppm must be employed. The compound is still useful for snail control under certain conditions.

Sodium pentachlorophenate. Sodium pentachlorophenate (NaPCP) has been developed within the past decade and has been used successfully for snail control in Japan and Venezuela, and in one area in Egypt.[72,73,74] It has not proved effective under certain conditions in Brazil and in the Transvaal. It is toxic to snail eggs and cercariae at the same concentrations used to kill snails. In the recommended concentrations for molluscicidal operations, it is not dangerous to human beings or domestic animals. Cases of poisoning in man have resulted from gross negligence, failure to properly instruct laborers in the safe handling of the compound, or exposure to concentrations far greater than those employed in snail control.[75,76] The chemical dust is very irritating to the mucosa of the respiratory tract. Although highly toxic to certain fish, amphibians and invertebrates, the effect on the aquatic environment is probably less lasting than that of copper sulphate. In flowing water, NaPCP has usually been applied at concentrations of 10 ppm for 8 hours. In still waters, good results have been obtained at 5 ppm. In irrigation canals and in streams with unobstructed flow, NaPCP has been carried for long distances and has retained its initial lethal concentration. The chemical has certain herbicidal properties. It has a serious disadvantage in being broken down by exposure to direct sunlight, especially in waters which are clear and free from suspended solids. Turbidity did not reduce its efficacy in Egypt. Under conditions with strong exposure to ultraviolet light, it should be applied in the late afternoon or on cloudy days. NaPCP is non-corrosive.

Copper pentachlorophenate. This compound is a highly effective molluscicide. It is non-irritating to snails and does not cause them to escape from the aquatic environment, a thing which has been reported in some areas following the application of NaPCP. The compound is in-soluble in water and can be prepared in the field by independently dispensing copper sulphate and NaPCP and mixing the two solutions in the snail habitat. CuPCP has a long residual effect, especially in still waters. However, it has been used with success in other types of habitats in Venezuela.[73/]

Bayer 73. Bayer 73 (5-chlorosalycilic acid (2-chloro-4 nitro-anilide)) is a recent development which shows great promise as a molluscicide.[77/] It is sparingly soluble in water but is formulated as a wettable powder, miscible with water as a stable suspension. The chemical is non-irritating and has a low level of toxicity to mammals. It is effective against snails in concentrations as low as 1 ppm. The snails are not irritated by the compound and make no effort to leave the aquatic environment. The chemical is affected adversely by strong sunlight but to a lesser extent than NaPCP. It loses much of its effectiveness in highly alkaline waters. Concentrations lethal for snails kill schistosome eggs and cercariae. It may scorch aquatic vegetation and destroy algae but this effect is short-lived. It is toxic to fish at concentrations employed against snails in the field. It would appear that the chemical can be marketed at a price to compëte with NaPCP.

Aqualin. This compound has been employed as an herbicide; the active agent is acrolein (CH_2: CH-CHO). It is effective against snails, ova and cercariae at concentrations of 3 ppm and is carried for long distances in flowing water.[78,79/] The compound would appear to be most effective in fast flowing streams. It vaporizes rapidly and cannot be employed as a spray. It is usually introduced directly into the discharge side of a circulating pump under water. The material is highly inflammable and should be handled and used under adequate precautionary measures.

Other molluscicides. Many other chemicals have been used for snail destruction, including I.C.I. 24223 (iso-butyl-triphenyl-methylamine), copper carbonate, Rhodiacid, dinitro-ortho-cyclohexyl phenol, calcium arsenate, calcium cynamide, etc. Some of these are effective under some circumstances and need further evaluation. Others have been superseded by more effective chemicals. Many other compounds have been laboratory and field tested. Some have evidenced high efficiency but are too expensive or are not readily available for control purposes.

Application of molluscicides. There is evidence that many of the disappointing results secured with molluscicides of recognized value have arisen because of a lack of understanding of the technical requirements for their use. Highly trained personnel are required. Due reconnaissance should be made of the area to be treated and a critical appraisal arrived at concerning the nature of the aquatic environment and the molluscicide and the method of application likely to produce the desired results. In the case of streams and irrigation canals, it is essential to estimate the rate of flow in order to accurately guage the amount of molluscicide required. In standing water, the average volume needs to be determined for the same purpose.

There are many ways of applying molluscicides; the selection of the most suitable method for any given site depends on the environmental conditions and the ecology of the molluscan intermediate host in the area. Molluscicides have been employed by means of sprays, by allowing the chemical to dissolve directly in flowing water, by the employment of apparatus which affords a constant output of the chemical for a given period of time, by broadcasting the chemical in powder form with a suitable vehicle, by applying the molluscicide along the shores of streams and irrigation canals, by the use of emulsifying agents, and other means.

Evaluation of molluscicide treatment. Once applied, it is essential to determine the concentration of the molluscicide in the water, whether stationary or flowing. If applied to streams or irrigation canals, the operator will wish to know how far the chemical is carried in lethal concentrations. Various means are available for such determination. In the case of sodium pentachlorophenate and Bayer 73, colormetric methods are available. The dispersion of Aqualin can be followed by the yellow color of the product in solution.

