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Epidemiology and control of schistosomiasis

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Expert Committee

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Geneva, 6–10 November 1978

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EPIDEMIOLOGY AND CONTROL OF SCHISTOSOMIASIS

Report of a WHO Expert Committee

A WHO Expert Committee on Epidemiology and Control of Schistosomiasis met in Geneva from 6 to 10 November 1978. Dr I. D. Ladnyi, Assistant Director-General opened the meeting on behalf of the Director-General.

INTRODUCTION

Since the meeting of the WHO Expert Committee on Schistosomiasis Control in 1972 (*1*), many important advances have been made in the control of this disease. In recent years there has been a marked movement towards an integrated approach to control. There is now less reliance on single control techniques such as mollusciciding, much used in the past, and this has followed the development of improved chemotherapeutic drugs and the realization of the preventive value of the installation of domestic water supplies in endemic areas. Current integrated control methods employ all the available forms of chemotherapy, the latest mollusciciding techniques, methods to meet basic health needs such as the supply of potable water at village level and the provision of sanitation, as well as continuing health education and socioeconomic improvement.

The moves towards an integrated approach to control depend essentially on an accurate ecological assessment—of the human community and its parasitological characteristics, of the biology of the snail intermediate hosts, and of the physical and geographical characteristics of the environment. Man's behavioural attitudes and customs are being given increasingly greater attention because it has been realized that they may play a crucial role in the success or failure of a control programme.

Reliable and effective schistosomiasis control measures have now become available but the most suitable combinations of these measures, applicable in different habitats and under various conditions of schistosomiasis transmission, still need to be worked out. Further studies on the ways of ensuring community participation in control activities are also needed.

Control may be subdivided into disease control in the human population and transmission control of the biological cycle. Both are essential to the concept of total control of schistosomiasis.

The advances in chemotherapy during the past 10 years make it clear that drug treatment will play an increasingly important role in both disease control and transmission control. However, there is a need for much operational research in order to define the best ways of using the available drugs.

In these changing circumstances it is essential to know to what extent the control measures against schistosomiasis can be integrated into the general health services and particularly those at the primary health care level. It is also necessary to ascertain which of the highly specialized biological techniques involving bionomics and control of the intermediate hosts can be taught to health auxiliaries. It appears that the present shortage of skilled personnel in communicable diseases control will continue for some years.

An increase, sometimes marked, in the prevalence of infection frequently occurs in association with different water resources development schemes. The creation of man-made lakes, and the introduction of new irrigation schemes or the extension of existing ones in endemic areas or in areas adjacent to existing transmission foci, are significant factors in the spread of the infection. This highlights the importance of planning for prevention and control not only of schistosomiasis but also of other communicable water-related diseases in such schemes. Inadequate planning may result in the spread of the infection, and this may nullify some of the planned economic benefits owing to the increased costs of control.

1. EPIDEMIOLOGY

The control of schistosomiasis depends on a profound understanding of the epidemiology of the disease complex, and in particular of the biology, ecology, and distribution of the parasites, their snail intermediate hosts and mammalian reservoir hosts. A sound knowledge of the role of man in transmitting and maintaining the infection is also important. Moreover, the ultimate success of any control programme is dependent upon a full comprehension of the local socioeconomic conditions and upon the appreciation by the health authorities of the benefits of the proposed measures to the population living in the endemic areas.

In view of the considerable recent advances in all aspects of the epidemiology of schistosomiasis, it appears desirable to review the present status of our knowledge in order to reformulate our strategy for control.

1.1 The parasite

1.1.1 *Schistosome taxonomy and physiology*

Efforts to delimit schistosome species and to understand further the interrelationships that exist between species have been directed towards studies of the egg and cercarial and adult stages of the parasite. Human cases of "terminal-spined-egg" schistosomiasis, due to infection with *Schistosoma haematobium* or *S. intercalatum*, may be distinguished relatively easily on the basis of differences in the egg excretion pattern in urine and stool, the clinical symptoms, and, above all, the length/frequency curves of the eggs (*2, 3*). It is more difficult, however, to distinguish *S. intercalatum* from *S. matthei* on the basis of egg morphology since the eggs of these two species are similar in size, though slightly different in shape (*4*). Differential staining techniques (Ziehl-Neelsen) appear to be of some use in distinguishing the eggs of *S. intercalatum* from those of *S. matthei* and *S. haematobium* in tissue sections (*5, 6, 7*).

The specific identification of cercariae may be of some practical interest in epidemiological surveys and several techniques have been developed for this purpose. The most frequently used technique is the enumeration and distribution of the argentophilic papillae. Several studies indicate that the number and distribution pattern of these presumably sensory organs on the cercarial body are relatively constant within one species and sufficiently different from those in other species to be taken as characteristic. Employing this technique, it has been possible to separate clearly cercariae of the *mansoni-rodhaini* group from those of the *haematobium-bovis* group (*8*), and a clear difference has been found between cercariae of *S. rodhaini* from Kenya and those of *S. mansoni* from Kenya and Brazil (*9*). The use of histochemical techniques has further demonstrated differences in the pre- and postacetabular glands of *S. mansoni* and *S. haematobium*, on the one hand, and *S. japonicum*, on the other (*10*). Isoenzyme techniques also show promise in differentiating cercariae,

particularly in distinguishing *S. haematobium* from *S. matthei* (*11, 12*).

Hybridization of adult worms in the definitive host and its implications on both the taxonomy of the various species and their transmission is of considerable interest and importance. Data supporting the hybridization of *S. matthei* and *S. haematobium* and of *S. intercalatum* and *S. haematobium* have given rise to speculations concerning the nature of these forms as "true" species. At present no information exists on the hybridization of *S. japonicum* strains, except, perhaps, for a possible hybrid between *S. japonicum* and *S. incognitum* in parts of Indonesia where the two parasite species are sympatric not only in geographical area but also in definitive hosts.

Recent data from Ghana suggest that two strains of *S. haematobium* formerly utilizing either *Bulinus truncatus rohlfsi* or *B. globosus* as intermediate hosts may have hybridized and that *B. t. rohlfsi* in Lake Volta may be able to transmit both these strains. Similarly, the spread of *S. intercalatum*, one strain of which normally utilizes only snails of the *B. forskalii* group, may now be adapting to the snails of the *B. africanus* group as a consequence of hybridization. An increase in the susceptibility of *Biomphalaria tenagophila*, noted recently, suggests that hybridization may be occurring in the Brazilian strains of *S. mansoni*.

The role of hybridization of parasite strains with respect to the response of the resultant hybrids to chemotherapeutic agents has not been adequately studied.

1.1.2 *Relation between intermediate snail hosts and parasites*

Although early studies on snail host–parasite relationships indicated relatively direct and uncomplicated interactions, recent observations on the interrelationships between many species and strains of *Schistosoma* and their actual or potential snail hosts have demonstrated a remarkable degree of variation in infection rates, duration of infection, cercarial production, and snail mortality due to infection.

In the early studies emphasis was placed on the varying susceptibility of the snail species, but later it became clear that schistosome infectivity was equally important. Recent research has confirmed this reciprocal approach, but because of the lack of standardized materials and methodologies, valid comparison of data has seldom

been possible. It has therefore become desirable to develop an objective quantitative measurement of compatibility between snails and parasites of known biological characteristics tested under standardized conditions.

Studies to elucidate the mechanisms governing compatibility between the parasite and intermediate host have been undertaken only recently. It has been postulated that miracidia can escape the defence mechanisms of the snail by covering themselves with snail host proteins. If the larval schistosome fails to mask its presence in the snail host, it is rapidly destroyed. The snail's response to alien material has been known for some years, but detailed knowledge of snail–parasite immune processes is still inadequate and warrants continued study.