It is assumed that the operator has, as a preliminary measure, made some determination of the snail population in the area to which the molluscicide is to be applied. With this determination as a base line, it is necessary after chemical treatment of the water to arrive at some estimation of the relative efficacy of the application. This can be accomplished in two ways. The first consists in carrying out a careful search and surveillance for living snails after the application of the molluscide, employing the same techniques that were utilized in conducting the pre-treatment estimation of the snail population. The second method of appraisal will usually make itself evident by a repopulation of the area in event that the molluscisiding has not been successful, or all snail eggs have not been killed, or there are opportunities for reinfestation from areas outside of the molluscisiding scheme. Even with the most efficient molluscicides, applied in the most effective manner, is it seldom that the total snail population is eradicated by one application. In most instances, repeated treatment is needed.

(b) Clearing of aquatic vegetation. This measure is essential when copper sulphate is employed as a molluscicide and is also advantageous in some circumstances prior to the use of other molluscicides. However, those chemicals with herbicidal properties can usually be utilized without the expense of prior clearing.

(c) Engineering practices and water management. There is no doubt that the engineering control of the molluscan intermediate hosts of the human schistosomes has not been adequately exploited. Engineering practices conducive to control consist in filling or draining small bodies of water providing good habitats for snails, straightening stream beds to increase water flow, lining of irrigation ditches to increase water velocity, the employment of fluctuating water levels, and other water management procedures which tend to render the aquatic environment unsuitable for the snail hosts. In some areas primitive agricultural practices and poor irrigation methods contribute materially to the spread of schistosomiasis. Inadequate provision for drainage causes the land eventually to become water logged and salted. Good water management in irrigated areas will frequently obviate snail harborage and prevent the introduction and dissemination of the disease. On the other hand, where little attention has been paid to such a remedy, irrigation systems have provided ideal conditions for the dissemination of schistosomiasis.

(d) Biological control. In economic entomology considerable progress has been made and success achieved by the introduction of insect enemies of other insects injurious to garden and field crops. In Brazil a micro-organism, Bacillus pinotti, has been found to be damaging to the snail hosts but apparently its use as a biological control agent has not been widely promoted. In Puerto Rico small colonies of the ampullarid snail Marisa cornuarietis were introduced into Australorbis glabratus habitats and the relative numbers of A. glabratus studied over an 81-week period. It was observed that while Marisa was devouring the aquatic vegetation it also ate the egg masses and young snails of Australorbis, so that with the multiplication of the predator the Schistosoma host snail was reduced almost to extinction. The experimental ponds remained free of vegetation and Australorbis has failed to recover at the end of the observation period (Radke, Ritchie and Ferguson.[80/] It remains to be demonstrated if similar results will be obtained in case the predator should be introduced into A. glabratus habitats in other endemic areas. Moreoever, precaution must be taken that the predator snail does not overrun streams and ponds into which it is introduced and thus produce more harm than good.

4. Safeguarding against non-human reservoirs. In the endemic foci of schistosomiasis in the Americas a rather impressive number of mammals have been found to be naturally infected. With the exception of the African green monkey (Cercopithecus sabaeus) in the central mountain forests of St. Kitts,[51/] these reservoirs have all been discovered in the heavily endemic foci of the northeastern states of Brazil and in the States of Bahia and Minas Gerais,[49/] and in Venezuela.[50/] The list includes three species of opossum, the black rat, the Norway rat, the white-bellied rat, two species of rice rat,

several species of native mice, and the native guinea pig from Brazil, and the rabbit from Venezuela. Of this group the only species which habitually frequents water is the rice rat (Oryzomys spp.). This rodent, reported to be a natural reservoir in two Brazilian states with high endemicity, is known to discharge viable Schistosoma mansoni eggs in its feces, and is therefore the most likely non-human carrier of the infection. It will be necessary to determine the significance of this reservoir and the others found naturally infected in Brazil or elsewhere before an evaluation can be placed on their relative importance in the propagation of schistosomiasis in endemic countries.

5. Treatment of human carriers. The individual who is daily evacuating viable eggs of Schistosoma mansoni in his feces constitutes a public health menace. As a carrier of the parasite he is the most likely agent for reinfection of the susceptible snail host. Even though it may not be feasible to treat all carriers with curative anti-schistosomal drugs, it may be of practical value to administer certain drugs (antimonials intramuscularly or lucanthone /Miracil D/ by mouth in coated tablets) in short courses periodically in out-patient clinics, to reduce temporarily the excretion of viable aggs.[81] This program should be conceived primarily as a public health measure.

6. Public health education. In connection with education of the community concerning parasitic and other infectious diseases, persons residing in endemic schistosomiasis areas require simple explanations of the seriousness of schistosomiasis for the infected individual and for his associates, how the disease is perpetuated from man to snail and back again to man through the contaminated water in which the snail lives, and the measures which will insure against infection of the

snail and against human exposure. Not only should such public health education be directed towards the individual but to an even greater degree towards the community as an integral socio-economic unit.[82,83] Practical acceptance of the reasons for combating schistosomiasis must be accompanied by active cooperation of the community with the local public health authorities in charge of the program. This cooperative effort will require changes in the habits, customs, and even cultural standards of the community; since the effectiveness of the control program can not be measured in terms of two or three years, but rather over longer periods of time, it will not be expected that low standards of personal and group hygiene and environmental sanitation which have been practiced for generations will be changed overnight, but only gradually.

7. Central administrative control and direction. In each country in which endemic areas of schistosomiasis exist, a problem as serious and many-facetted as the control and eradication of schistosomiasis must have central administrative control and direction. In Brazil there is constitutional requirement that the Federal Ministry of Public Health be responsible for all health programs in the States and their political subdivisions. To this end in Brazil and other countries where schistosomiasis exists there should be first of all close cooperation between the Ministry of Public Health and the other national ministries, to assure uniform and concerted effort in combating the disease, and a single experienced public health administrator should be assigned full-time responsibility for this program. Furthermore, there is need for constant communication between the national organization and local health units, to provide both inform-

ation and services, so that consistent plans will be organized and programs conducted on the basis of the best scientific knowledge, along the most efficient and economical pathways.

VI. EVALUATION OF CONTROL PROGRAMS IN SCHISTOSOMIASIS MANSONI

In order to have a basis for evaluation of the effectiveness or ineffectiveness of control methods and programs, it is necessary to have considerable information to compare with the results to be obtained as the program proceeds.

(1) In the first place, there should be substantial data on the geographical extent and intensity of the disease in each endemic area. In some regions, as the coastal and adjacent forest zones of the northeastern states of Brazil and in north central Venezuela, the endemic foci are more or less contiguous, whereas in other regions of endemicity they may be separated from one another by natural physiographic or climatic barriers; or they may be distributed widely but in multiple locales throughout an extensive terrain, as in the State of Minas Gerais, Brazil.

(2) In the second place, competent workers should have provided overall and location spot maps of the snails responsible as intermediate hosts of the disease. Such maps should include, if possible, not only those areas known to be endemic foci with demonstrated human infections but also adjacent regions or non-contiguous ones where the susceptible snails are present but as yet are not known to be infected. These data are essential before any type of molluscicidal procedures are undertaken.

A further requirement concerns intimate knowledge of the ecology of the molluscan intermediate host or hosts within the area. While the acquisition of such knowledge may require some time and effort, it is advisable to make such observations prior to any program aimed at snail destruction.

Assuming that data on the extent and intensity of the disease in man are provided for such endemic foci, that there is relatively accurate mapping of the habitats of the snail hosts and some information concerning their ecology, it will probably be desirable to test the control measures which have been decided upon in a relatively modest pilot project, to discover the pitfalls and inadequacies as well as the most practical and effective methods of conducting a more pretentious program. Field testing of the project on a small scale is particularly important if the funds and manpower available are meager, since a well-planned and satisfactorily conducted pilot test which shows potential practical value of the control measures employed should stimulate the allocation of larger appropriations and more trained personnel for the project.

In setting up the project, each of the following items of control should be considered and evaluated from the standpoint of the nature and extent of the problem, the available facilities, the amount of funds, and the number and type of trained personnel: (1) safe water supplies for domestic use and sanitary disposal of human excreta; (2) molluscicidal control measures; (3) biological control of snail hosts; (4) engineering methods of control; (5) the influence of potential mammalian reservoirs of infection; (6) treatment of human carriers; and (7) public health education. Each of these aspects will now be considered.

It is difficult to place relative values on various methods of schistosomiasis control for the reason that nearly all available procedures have been employed in the endemic areas in which control has been attempted. This has necessarily followed because no one method of control is singularly effective from a practical standpoint.

1. Control by sanitary measures. The installation of sanitary facilities, including safe water supplies, properly constructed latrines or sewage systems, and bathing and laundering facilities represents a capital expenditure not only of benefit in the control of schistosomiasis but of other water-born and fecal-borne diseases as well. Such a program should be tied to general health improvement schemes and not carried out for a single disease. The installation of such facilities will need to be accompanied by an intensive health education program so that the populations will realize the importance of using them. Populations in many areas are slow to alter age-old habits and benefits from new installations cannot be expected to materialize rapidly. In some cases salutary results are only of a temporary nature and the installation remains as a monument to another lost cause. For instance, in the WHO assisted pilot project in Leyte, an environmental sanitation campaign proved to be ineffective as a control measure.[84] Nevertheless, sanitary control of schistosomiasis is a *sine qua non* and the ultimate goal to be kept constantly in mind.

2. Molluscicidal control measures. The successful application of molluscicides results in a rapid interruption of the transmission of infection. If the chemical is effective also against snail eggs, the cycle of transmission continues to be interrupted until reinvasion of the treated area. Certain herbicidal effects possessed by certain molluscicides may in some places obviate expensive weed control and clearing of irrigation canals. All of these advantages accrue without the active cooperation of the exposed population, a cooperation which

is essential and sometimes difficult to secure in the application of other control measures. In many endemic areas, mollusciciding will aid in the control of certain trematode diseases of domestic animals.