Compatibility between the parasite and intermediate snail host is largely governed by genetic factors. Recent experiments involving *Biomphalaria glabrata* populations and a known strain of South American *S. mansoni* made it possible to categorize the snail populations according to their infection rates; some were susceptible and some refractory, others were susceptible when juvenile but refractory when adult, and a fourth category was susceptible in the juvenile stage but revealed varying degrees of susceptibility in the adult stage. The juvenile susceptibility status was determined by a complex of four or more genes; accordingly, genes for the lack of susceptibility may be present even in susceptible snails and vice versa.

During the present decade research on the interactions between *S. japonicum* and *Oncomelania* spp. has been relatively modest in comparison with the many interesting findings of earlier years. However, recent studies have shown that the intermediate host spectrum and pathogenesis in the definitive host can be altered by passage through the snail host and that the sex of the snail has no influence on the sex of the schistosome. Interesting studies have been conducted on the differences between populations of schistosomes and snails in the Philippines and China (Province of Taiwan). The most dramatic finding, however, has been the discovery in the Mekong river area of Indochina of a new strain of *S. japonicum* for which the intermediate host is *Tricula aperta*, an aquatic species distantly related to *Oncomelania*. Three races of *T. aperta* have been described, each of which shows a significant variation in compatibility with the newly found strain. Laboratory experiments have shown that this strain cannot infect *Oncomelania* spp. and it is also

unlikely that *T. aperta* can be infected by other *S. japonicum* strains.

Experiments have confirmed that all *Biomphalaria pfeifferi* populations are highly compatible with all known *S. mansoni* strains; however, other African *Biomphalaria* species display marked differences in compatibility with various *S. mansoni* strains.

The South American *S. mansoni*, probably the most studied of all schistosomes, shows excellent compatibility with most *B. glabrata* populations, with by far the highest known production of cercariae per snail, but in some localities in Brazil refractory populations also occur. Two other *Biomphalaria* species (*B. straminea* and *B. tenagophila*) in South America can function as important intermediate hosts, but they generally reveal a poorer compatibility with the local schistosome strain than does *B. glabrata.*

Although *S. haematobium* is considered to be a single species, it is believed that several strain variants exist. The two major strain variants are *truncatus*-borne and *africanus*-borne. A third strain has been described for which members of the *forskalii* group act as intermediate snail hosts. Recent laboratory and field observations have shown that a *truncatus*-borne *S. haematobium* exists on the west coast of Africa as far south as Zaire. In East and central Africa there is a diploid *Bulinus truncatus*-like snail from Southern Rhodesia, as well as the normal tetraploid *B. truncatus* from Malawi, Kenya, and United Republic of Tanzania, all highly susceptible to the North African *S. haematobium.*

S. intercalatum has been the subject of considerable research during recent years and two distinct strains have been recognized—*forskalii*-borne from Gabon and the United Republic of Cameroon and *africanus*-borne from central Zaire.

1.1.3 *Animal hosts of human schistosomes*

Many kinds of animals are found naturally infected with *Schistosoma japonicum, S. mansoni, S. intercalatum,* and *S. haematobium*; however, their role as reservoir hosts, especially of those schistosomes producing terminal-spined eggs, in maintaining the infection in nature and in serving as a source of material for infecting the snail hosts is in most situations minimal. In assessing the epidemiological importance of those nonhuman hosts, the following factors must be

considered: (1) the ability to produce viable eggs; (2) the number of eggs produced; (3) the hatching rate of eggs produced; and (4) the infectivity of miracidia derived from the eggs.

Recent data on infections of nonhuman mammalian hosts by human species of schistosomes indicate that, in addition to the existence of several reservoir hosts of *S. japonicum* (among which are dogs, cats, cattle, pigs, sheep, goats, water buffaloes, and horses), wild rodents may, in some areas, be of considerable importance in the dissemination of *S. japonicum* infection. The dog appears to be a reservoir of the new *S. japonicum* strain found in the Mekong river area. The epidemiological significance of rodents as reservoirs of strains of *S. mansoni*, especially in South America, some Caribbean islands, and in parts of central Africa, should be studied more closely. For example, recent records of rodents being infected with *mansoni*-type schistosomes in Brazil and Guadeloupe raise the question of the possible existence of *S. rodhaini* in the Americas, and of the possible role of these rodent strains in the epidemiology of schistosomiasis due to *S. mansoni*.

It should be noted that frequently common or nonspecific terminology has been used in designating animal hosts, a practice which may result in undue confusion and hinder comparative insight. The Latin or scientific name should always be given wherever there is a danger of misinterpretation.

1.2 The snail intermediate host

1.2.1 *Snail taxonomy and classification*

In the control of the snail intermediate hosts of schistosomiasis a sound taxonomy is vital. To this end, malacologists have employed, during the past decade, a variety of techniques for delimiting and identifying the nominal snail species. These include elaboration of shell and internal morphology (particularly of the genital system); karyotypic analysis; utilization of electrophoretic and electrofocusing techniques employing egg, haemolymph and tissue extracts; chromatographic analysis; and immunological procedures. Although considerable progress has been made in snail taxonomy and classification employing the above-mentioned techniques (singly or in combination with one another), the difficulties inherent in the various techniques have not always been fully appreciated and the samples

and controls considered to be adequate are frequently below the optimum level. Thus, there is a need for cautious interpretation of the available data and for more rigorous comparative studies.

Table 1. Classification of snail hosts of oriental schistosomes along with other closely related taxa

Subclass: Prosobranchia	
Superfamily: Rissoacea	
Family: Pomatiopsidae Stimpson, 1865	
Subfamily: Pomatiopsinae Stimpson, 1865	
Genus: *Oncomelania* Gredler, 1881	
O. minima (Bartsch, 1936)	Japan
O. hupensis (Gredler, 1881) [a]	
O. h. chiui (Habe and Miyazaki, 1962)	China (Province of Taiwan)
O. h. formosana (Pilsbry and Hirase, 1905) [a]	China (Province of Taiwan)
O. h. hupensis (Gredler, 1881) [a]	China
O. h. lindoensis (Davis and Carney, 1973) [a]	Indonesia (Sulawesi)
O. h. nosophora (Robson, 1915) [a]	Japan
O. h. quadrasi (Möllendorff, 1895) [a]	Philippines
Subfamily: Triculinae Annandale, 1924	
Tribe: Triculini Davis, 1978	
Genus: *Tricula* Benson, 1893	Asia
T. aperta (Temcharoen, 1971) [a]	Mekong River Lao People's Democratic Republic Democratic Kampuchea

After DAVIS, G. M. *The origin and evolution of the gastropod family Pomatiopsidae, with emphasis on the Mekong River Triculinae.* Monograph of the Academy of Natural Sciences of Philadelphia (in press).

[a] Snail hosts actually transmitting their respective parasites in nature

Hosts of S. japonicum. The present status of the snail hosts of *S. japonicum* and other closely related species is given in Table 1. *S. japonicum* is transmitted by populations of polytypic *Oncomelania hupensis* and the new strain of *S. japonicum* found in the Mekong river area is transmitted by *Tricula aperta* (= *Lithoglyphopsis aperta*). Population variants occur in the subspecies of *O. hupensis.* The physicochemical differences in these variants can be detected by electrophoresis and their biological differences can be appreciated by investigation of their potential in transmitting the infection. The identity of the snail hosts transmitting *S. japonicum* infection in Borneo and Peninsular Malaysia is not known.

Hosts of S. mansoni. The genus *Biomphalaria* is represented in the Americas by about 20 species, of which 15 have been well defined by

morphological (conchological plus anatomical) criteria, the definition being substantiated in especially difficult cases by genetic criteria (crossbreeding experiments). Of these 15 well defined species, only *B. glabrata, B. straminea,* and *B. tenagophila* have been found naturally infected with *S. mansoni.* Several additional species have been implicated as experimental hosts, but the taxonomic status of some of these is questionable. Of the three species found naturally infected, *B. glabrata* appears to be the most efficient in terms of transmission. Populations of both *B. glabrata* and *B. tenagophila* show considerable variation in levels of susceptibility in different geographical areas.