On the disadvantageous side, the employment of molluscicides is relatively costly since applications must usually be repeated over a period of time; in fact in the past it has required a period of years before substantial control has been achieved. The problem of reinfestation has not been solved and it is not always possible to ascertain the means by which repopulation occurs, assuming that the molluscicide has been effective in destroying all snails and eggs. Consideration must be given to the relative values to be placed on the long-term use of molluscicides versus the benefits to be derived from capital expenditures for permanent sanitary improvements or engineering works to obviate snail harborage. Under some circumstances, it may be found that the latter offer the best investment. A mollusciciding campaign will lack permanent value unless snail eradication can be accomplished. At present, such a goal is difficult to achieve. However, in nearly every area in which progress has been made in the control of the disease, molluscicides have played a prominent role. No doubt more effective compounds will be developed and better methods will be devised for their use.

3. Biological control of snail hosts. Biological methods of control have been tried in certain localized foci. The most promising has consisted in the introduction of the ampullarid snail *Marisa cornuarietis* in certain areas in Puerto Rico, with resulting control of the molluscan intermediate host, *A. glabratus*. Other biological methods have been less successful. However, before the introduction of *M.*

cornuarietis into any endemic area, it would be necessary to evaluate the potential danger of placing the predator snail in unrestricted locales, where its demonstrated propensity to consume vegetation may damage irrigated rice fields or vegetable truck farms, and thus produce a greater menace than help to the economy of the area.

4. Engineering methods as applied to control. Engineering techniques such as drainage and filling, alteration of agricultural practices, lining of ditches and canals, straightening of channels, weed removal to increase water velocity, damming and ponding, fluctuation in water levels and other practices have been utilized locally, frequently in conjunction with other control methods. Their usefulness is tied to the type of topography, the nature of the snail harborage, the conformation of infested waters and agricultural practices. Such procedures are capital expenditures from which long-term benefits can be expected in many cases. The degree of effectiveness and the relative permanence of the procedure will indicate whether the capital expenditure is warranted. In some cases the cost will not exceed that of prolonged mollusciciding; given comparable results in control, the advantage would lie in the adoption of the engineering methods.

5. The influence on control of potential mammalian reservoirs of infection. As previously indicated, many lower animals in some endemic areas have been found to harbor S. mansoni. The potential importance of these reservoir hosts needs to be more thoroughly evaluated before any extensive control campaign is launched. The present evidence would not indicate that lower animals constitute a serious threat or play a significant role in the transmission of the disease. Perhaps

in localized areas, however, they may be sufficiently important in this regard that control measures should provide for such contingency.

6. Treatment of human carriers. Experience has demonstrated that the largest proportion of viable eggs produced by *Schistosoma mansoni* in the smaller intestinal veins of man are evacuated in the feces during the active stage of the infection. In chronic cases the eggs tend to remain in the intestinal wall or are carried into the liver. Repeated exposure tends to reactivate the infection as newly matured worms produce new batches of eggs. Therefore, in a practical sense, the active cases constitute the important source of eggs for reinfecting the snails. In countries in which large scale treatment campaigns have been carried out, there is some question as to the net benefits. It is difficult, if not impossible, to carry out treatment on a large segment of the population. Present drugs lack desired efficacy and side reactions are frequently so disagreeable that a relatively small percentage of individuals consents to complete the treatment. It is the consensus of opinion that large scale chemotherapy has not contributed materially to the control of the disease, although it has been of benefit in reducing the intensity of the infection and thereby has obviated some of the complications. Its employment will depend largely on the characteristics of the endemic area and on the willingness of the population to cooperate.

7. Public health education. Any campaign for the control of schistosomiasis should be fortified by an earnest effort to acquaint the population of the endemic areas with the nature of the disease, the manner in which it is transmitted, and the purposes of measures which are being taken to alleviate the situation. Effort should be

made to stimulate the interest in the local inhabitants of the area and, where possible and feasible, endeavor to have them take an active role in helping to promote the control efforts. In nearly every country in which some progress has been made in arresting the disease, public health education has played an important role, even though it may have taken considerable time to awake and maintain the necessary interest on the part of the local citizenry.

The task is one in which the public health educator has the important role. Other individuals, such as the sanitarian, public health nurse, etc., must have had training in this phase of the program; and he (or she) must have a sympathetic understanding of the background, the education, mores, habits and superstitions of the people of each endemic community. Without the cooperation of the community the entire program may fail. This part of the campaign will not be easy and will require great effort and much time to accomplish. Hence evaluation of failure or success of control will need to include progress in community education.

VII. ACTUAL AND POTENTIAL EXTENSION OF SCHISTOSOMIASIS IN THE AMERICAS

As previously indicated, establishment of the disease in the Americas was actually an extension from its African habitat. There are relatively few recent records of its introduction from one to another completely different focus in the Western World; of these the development of an endemic center at Fordlandia, State of Pará, Brazil[85/], following introduction of laborers from coastal Brazil, is an outstanding example. Yet today there are known extensions of the disease within the past quarter of a century in Puerto Rico[86,10/], Venezuela[14/], and particularly in Brazil, where it has become endemic in new centers to the south, and southwest of the hyperendemic coastal areas in the northeastern States[17/]. With increasing migration of inhabitants from this relatively dry, agriculturally unproductive region to the fertile, as yet sparsely settled regions of the States of Goiás, Pará, Mato Grosso and inland São Paulo, there is every likelihood that infected newcomers will "seed" the previously uninfected territory wherever the carriers of the disease provide the inoculum for the susceptible snails, which will, in turn, provide opportunity for exposure of other settlers in the new territories. Similarly the present concentration of schistosomiasis in Venezuela and Surinam along heavily populated coastal areas will unquestionably work inland if any "population explosion" causes individuals and families to seek relief from the overpopulated districts. Wherever the appropriate snails are established these inland regions will be subject to the disease. Moreover, in British Guiana and parts of Chile, where susceptible snails are present, there is the liability that the infection may become established. French Guiana may also be a favorable territory, although thus far the snails tested have proved to be refractory. In Puerto Rico essentially all of the island where Australorbis glabratus breeds is already schistosomiasis endemic territory.

The proposed reclamation of agricultural lands in northeastern Brazil through the extension of existing irrigation systems and the establishment of new systems will increase the possibilities for spread of schistosomiasis in an area in which the disease is already a major health problem. Any plans for the rehabilitation of the area should undoubtedly take into consideration the potentialities for the spread of infection.

In addition to the extension of the disease into previously non-endemic regions, the rapid increase of population since 1940 in Brazil, Venezuela, Surinam and the Dominican Republic indicates that, at the present growth trend, by the year 2000 there will be nearly a five-fold increase over 1960 (viz., in Brazil from 66.3 to 400.0 million, in Venezuela from 7.36 to 37.5 million, in Surinam from 0.295 to 3.3 million and in the Dominican Republic from 3.0 to 14.2 million.) With increased migration of workers from congested to sparsely settled areas in each of these countries there is a possibility that the calculated Schistosoma-infected persons will increase respectively from the 1960 estimates of 5 million to 28.5 million in the year 2000 (Brazil), from about 30 thousand to 150 thousand (Venezuela), and from 9,300 to 75 thousand (Surinam). In view of lack of sufficient information concerning the extent of the disease in the Dominican Republic, it is impossible to provide an estimate of the present or a forecast for the future of this disease in this country.

The above extrapolation is based on the concept that the increased populations will be exposed to schistosomiasis and become infected to the same degree as at present; that there will be no extension of control measures; or that control measures, if applied, will be totally ineffectual. At present, there is no indication that such a concept may prove to have any validity.

However, the data do indicate the grave future potentialities of the disease unless effort is made to curb it.

VIII. REPORTING OF SCHISTOSOMIASIS

Nowhere in the Americas is schistosomiasis a reportable disease. Yet in some regions of the hemisphere it constitutes one of the major baffling medical and public health problems of our time. Even in New York City, the City Health Department is able to tabulate annually only 5 per cent of the estimated infected Puerto Rican population living in the City; and in Puerto Rico itself only 5.8 per cent of the positives were reported in 1958. In Venezuela 13.4 per cent of the cases were listed in the same year, while in the Dominican Republic 49 cases were recorded for that year.

In view of the seriousness of the situation in endemic areas and potentially serious development of the disease in other areas, it would be advantageous to include schistosomiasis in the list of reportable diseases in countries with known endemic foci. Inclusion of schistosomiasis among the notifiable diseases in these countries:

(a) Will make it easier to define its present prevalence and geographic confines.

(b) Will provide a better basis for the health authorities of the countries to evaluate progress or failure in the attack on the disease within the country, and

(c) Will make surveillance and evaluation of its present and prospective status a simpler task for PAHO.

IX. NEED FOR FIELD AND LABORATORY RESEARCH

The basic facts concerning schistosomiasis and its methods of propagation have been known for several decades, yet attempts to eradicate or even to control it have been disappointing or at least equivocal. Many facets in the epidemiology of the disease in each endemic region are still obscure and need elucidation. This means additional research, both in the field, the laboratory and the hospital and clinic.

Field investigation. Biologists who are specially trained in the ecology of the snail hosts of the infection must provide more adequate information on the climatic, physiographic and other macro and micro-environmental factors favorable to the breeding of these molluscs, and must direct their attention especially to the reactions of these snails to older and newer molluscicidal agents.

Field epidemiologists must be constantly on the alert for apparent or actual increase or diminution in the number of infected persons in an endemic area, and be prepared to interpret the significance of their observations. When new human cases are diagnosed, the epidemiologist must discover if this indicates the beginning of new foci. If the cases are isolated ones which have come from a previously known focus to an as yet non-infected area, he should be prepared to forecast the chances of initiation of the disease in the new area. Careful field investigation will also provide evidence of the extension of the disease to contiguous areas, a situation which is today probably the most serious one.