The taxonomy of the African species has, to some extent, lagged behind that of the American forms, which can be identified with a greater degree of confidence. There has been little change, in fact, in the taxonomic status of African biomphalarids during the past two decades, and most workers still follow the classification proposed by Mandahl-Barth (*13*), in which the genus is divided into four species groups: (1) the *pfeifferi* group, (2) the *alexandrina* group, (3) the *choanomphala* group, and (4) the *sudanica* group. These groups comprise a total of nine nominal species, as follows: *B. alexandrina* (Ehrenberg, 1831); *B. angulosa* (Mandahl-Barth, 1957); *B. camerunensis* (Boettger, 1941); *B. choanomphala* (Martens, 1879); *B. pfeifferi* (Krauss, 1848); *B. salinarum* (Morelet, 1868); *B. smithi* (Preson, 1910); *B. stanleyi* (Smith, 1888); and *B. sudanica* (Martens, 1870). Several of these species comprise numerous subspecies. The validity of many of the subspecies is questionable and many of the named forms may be no more than ecophenotypes. The taxonomic status of the African species of *Biomphalaria* requires further careful evaluation.

The relationship between the African species of *Biomphalaria* and *S. mansoni* may parallel the relation that occurs in the Americas, and more studies are desirable. While, in general, all the African species are susceptible to infection with at least some strains of *S. mansoni,* there are indications that levels of susceptibility may vary considerably among populations of a particular species.

Hosts of S. haematobium. The taxonomy of the snail hosts of *S. haematobium* is particularly complex and is, to some extent, in a state of flux. At present, the genus *Bulinus* has been subdivided into two subgenera comprising a total of four species-groups or complexes as shown in Table 2.

Table 2. Species recognized in the subgenera *Bulinus* and *Physopsis*, arranged within groups in alphabetical order

1. Subgenus *Bulinus* Müller, 1781
   - 1.1 *B. forskalii* group
     - *B. bavayi* (Dautzenberg, 1894) [a]
     - *B. beccarii* (Paladilke, 1872) [b]
     - *B. camerunensis* (Mandahl-Barth, 1957) [b]
     - *B. canescens* (Morelet, 1868)
     - *B. cernicus* (Morelet, 1867) [b]
     - *B. crystallinus* (Morelet, 1868)
     - *B. forskalii* (Ehrenberg, 1831)
     - *B. scalaris* (Dunker, 1845)
     - *B. senegalensis* (Müller, 1781) [b]
   - 1.2 *B. reticulatus* group
     - *B. reticulatus* (Mandahl-Barth, 1954) [a]
     - *B. wrighti* (Mandahl-Barth, 1965) [b]
   - 1.3 *B. truncatus/tropicus* complex
     - *B. angolensis* (Morelet, 1866)
     - *B. coulboisi* (Bourguignat, 1888)
     - *B. depressus* (Haas, 1936)
     - *B. guernei* (Dautzenberg, 1890) [b]
     - *B. hexaploideus* (Burch, 1972)
     - *B. liratus* (Tristram, 1863)
     - *B. natalensis* (Küster, 1841) [a]
     - *B. nyassanus* (Smith, 1877)
     - *B. octoploideus* (Burch, 1972) [a]
     - *B. permembranaceus* (Preston, 1912)
     - *B. rohlfsi* (Clessin, 1886) [b]
     - *B. succinoides* (Smith, 1877)
     - *B. transversalis* (Martens, 1897)
     - *B. trigonus* (Martens, 1892)
     - *B. tropicus* (Krauss, 1848)
     - *B. truncatus* (Audouin, 1827) [b]
2. Subgenus *Physopsis* Krauss, 1848
   - 2.1 *Bulinus (Physopsis)* complex (= *africanus* species group)
     - *B. abyssinicus* (Martens, 1866) [b]
     - *B. africanus* (Krauss, 1848) [b]
     - *B. globosus* (Morelet, 1866) [b]
     - *B. hightoni* (Brown & Wright, 1978) [a]
     - *B. jousseaumei* (Dautzenberg, 1890) [b]
     - *B. nasutus* (Martens, 1879) [b]
     - *B. obtusispira* (Smith, 1882) [b]
     - *B. ugandae* (Mandahl-Barth, 1954)
     - *B. umbilicatus* (Mandahl-Barth, 1973)
     - *B. obtusus* (Mandahl-Barth, 1973)

Partly after BROWN, D. S. *Freshwater snails of Africa. The composition and distribution of a fauna with special reference to medical and veterinary importance.* London, Taylor and Francis (In press).

[a] Species compatible to some degree with *S. haematobium* in the laboratory.

[b] Species known to serve as natural intermediate hosts of *S. haematobium*.

Members of the subgenus *Bulinus* present difficult taxonomical problems owing to their unstable characteristics and the occurrence of intermediate forms. Efforts to resolve these problems by electrophoretic or karyotypic techniques have not been entirely satisfactory. This subgenus appears to be playing an increased part in the transmission of the disease in Africa.

The significance of *Planorbarius metidjensis* in certain areas bordering the western Mediterranean and of *Ferrissia tenuis* in India requires further evaluation.

1.2.2 *Genetic aspects*

Genetic studies on host snails have been largely limited to studies of clonal populations of *Biomphalaria glabrata* (see section 1.1.2). To date, twelve types of *B. glabrata* with genetically different susceptibility to infection by *S. mansoni* have been derived by testing and selection.

Susceptibility in a snail population is a dynamic process subject to change by mutations or shifts in gene frequencies. If genetic changes result in a less susceptible snail population, then survival of the endemic parasite strain may depend on increased parasite infectivity through genetic changes. Such changes may affect the relation of the parasite strain to human hosts. Crossing experiments indicate that some of the genetic differences in snail susceptibility are determined by gene complexes while others are determined by single genes. It should be noted, however, that, although stocks of either susceptible or resistant snails have been derived, they do not continue to breed true over long periods of time.

Efforts to study population genetics by means of isoenzyme analysis are in their infancy, although studies in Brazil indicate that this type of analysis permits the detection of basic differences in gene frequencies among populations of *B. glabrata* and *B. tenagophila.*

1.2.3 *Snail physiology*

During the past 2–8 years, a limited number of studies have been undertaken in efforts to understand the physiological consequences and the mechanisms of action of molluscicides on the intermediate host. These investigations have been mainly oriented towards the study of intermediary metabolism, structure-activity relationships,

physiological effects, and resistance. Although to date these types of studies have provided only limited data, they should be encouraged as they offer promise in aiding the development of more specific and effective chemical control agents.

The recent documentation of molluscicide resistance in *Bulinus truncatus* has caused considerable concern; the phenomenon is reported to have occurred in a population from the Gezira, Sudan (*14*), where trifenmorph was used for several years. In view of these observations, a test kit for the detection of molluscicide resistance is under development and will soon become available through WHO. However, recent trends towards the focal application of molluscicides rather than blanket or area-wide dispersal may impede the development of resistance.

In addition to studies associated with the effects of molluscicides, a number of investigations of snail physiology have been undertaken recently and have provided data that may considerably enlarge our understanding of snail biology and the transmission of infection. As a result of these investigations there have been advances in the maintenance of snail tissue-culture systems, the clarification by ultrastructural studies of the encapsulation process in the snail's defence mechanism, the identification of the "pore cell" as the site of haemoglobin synthesis, and the identification of the haemopoetic organs that produce amoebocytes.

1.2.4 *Snail ecology*

More information on the ecology of snail intermediate host populations and schistosome transmission is needed in order to establish general guidelines for control that can be applied to a variety of habitats in broad climatic or geographical zones. Such information will be particularly useful in planning major water resources development projects. Moreover, the marked difference between the ecology/biology of the amphibious hydrobiid snail hosts of *S. japonicum* and that of the aquatic intermediate hosts of the other human schistosome species, have significant implications that are especially relevant to the choice of control methods.

The chief priority in snail biology and intermediate host–parasite studies is the definition of the locations and the time patterns of transmission within any particular area.

Studies of the ecology, bionomics, and population dynamics of the snail host are usually necessary for planning any measures against

it and much more specific data are required if cost-effective methods involving habitat modification and environmental changes are to be applied.