The Laboratory. Laboratory workers should be specialists in biological, physiological and biochemical disciplines, with their sights directed towards the snail on the one hand and towards the infection in man and reservoir hosts on the other. The problems of the laboratory personnel include inquiries into the specific physical and physiological norms of a host snail such as Australorbis glabratus, which permit it to populate an aquatic habitat in 50 days or less, and how best to interrupt the life cycle of the snail without permanently altering the biological balance of the area. The as-yet unsettled question of the role played by non-human mammalian hosts urgently requires an answer. Problems such as these can best be studied experimentally in the laboratory; later the laboratory results can be tested under natural conditions in the field.

An additional important role for workers in laboratories close to hospitals is to provide skilled technical aid to the physician in studying his patients in the clinic and in the hospital wards. This much needed cooperative type of endeavor will be mutually rewarding.

The hospital and clinic. The clinician represents an important cog in any effort to control schistosomiasis. He is usually the first to observe clinical cases and the first to become aware of sub-clinical cases which may represent new foci of infection. Of necessity, the epidemiologist will have to maintain close liaison with the physician.

It has already been noted that present day treatments for schistosomiasis lack desired efficacy and have annoying side reactions. This situation obviates to a considerable extent the employment of mass therapy in the control of the disease. Vigorously pursued research is needed for the development of new and more effective methods of chemotherapy. It is here that the clinician can play a major role.

Laboratories having major concern with schistosomiasis at a national level are carrying on fundamental and applied research in Brazil, Venezuela and Puerto Rico. In Brazil the center of research activity on schistosomiasis is located at Belo Horizonte, in the State of Minas Gerais, which lies in the midst of an extensive area of endemicity, with a branch laboratory at Recife in the northeastern hyperendemic area. In Venezuela most of the investigation has been associated with the Ministry of Public Health, including its Institute of Hygiene and the Department of Tropical Medicine in the Medical School of the Central University in Caracas. In Puerto Rico the original School of Tropical Medicine, which later became a part of the Medical School of the University, has for many years conducted laboratory and field investigation on schistosomiasis. In recent years collaborative research in Puerto Rico has been fostered by the Department of Parasitology of the Medical School, the U.S. Army Tropical Research Medical Laboratory and the U.S. P.H.S. Puerto Rico Field Station. All of the laboratories in Brazil, Venezuela and Puerto Rico are in endemic schistosomiasis areas, where the laboratory findings are being tested in the field and clinic. They constitute the type of fundamental and applied scientific research which, on a more modest scale, might be undertaken in other endemic areas of schistosomiasis in the Americas.

X. SOME RESEARCH PROBLEMS IN SCHISTOSOMIASIS IN THE AMERICAS

Present inability to control schistosomiasis is linked largely with a past dearth of research effort which has been distinctly limited, for instance, when compared to the vast amount of investigation which has taken place in the field of malaria. As a consequence, answers are lacking for many of the vital questions which pertain to control. The following research problems are suggested as being some of the ones which are of most immediate concern and which have a bearing on the public health aspects of the disease.

1. Research on the Molluscan Intermediate Hosts.

(a) The preparation of a guide for the neotropical planorbids for use by public health workers involved in survey work and control programs of schistosomiasis in the Americas, as recommended by the PASB/WHO Working Group for the Development of Guidance for Identification of American Planorbidae Involved in Schistosomiasis at its meeting on 6 - 9 November 1961.

(b) Distribution of intermediate hosts and potential intermediate hosts with special reference to Brazil.

(c) Additional studies on the biology and chemistry of the aquatic environment to determine the factors conducive to snail harborage.

(d) Further evaluation of the role of *Australorbis tenagophilus* in transmission of the disease.

(e) The genetic and physiologic constitution of various strains of molluscan intermediate hosts in relation to their susceptibility to schistosome infection.

2. Research on the Control of the Molluscan Intermediate Hosts.

(a) Intensive effort to develop more efficient and cheaper molluscicides.

(b) New formulations of known effective molluscicides with synergists, spreading or emulsifying agents or other physical and chemical mechanisms to provide for more effective distribution and to promote residual activity.

(c) Biochemical and physiological studies to determine the mode of action of molluscicides.

(d) Research on more reliable methods for the automatic dispensing of molluscicides.

(e) Development of effective tests for the detection of low dilutions of molluscicides.

3. Research on the Parasite.

(a) Development of *in vitro* axenic cultures of *Schistosoma mansoni* to determine basic physiological and biochemical patterns, knowledge which would be of value in the development of new drugs aimed at destroying the parasite or inhibiting the egg laying capacity of the female.

(b) The significance of lower animal reservoirs in the transmission of the disease and their possible influence on control schemes.

4. Research Relating to the Human Host.

(a) Development of more effective and safer drugs without appreciable side effects for treatment of human schistosomiasis.

(b) Further studies on the mode of action of schistosomicidal drugs.