Studies of the *total* populations of snails involved in a given transmission area have been few. While more studies of this nature would be desirable, it will be necessary to solve certain problems such as sampling bias, measurement of total volume of habitat, and assessment of the proportion of snails potentially exposed to transmission.

The second need—a more important one in practice—is for the collection and analysis of valid data on the proportion of snails infected. This is typically lower when based on shedding, especially in flowing water. Since the mortality of infected snails may be significantly greater than that of uninfected ones and since the incubation period of infection may be long in relation to expected snail survival in several places, the proportion of snails actually infected may greatly exceed the proportion shedding cercariae. However, by making separate life-tables for infected and uninfected snails it may be possible to estimate the actual proportion of snails infected. True incidence and prevalence of infection in snails must be known in order to understand the factors regulating transmission, and thus to predict the consequences of different approaches to control. In particular, the value of improved disposal of human excreta as a control method, especially for intestinal schistosomiasis, depends heavily on the rate of infectivity among snails.

A thorough understanding of snail ecology is also a basic requirement for the success of control measures relying heavily on appropriate technology implemented by the community on a self-help basis. Experience in malaria has clearly shown the need for sophisticated knowledge wherever simple control techniques are to be successfully applied. In this context it is essential to relate snail habitats to sites of pollution and of human exposure to water if the transmission pattern is to be understood for control purposes.

Understanding of snail ecology in relation to water resource development is greatly needed to guide preventive measures. More attention must be given to small-scale water development projects since information gained from a few such projects may be applied to many more in the same region, whereas the necessary studies on large man-made lakes have less application outside their own basins simply because such large developments are not locally replicated.

1.3 Human infection

1.3.1 *Epidemiological models*

Considerable interest in mathematical models of schistosome transmission and their relevance to control strategy has been generated by the original work of Hairston(*15*) and Macdonald(*16*). A useful predictive model of the whole life cycle has not yet been developed, but work towards this goal has clarified epidemiological understanding and has led to the development of useful submodels of parts of the cycle. Key features of Macdonald's model were the bisexual nature of the parasite and the regulation of the parasite population by snail saturation. Recent work has reconstructed the detailed functioning of that model, allowing for the latent period prior to cercarial release as well as for the survival of infected and uninfected snails to differ.

Some qualitative features of transmission that are now understood relate to breakpoint and threshold behaviour. Two types of areas are defined—one where transmission is entirely impossible and one where transmission is possible but need not necessarily occur. A control scheme that changes an area from being capable of supporting transmission to being incapable of supporting any transmission at all is said to have passed a threshold and is thought to have lasting effect. Any scheme that eliminates transmission (by changing the values of variables) but does not render the area incapable of future transmission is said to have passed a breakpoint and is not thought to have a lasting effect.

The influence of various properties of models is studied more by the effects on breakpoint and threshold behaviour and less by the numerical accuracy of predictions. Factors of greatest influence are immigration and emigration of infection, aggregation of worms in hosts, and spatial heterogeneity of contact with infection. It is expected that immunity will have drastic effects but an adequate model is not yet available.

An important consequence of the bisexual nature of the parasites was formerly held to be that, even if the level of transmission factors (such as snails, water contact, and pollution) still allowed potential transmission, the infection would die out if the worm population in man fell felow a critical level. It has recently been shown, however, that this level is more sensitive to deviations of the worm distribution in man away from the Poisson distribution than had been previously realized. The expectation that a reduction of infection in man to a

low level would be followed by natural extinction is thus weakened.

The prediction from Macdonald's model that sanitation is an ineffective control approach depends upon the very high transmission to snails assumed rather than upon the model structure. His conclusion therefore has no general validity.

Simpler submodels of snail populations have been used to optimize the times of molluscicide. One such model has been of value in predicting prevalences of schistosomiasis in irrigation schemes in Iran.

More work on the various transmission factors needed to construct predictive models is warranted, and the incorporation of more realistic assumptions on snail population dynamics will also be of benefit. Furthermore, the phase of transmission within the human host, from cercarial penetration to egg release, may alter the qualitative behaviour of transmission considerably.

In future, the development of models will need to be more closely linked to the recorded data, and factors such as seasonal variation of transmission, immune phenomena, and differences in transmission situations will have to be taken into account.

1.3.2 *Resistance and the immune response*

The last decade has seen an immense output of experimental work on acquired resistance to schistosomiasis, using a wide range of animals from mice to cattle. The occurrence of acquired resistance has been clearly demonstrated and the complex mechanisms involved have been partly analysed. Understanding of the phenomenon in man has developed slowly by comparison because direct experimentation is ethically impossible and because the interpretation of reductions in egg output with increasing age in natural epidemiological conditions is confused by parallel changes in human water contact. It is thus still possible to maintain that there is no direct evidence proving that man acquires resistance to schistosomiasis. Nevertheless epidemiological evidence suggests that some degree of immunity to *S. haematobium, S. japonicum, S. intercalatum* and, possibly, *S. mansoni* occurs in man, but whether it is a factor providing a significant degree of control of the prevalence and intensity of infection remains uncertain. More epidemiological studies combined with precise measurements of water contact are necessary if these important questions are to be answered.

There is a complex relation between the intensity and duration of infection in man and the type and degree of immune response. The probability of a positive intradermal or serological test in infected children tends to be proportional to the intensity of the infection, whereas almost all infected adults will show positive tests.

1.3.3 *Man-made water resources*

In the past decade many water resource development programmes, were undertaken in endemic areas of the Eastern Mediterranean region, Africa, South America, and Asia, and during this period an increase has been observed in the transmission of communicable diseases, particularly of schistosomiasis, in the areas around man-made lakes and irrigation schemes. In view of this situation, concern must be expressed at the apparent lack of adequate interdisciplinary consultations at the planning stage in many such programmes.

While it is realized that governments are mainly concerned with the economic returns from such resource development projects, it must be emphasized to them, as well as to the international agencies and to development banks, that real economic returns may be seriously jeopardized by disease transmission resulting from failure to make provision for human welfare within the programmes at the planning stage. The lending agencies, by requiring, as a condition of the loan, that adequate measures for schistosomiasis prevention be made an integral part of the plans, can encourage the necessary cooperative action.

1.3.4 *Epidemiological studies*

Increasingly, epidemiological studies of populations in endemic areas of schistosomiasis are using standard quantitative methods to determine both the intensity of infection and morbidity. The use of these methods furthers the understanding of the relationship between intensity of infection and morbidity by allowing comparisons between different geographical areas. They will also provide reliable baseline data for studies on chemotherapy, malacology, sociology, and contamination patterns in defined communities and will provide information on the transmission potential of different population subgroups, which may be utilized in devising operational and assessment strategies for schistosomiasis control.

Selection of populations. Epidemiological studies are best undertaken jointly by research institutions and the agencies concerned with schistosomiasis control. To determine the precise control methods to be used it is necessary to carry out large population studies, which require a substantial research infrastructure.

Because schistosomiasis transmission is often focal it should be studied in small communities; such studies have several advantages. In small communities the entire population can be examined and short-term follow-up is facilitated. These communities also provide an excellent means of testing the guidelines for control programmes.

Since the meeting of the WHO Expert Committee on Schistosomiasis Control in 1972 epidemiological studies using quantitative methods have been reported from areas where *S. mansoni* and *S. haematobium* are endemic, but few studies on *S. japonicum* have been reported.

Quantitative methods of determining the presence and intensity of infection. Quantitative faecal and urine examination techniques have in recent years replaced qualitative procedures in community studies of schistosomiasis because of the useful information provided by quantitation of egg output. The sensitivity of the method used should be tested and the results expressed in terms that allow comparison with other studies—e.g., arithmetic mean, geometric mean or Williams' mean, and median egg output. In this connection, recovery studies, such as adding a known number of eggs to uninfected faeces or urine and determining the proportion of eggs recovered by the method, are indicated.

Filtration, thick smear, or concentration techniques are recommended for detecting *S. mansoni* infections; any of the three techniques may be used depending on personal preference, available laboratory support, and the objectives of the epidemiological studies. For *S. japonicum* infections, modified thick smear and concentration techniques are recommended, while for *S. haematobium* infections filtration methods with paper or synthetic filters are recommended.

Miracidial hatching tests for *S. haematobium* and *S. mansoni* have been advocated for longitudinal evaluation of efficacy of chemotherapy or in control efforts in large populations; however, they have not been used in epidemiological studies or compared with quantitative egg counts in populations.

Immunological techniques. Immunodiagnostic techniques are of two types—those that depend on cutaneous hypersensitivity and those based on the detection of serum antibodies. The intradermal tests currently available correlate poorly with parasitological observations, and so their use in epidemiological studies is limited.

Currently available serodiagnostic tests have limited specificity, which restricts their widespread use for epidemiological studies and individual diagnosis. Biochemical and immunological characterization of standard and specific antigens and the availability of such characterized antigens for immunodiagnostic tests in schistosomiasis command high priority in research. Nevertheless, under conditions of low transmission or where the tests correlate with parasitological observations, serological tests can be used and may facilitate epidemiological survey work, particularly as recently developed tests can be performed on blood from a finger-prick.

Standardization and quality control of egg counting techniques. Little progress has been made either in standardization of egg-counting techniques or in developing methods to increase the comparability of results from different techniques. Sensitivity of the diagnostic method is the most important criterion for the comparison of results by different techniques and has a profound effect on all population measures of egg output—prevalence, incidence, intensity, and other related indices. In addition to the validation of the microscopist's ability, comparison of different methods should take into account the amount of excreta examined, the number of eggs present, and the randomness of distribution of eggs in the specimen.

Criteria for selection of the most appropriate parasitological technique for a given study are not well developed. In general, a technique should be sufficiently sensitive to minimize the occurrence of false negative results; for populations with light infections, high sensitivity of the technique is essential. However, when transmission is intense or when it is desired to detect those individuals in a population who have high egg output and are thus most at risk of pathological complications, the use of a less sensitive parasitological technique may be appropriate.

The control of the accuracy and reliability of egg counts in large-scale epidemiological studies has been a major concern. Recently a quality control method based on missed positive specimens has been introduced, but the limitations of this approach in areas of low prevalence are recognized. Application of high standards of quality

control should be encouraged in all laboratories in the collection of specimens, maintenance of equipment, systematic checking of egg counts, and labelling.

Measurement of morbidity. Epidemiological studies in communities of different endemic areas with varying intensities of *S. mansoni* infection have clearly demonstrated a positive correlation between egg output and prevalence of clinically diagnosed disease. Such studies have led to improved reproducibility and comparability of methods of measuring morbidity. In recent years few studies have been published on morbidity due to *S. haematobium* infection and no such studies on *S. japonicum* are available. New field methods for evaluation of urinary tract morbidity in *S. haematobium* infections, such as portable isotope renography, would be useful.

Mortality data. Data on mortality due to schistosomiasis have not appeared even in countries with relatively developed health infrastructures and vital statistics systems.

Behavioural studies. Studies to quantitate human contact with water and other behavioural studies directed at determining the pattern of faecal and urinary contamination in communities are highly desirable. Human population movements also need to be studied because they may influence the patterns of transmission and confuse analyses, especially when longitudinal studies are involved.

Snail studies. Cross-sectional and longitudinal determination of the distribution, density, and infection rates of snail intermediate hosts should be an integral component of all epidemiological studies in communities. Contamination may be conveniently monitored by the use of sentinel snails.

2. CONTROL

2.1 General situation

The most recent estimate of the global prevalence of schistosomiasis has been 200 million cases. Since this estimate was arrived at, the world population has continued to increase with an enlargement, in most endemic areas, in the lower strata of the population pyramid, i.e., an increase in the age-groups known to have the highest prevalence of disease and to be most responsible for transmission. Concomitantly, worldwide demand for water has resulted in the spread of schistosomiasis to new areas, and the overall infection rate appears to have increased. It is clearly desirable to

obtain some idea of global prevalence as well as of the prevalence and incidence of disease in discrete endemic areas. To this end, WHO has recently attempted to obtain the necessary data by the following means.

Information was requested from 121 countries in 1976 with respect to the endemicity of schistosome species, the population at risk, and the nature of existing control programmes (e.g., budget, methods of control, agents employed, and individuals tested). Ninety-five countries responded (78%), and the results are being analysed and prepared for publication. Efforts have also been made to collate available information from various sources on both prevalence and incidence of schistosomiasis in selected endemic areas. The present compilations have been derived from the literature covering the years 1969–77, in both English and French, and from the literature and government agencies of 19 selected African countries. This information is similarly being prepared for publication.

Until a more precise picture of the schistosomiasis situation becomes available, it may only be stated in general terms that projects for water-resources development have exacerbated transmission in many endemic areas during the past decade and that schistosomiasis is continuing to spread in many parts of the world. Evidence of the relationship between intensity of infection and morbidity has been established in many places and authorities are becoming aware of the public health significance of the disease and are beginning to accord it some priority in relation to other health problems for purposes of planning and allocation of resources.

There is ample evidence that snail control by area-wide mollusciciding has been successful in some control programmes and that transmission control of the disease foci has been achieved by mollusciciding and surveillance. Those responsible for undertaking control measures should realize that schistosomiasis control will require sustained efforts over a long period of time.

It is essential that control measures should be identified and applied in order to achieve effective control over short, medium, and long periods. It is probable that molluscicides will continue to play a role in the integrated control of schistosomiasis.

2.2 Review of progress in selected national control programmes

The Committee reviewed reports from 12 countries or areas —Brazil, Egypt, Iran, Iraq, Kenya, Morocco, Puerto Rico, St Lucia,

Saudi Arabia, Swaziland, Tunisia, and Venezuela—and general summaries of programmes in China and the Caribbean. Although critical analysis of reported progress must await the presentation of detailed quantitative data, there is no doubt that in many instances real progress has been made in the reduction of both the incidence and the prevalence of the disease. As noted in section 1.3.4, it is hoped that standardization and the quality control of evaluation techniques will be used widely in schistosomiasis programmes.

In the following progress reviews the cost analyses cited may not always be comparable owing to different methods employed in the computations.

(1) *Brazil.* Although pilot control projects, using only molluscicides with niclosamide, have been conducted both in areas of natural drainage and in those with primitive irrigation in Belo Horizonte, São Lourenço, and Taquarendi (Bahia), the deficiencies of the control tools and the high capital costs of environmental modifications prevented ongoing campaigns from having the intensity and continuity necessary to achieve lasting success.

In 1975, the Ministry of Health, through the Department of Public Health Campaigns, began a prevalence survey using the Kato technique on one stool in the 7–14-year-old age-group in a randomly selected sample of counties. Simultaneous snail collections were made with the object of achieving a nationwide taxonomic classification of the intermediate hosts.

A national schistosomiasis control programme was launched in 1976 using chemotherapy with oxamniquine, environmental sanitation improvement techniques, and selective molluscicides. The programme was allotted 1 750 million cruzeiros (approx. US $195 million)[1] up to 1979.

Under this programme, the Special Public Health Services Foundation is responsible for the improvement of environmental sanitation in endemic areas and this involves the provision of rural water supplies, showers, laundry facilities, and privies.

The Special Programme for the Control of Schistosomiasis is responsible for stool surveys, malacological collections, and the provision of chemotherapy. In areas where prevalence is over 20%, chemotherapy is given to the total population; where prevalence is between 5% and 19%, only people aged 5–25 years are treated; and where prevalence is 4% or less, only positive cases are treated.

[1] At the December 1975 rate of exchange, US $1 = 9 cruzeiros.

The campaign started in the north-east of Brazil where the endemic area consists of 8 states (270 counties), extends over 85 421 km^2, and has an estimated population of 4 783 000. To date 71 counties are in the attack phase and more than one million people have been treated.