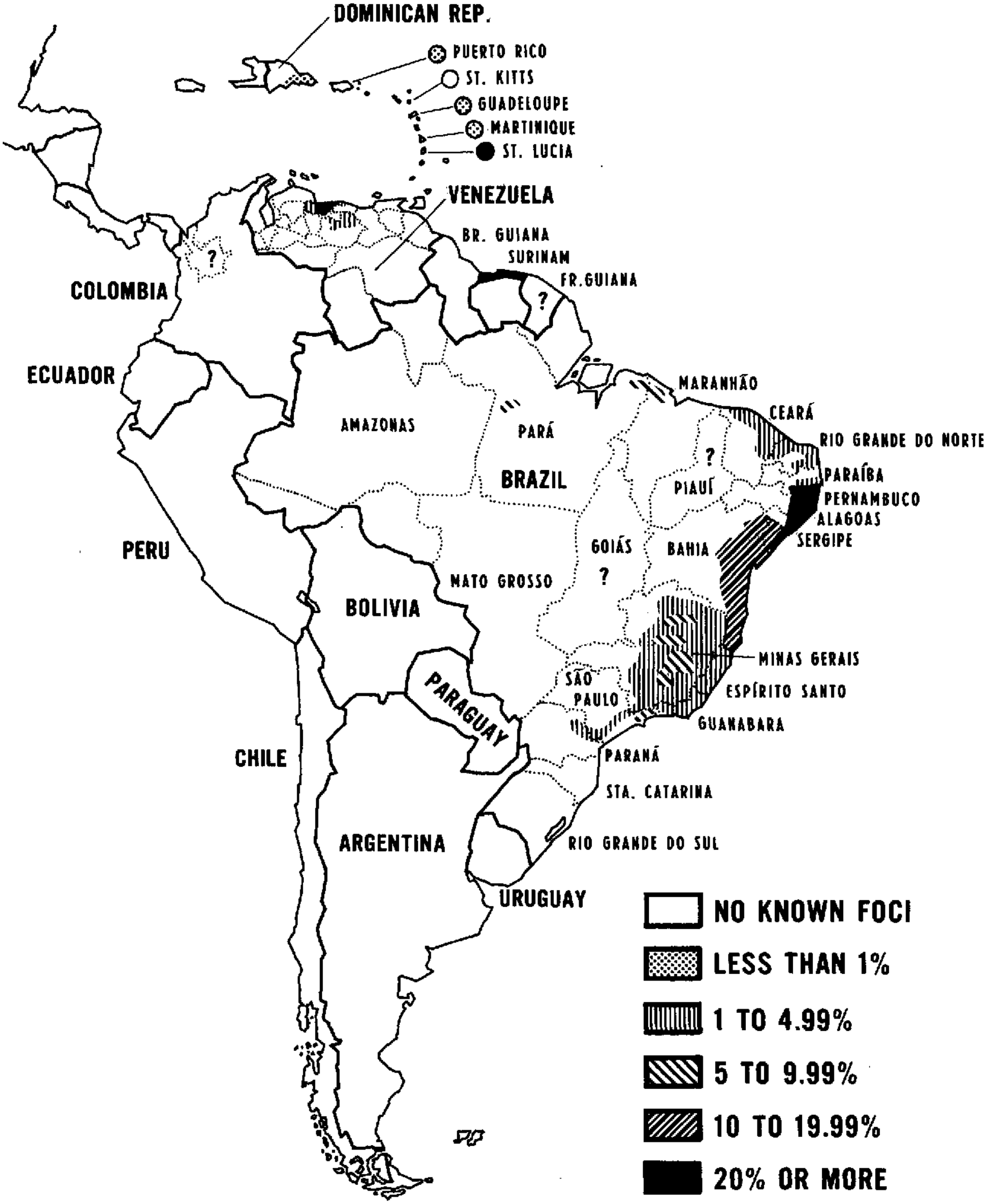
(c) Additional studies on the fluorescent antibody technique for the diagnosis of schistosomiasis and evaluation of its usefulness in epidemiological surveys.

(d) Studies on immune mechanisms in the human host.

(e) Carefully controlled group studies in a highly endemic area in which control measures are not operative to determine the effect of fortified diets on the symptomatology of the disease and the egg output of the female worms.

(f) Group studies to establish clinical gradient standards for schistosomiasis in the Americas to serve as a base line for determining the economic impact of the disease on the individual and the community.