(2) *Egypt.* In Egypt, rural populations throughout the country suffer from *S. haematobium* infection, while in the Nile Delta there is the country's biggest focus of double infection with *S. mansoni* and *S. haematobium.* The overall prevalence in the country was estimated at 22% in 1974.

In 1968 Egypt launched an antischistosomiasis project in the Faiyûm Governorate (population 1.16 million), which had a prevalence of 45.7% of *S. haematobium* infection. Snail control was carried out with niclosamide, and therapy by niridazole was given to patients under 20 years of age; tartar emetic was given to older infected persons. In 1977 the prevalence was estimated at 6.2%.

After the success of the Faiyûm Governorate project, the Middle Egypt project was started in 1976. The prevalence in the project area, which had a population of 4.5 million, was 31%. The approach used molluscicide combined with metrifonate at three doses each of 10 mg/kg of body weight at 14-day intervals. By the end of August 1978, 2.8 million persons had been examined and 675 000 treated. At present, there are three applications of molluscicide per year to all branches of main canals and to all drainage systems in the area. Starting in spring 1979, the project will be extended southwards to cover all the governorates of Upper Egypt, bringing under protection another 5 million people. The control strategy will remain the same.

In the above projects the success of case-finding and the delivery of therapeutic agents depended on Egypt's unique system of basic health services. In the rural areas there are 2300 health units and centres serving 4200 villages. All these have laboratories, and the smallest unit is staffed by a health team of nurses and technicians headed by a physician.

The annual cost of the Middle Egypt project during the active intervention phase was estimated at US $1 per capita of the population protected. Funds were made available by the World Bank, which agreed to include schistosomiasis control as a budget item in the credit agreement for the drainage programme now being implemented in Egypt.

(3) *Iran.* Control measures covering the endemic area of Khuzistan Province in south-western Iran started in 1966. Combined use of molluscicíding and mass chemotherapy was continued annually with a concentration of activities in spring and autumn. Niridazole was given in a total dose of 120 mg/kg body weight over 4 days and focal molluscicíding was carried out with niclosamide at a dose of 1 mg/l for 8 hours against *Bulinus truncatus*, the sole intermediate host of *S. haematobium* in the area. The prevalence of infection declined from 8.3% in 1970 to 1% in 1976 and 1977. The incidence of infection, determined by examining 2–15-year-old children from several representative villages, declined from 3.3% in 1970 to 0.04% in 1976 and 0.01% in 1977. In addition, *Bulinus*-infected habitats diminished from 10% in 1970 to 1.6% in 1977.

Data obtained in 1977 suggest that *Bulinus truncatus* from Dezful, where molluscicíding has been carried out for the past 10 years, may have developed resistance to niclosamide(*17*).

(4) *Morocco.* In Morocco only *S. haematobium* is endemic, with probably fewer than 50 000 cases. *B. truncatus* is virtually the exclusive snail host but in certain foci the role of *Planorbarius metidjensis* merits further investigation.

From the viewpoint of the epidemiology and control of *S. haematobium*, Morocco is situated almost at the extremity of its African distribution; therefore, seasonal climatic effects, particularly those of temperature, play a crucial role in the pattern of transmission.

In the past, many foci of *S. haematobium* tended to be unstable and some even disappeared. In recent years, however, with the development of permanent water resources, mainly for irrigation, some "new" and more stable foci of *S. haematobium* have given cause for concern. Thus, with the threat of even more widespread and more intense *S. haematobium* infection, the Moroccan health authorities have recently initiated a nationwide control and surveillance programme under the aegis of a National Schistosomiasis Commission. This body functions at the provincial level through the integrated activities of Provincial and Prefectoral Infrastructure and Outpatient Services, which combines control activities against both malaria and schistosomiasis.

Manuals have recently been published by the Ministry of Health providing standard practical procedures for the early phases of control commensurate with local resources of personnel, facilities, and equipment. The essential groundwork for a national control

programme is now being satisfactorily established and this augurs well for the future.

(5) *Puerto Rico.* Under a programme to control schistosomiasis, initiated in 1953, the population of Puerto Rico was provided with improved public water supplies, hygienic latrines and limited chemotherapy, and snail control by environmental, biological, and chemical means was carried out. The impact of the programme was evaluated by faecal examinations until 1966, and subsequently by three nationwide surveys using adult worm antigen for skin tests on schoolchildren in the fifth grade. There was a decrease in the proportion of positive reactors to the skin test from 24% in 1963 to 5% in 1976. From 1969 to 1976 the decrease in positive skin tests was over twice as great in the area under snail control as in the rest of the endemic area. Tests indicated a similar decrease (from 15% in 1963 to 3.4% in 1976) in prevalence among the entire population, determined by multiple faecal examinations. In 1976 the geometric mean was 28 schistosome eggs per gram of faeces of the infected persons and the estimated number of persons passing eggs in Puerto Rico was 100 000. The cost of snail control was minimized by emphasizing environmental and biological methods instead of chemical methods, and the results showed that the disease can be controlled on a large scale with simple methods. Eradication of the parasite is quite likely to be achieved in the next few years within a total cumulative cost of US $3 per person for the 3 million people protected.

(6) *St Lucia.* The provision of piped water, chemotherapy, and snail control have reduced the prevalence and intensity of infection to such low levels that the detection of infection by stool examination is becoming difficult and unreliable. For this reason, and because future monitoring of transmission during the consolidation phase of the control programme will necessitate a diagnostic method that is rapid, sensitive, specific, and more cost-effective than stool examination, a radioimmunoassay for the detection of *S. mansoni* infection is being evaluated.

(7) *Saudi Arabia.* The focal nature of schistosomiasis transmission (wells, small canals, cisterns, small swamps, temporary streams, residual pools, and ponds) in most parts of the country offers the opportunity to reduce it by snail control operations with an excellent prospect of good results. Control of *Bulinus truncatus, B. beccarii, B. reticulatus wrighti* and *Biomphalaria arabica* populations is currently being carried out using niclosamide.

Routine chemotherapy has been conducted with stibophen and niridazole, but it is anticipated that metrifonate for *S. haematobium* infection and oxamniquine for *S. mansoni* infection, both of which are endemic, will be introduced in 1979.

(8) *Swaziland.* Schistosomiasis is widespread in Swaziland and it is estimated that 150 000 individuals are infected with one or both forms of the disease, the more common being *S. haematobium* infection. The intermediate snail hosts (*Bulinus globosus* and *Biomphalaria pfeifferi*) are widely distributed. Sugar and rice irrigation schemes favour the distribution of these snails and the numerous small water reservoirs play an important role in transmission.

The Government's malaria/schistosomiasis unit at Manzini has overall responsibility for the control of schistosomiasis. Mobile teams carry out routine examinations of schoolchildren and arrange mass treatment of infected individuals. During 1974 and 1975 hycanthone was given extensively. Niclosamide is used during the transmission season (October to March) for the focal control of the snails in limited areas.

The strategy of snail control, adopted in 1970 in the irrigation schemes was the treatment of all snail habitats with trifenmorph every seven weeks during the transmission season (October to March) with the aim of controlling transmission throughout the irrigation systems. These measures were a joint effort between the irrigation estates and the Ministry of Health.

In 1976 a school health programme was started in which special attention was paid to schistosomiasis. Four mobile teams, each with a public health nurse in charge, examined all new school entrants.

The control programmes described have reduced the prevalence of schistosomiasis in Manzini and some of the sugar estates, but they do not appear to have been effective in the system of reservoirs.