DISTRIBUTION AND INTENSITY OF INFECTION WITH SCHISTOSOMIASIS MANSONI IN THE AMERICAS



POPULATION TRENDS OF AMERICAN COUNTRIES WHICH HAVE ENDEMIC FOCI

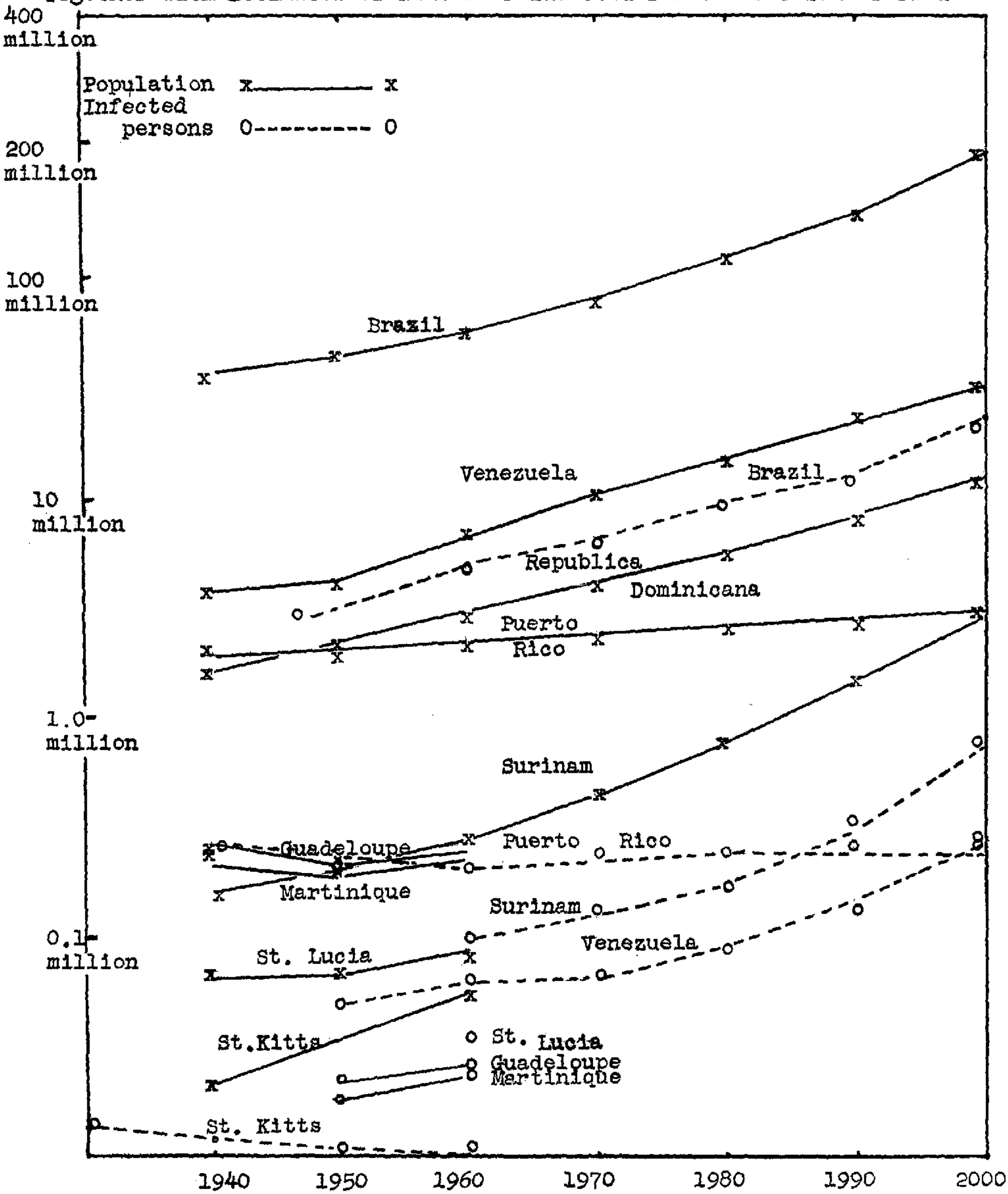
of

Schistosomiasis Mansoni

(From Census Figures of 1940-1960, with Extrapolation to 2000)
Together with Estimates of Number of Infected Persons
for the Same Period
(All Figures and Estimates in Millions)

Country	1940	1950	1960	1970	1980	1990	2000
BRAZIL							
popln.	41.356	51.976	66.302	90.000	135.000	215.000	400.000
infect.	2.800	3.220	5.000	6.850	9.500	15.000	28.500
VENEZUELA							
popln.	3.493	4.986	7.362	10.800	16.800	28.500	37.500
infect.	0.045	0.050	0.060	0.070	0.095	0.150	0.300
PUERTO RICO							
popln.	1.865	2.211	2.350	2.500	2.550	2.600	2.650
infect.	0.270	0.235 (1945)	0.235	0.250	0.255	0.260	0.265
SURINAM							
popln.	0.178	0.209	0.295	0.460	0.800	1.500	3.300
infect.	0.075	0.080	0.100	0.133	0.200	0.360	0.800
REPUBLICA DOMINICANA							
popln.	1.617	2.121	3.014	4.150	6.500	11.000	14.000
infect.	?	? 2 small foci (1952)	?	?	?	?	?
St. KITTS							
popln.	0.022		0.057				
infect.	0.011 (1932)	neg.	neg.				
St. LUCIA							
popln.	0.071	0.070	0.086				
infect.	*	0.035	0.036	*first case diagnosed 1925			
GUADELOUPE							
popln.	0.304	0.229	0.275				
infect.	?	0.018	0.0275				
MARTINIQUE							
popln.	0.247	0.237	0.275				
infect.	?	0.0143	0.0275				
TOTALS							
popln.	49.153	62.039	80.016	107.910	161.650	258.600	457.450
infect.	3.201	3.6523	5.4860	7.303	10.050	15.770	29.865

GRAPHS SHOWING POPULATION TRENDS IN AMERICAN COUNTRIES ENDEMIC FOR Schistosomiasis
(From Census Figures for 1940-1960, and Extrapolation to 2000)
Together with Estimates of Number of Infected Persons for Same Period



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