(9) *Tunisia.* Until a few years ago urinary schistosomiasis was endemic in southern Tunisia, occurring in many localities, mostly oases, of the Governorates of Gabès and Gafsa, with an isolated focus in the Governorate of Kairouan. The population of 150–200 thousand at risk was submitted to a parasitological survey that identified 11 596 positive cases. The overall prevalence in endemic areas was 6.6%, but many localities presented infection rates of 30–70%. The only snail vector was *Bulinus truncatus.*

A WHO-assisted control project was established in June 1970, with the recruitment of national personnel, training activities, and

survey planning. Control measures were started in December 1971 at the oasis of Guettaya and were gradually extended to the entire endemic area. These measures comprised the application of niclosamide to every water collection containing *Bulinus*, in or around the locality and the treatment of every person with a positive urine examination with niridazole (20–25 mg/kg/day, for 7 days) provided there were no contraindications. By September 1978, a total of 10 658 cases (i.e., 91.9% of those diagnosed) had been treated.

In 1972, snail hosts were found in 42.6% of water sources, comprising natural springs, artesian wells, and irrigation canals. The first treatment was efficient in 75% of the places treated. The others required two or more applications of niclosamide. Of the 440 places surveyed, 40 were reinfested in 1973, 27 in 1974, 11 in 1975, 3 in 1977, and 1 in 1978; 525 water places were then under survey. The last transmission foci were identified at Nouail in 1975 and at M'naga oasis (Gafsa) and Oulad Majed (Dégache oasis) in 1976.

Project evaluation was carried out each year in addition to malacological surveys. This was done by means of parasitological examination of the total population of 10 localities selected among those originally most affected by schistosomiasis and representing different endemic areas. The prevalence in these localities, which have a total of 14 000 inhabitants, fell from 34.1% in 1972 to 0.6% in 1978. Each new batch of primary school children of the entire endemic area was examined for infection. The positivity rate fell from 0.37% in 1975 to 0.06% in 1977–78. The follow-up of positive cases not treated owing to contraindications to niridazole showed the usual decrease (with increasing age) in the residual positivity of urinary sediments from 21.1% in 1975 to 17.9% in 1978.

At present, every positive case is the object of an epidemiological inquiry to establish whether it is a new case or not and to assure identification of any active transmission site. No transmission has been registered in Tunisia during the last two years.

These data suggest that, through control measures and spontaneous cure of untreated cases, human sources of schistosomiasis will disappear in the years to come.

(10) *Venezuela.* After 35 years of a schistosomiasis control programme, the number of active cases of schistosomiasis in Venezuela is estimated at about 10 000. The number of persons at risk, living in a 15 000 km^2 endemic area in the north-central part of the country, is estimated at about 250 000. The general prevalence of

14% at the beginning of the programme had fallen to 1.8% at the 1977 evaluation. The control programme includes (1) diagnosis of all cases followed by treatment with oxamniquine (effective in 92% of the cases without important side-effects), (2) control of the snail host, *Biomphalaria glabrata*, by the use of copper preparations, niclosamide, and trifenmorph, (3) environmental and sanitary improvements, and (4) health education.

Collaborative research by the Ministry of Health in association with universities and research institutes is being carried out.

In recent years new foci of *B. glabrata* have been identified in two western and two eastern states, and in at least one of these foci transmission of schistosomiasis was occurring. More than 10 cases of schistosomiasis with spinal cord involvement and two patients with generalized schistosomiasis have been encountered, thus indicating the need to reevalutate the severity of morbidity produced by the infection, which is usually considered as mild.

2.3 Control tools and techniques

The composition of any control programme will necessarily vary according to the emphasis placed upon one or more different approaches with respect to local conditions, objectives of the control programme, available resources, and the strategy employed.

2.3.1 *Chemotherapy*

(1) *Use of chemotherapy in control.* The use of chemotherapy in control requires a clear definition of aims, selection of the appropriate chemotherapeutic agent, and decisions on the dosage and frequency of administration to be followed as well as on the organization of the delivery system.

While other means of schistosome control merely reduce transmission without any direct effects on human worm load, chemotherapy reduces the output of live eggs from the patient's body and, in doing so, diminishes transmission. Moreover by killing worms in the treated individual it not only reduces the risk of morbidity and mortality due to the disease, but also enables the patient to recover from reversible lesions. It is important to distinguish between these two beneficial effects. The second benefits only those who are treated, while the first helps the whole community. Even when the reduction in transmission is incomplete,

the fall in disease risk may still be considerable. Chemotherapy is thus a tool for both primary and secondary control of schistosomiasis.

The object of primary control is clearly to end egg output, especially in those most likely to pollute transmission sites. In situations where egg output cannot be reduced to zero, it is not known at what level persisting egg excretion ceases to be a public health problem. Some epidemiological models suggest that egg production is so great relative to what is needed for continued transmission that even a small residual percentage of egg output will be sufficient to maintain transmission at a considerable level; however, data are not yet available to test this hypothesis. Nor is it possible to say whether a few people with high egg excretion rates are epidemiologically more or less of a problem than a large number of people with a low egg output. It follows that the goal of primary control should be to reduce the egg output of as large a part of the population as possible to as near zero as can be obtained within the constraints of drug toxicity, cost, and possible effects on immunity.

The severity of schistosomiasis increases with rising egg output and intensity of infection. An appreciable proportion of patients with low egg excretion rates also show severe lesions, though it is not clear whether these lesions are due to a previous heavy infection or greater susceptibility to pathological consequences. It is therefore desirable to treat *all* infected individuals to achieve maximum secondary control; in situations where there are operational constraints priority must be given to the heavily infected or to other high-risk groups such as schoolchildren.

The drugs available for the control of schistosomiasis are shown in Table 3. Decisions on the dosage to be used in the field can be difficult. The aim is to provide enough of the drug to kill all the worms in all those treated; however, the use of chemotherapy in the field may be limited by the following three constraints.

Toxicity. For some drugs, the dosages required to cure all schistosomiasis patients may produce side-effects in some and may even be occasionally lethal. Therefore, in the past, the doses of the then available antischistosomal drugs administered were below the level considered clinically ideal. Although the drugs available today are far less toxic than earlier drugs, the dosage for some drugs may still have to be reduced below the optimum clinical level in order to make them more acceptable to the population.

Cost. With the exception of metrifonate, the antischistosomal drugs are expensive in relation to the health budgets of many developing countries. Both the drug costs and the expenses of administering a multiple-dose regime may be reduced by shortening the course of treatment or decreasing the dose. The consequences of such reductions in parasitological terms must be assessed for each proposed regimen.

Effects on immunity. A third possible argument against full treatment is that complete removal of worms might abrogate such acquired resistance as has been induced, rendering people more susceptible to reinfection. Much more evidence will be needed, however, before this argument can be taken into account in treatment policy.

It is clear that the lower toxicity and simpler dosage regimens of the drugs now available will enable chemotherapy to play an increasing part in control programmes. Already over one million persons have been treated for *S. mansoni* infection in the Brazilian control programme, while hundreds of thousands have received metrifonate in the Egyptian *S. haematobium* control measures.

When the prevalence is high in a community and mass treatment is required, two main approaches are possible. In one, the whole population is examined and those found infected are treated. In this case the treatment is on an individual risk basis and the efficiency and cost of the examination will have to be considered before opting for this approach. In the alternative approach, high-risk groups with high prevalence of infection are identified and treatment is given to all members of those groups regardless of whether each individual is infected or not. This may be called a group risk approach.

Several factors must be considered in deciding between the two approaches. The safety of the treatment is the overriding consideration, since it is not wise to give a hazardous drug to an uninfected person. However, in economic terms, the cost of identifying infected persons must be balanced against the cost of chemotherapy given unnecessarily and this has to be worked out individually for each programme. Both these costs will rise as prevalence falls. For some drugs the cost is relatively low compared with that of case detection; but, since the drugs have to be imported into most endemic areas, the use of shadow pricing, in which such items as foreign exchange and local labour are differentially weighed, may alter this balance.

Most schistosomiasis control programmes use diagnosis based on the examination of excreta and apply treatment on the basis of

Table 3. Properties of antischistosomal drugs

Property	Type of schistosomiasis	Niridazole	Metrifonate	Hycanthone	Oxamniquine
Therapeutic efficacy: estimated cure rates	*S. haematobium*	40% to over 80%	40% to over 80%	40% to over 80%	ineffective
	S. mansoni	40–80%	negligible curative effect	40% to over 80%	50% to over 90%
	S. japonicum	40–80%	negligible curative effect	ineffective	ineffective
Estimated population acceptance of the standard dose[a]		33% to over 66%	50% to 90%	75%	over 85%
Estimated population tolerance[a]	*S. haematobium*	moderate to good	good	moderate to good	not applicable
	S. mansoni	moderate	not applicable	moderate to good	good
	S. japonicum	poor to moderate	not applicable	not applicable	not applicable
Mode of administration		5–10 days oral	3 doses at 2-week intervals	single intramuscular injection	In South America and Caribbean, single oral dose. In Africa treatment over 2 days usually necessary.
Cost		high	low	moderate	high

[a] Varies markedly with age.

individual risk. This is true, for example, of the large Egyptian programme, which uses an inexpensive drug distributed through the national primary health care facilities. However, in the extensive Brazilian programme, treatment of the whole community is undertaken at defined prevalences of *S. mansoni*.

The Committee was of the opinion that community examination followed by treatment of the individuals found to be infected was the preferred method of chemotherapy and viewed with concern the treatment of entire communities on the basis of rather low prevalences of infection. However, the Committee felt that there were circumstances in which, due to very high prevalences of infection coupled with economic constraints, treatment of the entire population in specific age-groups might be undertaken. A particular example was provided by schoolchildren, who often show the greatest intensity of infection and are accessible for therapy. Similarly in some areas of *S. mansoni* infection, when a 60% prevalence is revealed by single stool examination and probably over 80% of the population is infected, a rational case for treatment of the entire population can be made.

(2) *Present status of antischistosomal drugs for large-scale use.* Although many drugs display antischistosomal activity, only a few can be considered for selected large-scale chemotherapy. Some of the properties relevant to large-scale use are listed in Table 3. The prospects for successful treatment of a population are equal for *S. haematobium* and *S. mansoni* and lower for *S. japonicum*.

The merits and drawbacks of niridazole, metrifonate, and hycanthone were extensively discussed in the report of the WHO Expert Committee on Schistosomiasis Control(*1*). Therefore, in the present report the discussion on these drugs will be restricted to new findings made since 1972. The use of oral oxamniquine has increased greatly since then and properties of this drug will be discussed separately.

Niridazole and hycanthone. The main concern regarding niridazole and hycanthone was that they were believed to be potential carcinogens. The first results of experimental studies suggesting that niridazole has a carcinogenic effect in mice were reported in 1975. Since then more studies have been completed, and niridazole has also been investigated by the International Agency for Research on Cancer, which reported that tumorigenic effects had been demonstrated in mice and hamsters(*18*). The presence of living schistosomes did not affect the findings.

Several studies on mutagenicity have been performed by the manufacturer of niridazole. These investigations have revealed that niridazole exerts a mutagenic effect on the male germinal epithelium and have indicated a cytotoxic action on spermatogonia, spermatids, and spermatozoa in mice. However, there was no evidence of mutagenic effect on somatic cells in various mammalian systems.

In contrast to these findings hycanthone has only a limited genetic effect, if any, on mammalian germinal tissue; however, it proved mutagenic in mammalian somatic cells and induced chromosomal alterations in each system used. In limited evaluation in humans (13 patients) treated with a clinical dose (2.5 mg/kg) of hycanthone, no evidence of chromosome abnormalities in circulating lymphocytes was found.

The data available from carcinogenicity tests with hycanthone in mice and hamsters, some of which were infected with *S. mansoni*, do not permit a definite judgement on this drug's tumorigenic potential.

The Committee recognized the value of the research being carried out in many countries on improved predictive tests for mutagenic, carcinogenic, and teratogenic hazards of chemicals, including pharmaceuticals and pesticides, and it pointed out the desirability of parallel clinicoepidemiological monitoring of populations being given potentially hazardous drugs.

Oxamniquine. Oxamniquine was initially tested as an aqueous suspension administered by deep intramuscular injection; it has now been studied extensively for administration by the oral route. The effective dose against *S. mansoni* varies for each geographical location, and the compound seems to be ineffective against other schistosome species.

Lowest effective doses were those required in Brazil, where cure rates of 80–95% were observed after a single dose of 12.5–15 mg/kg of body weight. In those not cured an average egg reduction of 97% was noted. As with other drugs, infection in children was more difficult to eradicate. The recommended adult dosage of 12.5–15 mg/kg effected a cure rate of only about 50% in children, although egg reductions of up to 70% were seen. By increasing the total dose to 20 mg/kg, cure rates of 80–85% were observed with egg reductions of up to 76% in those not cured. The recommended dosage for children is consequently 10 mg/kg administered twice in one day.

Similar results were obtained in adults in West Africa, whereas in East Africa (Kenya and United Republic of Tanzania) a total dose of 30 mg/kg, given as either 15 mg/kg administered twice in one day or 15 mg/kg daily for two days, was needed to bring about a comparable antiparasitic effect. The same dosage regime in Uganda gave a slightly lower efficacy.

A total dose of 40–60 mg/kg administered as 10–15 mg/kg twice daily for two days was necessary to produce a cure rate of approximately 80–90% in Egypt, South Africa, and the Sudan.

Tolerance of oxamniquine is good at all dose levels. The most frequent side-effects are dizziness and drowsiness, which occurred in 559 out of the 1717 (33%) patients assessed; they were usually of a mild and transient nature. Other side-effects that have been reported are headache, vomiting, and diarrhoea; these are difficult to differentiate from the symptoms of the disease. Hallucinations and psychic excitement have also been reported; in one large study three cases of hallucinations were observed out of 600 treatments. Five cases of epileptiform convulsions have been reported after an estimated 250 000 treatments with oxamniquine. No important changes in haematological functions or in liver function tests and no consistent electrocardiographic (ECG) abnormalities were noted.

Conclusion. The choice of any particular drug or drugs for use in any control programme is dependent upon a number of factors among which the local estimate of relative risk ratios of death or disability from severe disease, transmission characteristics of the infection, health delivery systems available, costs of population examination, costs of antischistosomal compounds, and known or estimated population acceptance and tolerance of the various alternative drugs must be considered. It is not possible to make general recommendations to cover all situations.

(3) *Development of new drugs.* The Committee noted that four new drugs belonging to different chemical classes were in various stages of investigation and development.

Praziquantel, an isoquinoline-pyrazino derivative of a new heterocyclic system, is effective, both experimentally and clinically, against *S. mansoni, S. haematobium,* and *S. japonicum* when administered orally. In animal models it is also effective after parenteral administration. Many test systems were used in its evaluation. Among them were: *S. mansoni* in mice, multimammate rats *(Mastomys natalensis),* Syrian hamsters, and vervet monkeys *(Cercopithecus aethiops)*;

S. haematobium in Syrian hamsters and baboons (*Papio* spp.); and *S. japonicum* in Syrian hamsters and vervet monkeys *(Cercopithecus aethiops).* In all these models, the activity of the drug against adult worms was pronounced as evidenced by reduction of the parasites in the autopsied test animals. The drug was less effective against schistosomules and lacked prophylactic effect. Praziquantel was also found to be effective against trematodes other than schistosomes (*Clonorchis sinensis, Paragonimus westermani, Dicrocoelium dentriticum,* and the intestinal fluke *Istmiophora melis*) in several host animals. In addition, it is highly effective against numerous cestode species in the larval as well as in the adult stage.

In clinical trials against *S. haematobium* in Zambia, *S. mansoni* in Brazil, and *S. japonicum* in Japan and the Philippines randomized groups of patients were given regimens containing oral doses of 1×20 mg/kg, 2×20 mg/kg, 3×20 mg/kg and 1×50 mg/kg with excellent antiparasitic results at follow-up examinations 6 months later. Of 79 Zambian children infected with *S. haematobium* 66 were re-examined a year later and only two were found to be egg positive. Among 74 Brazilian patients infected with *S. mansoni,* 43 were treated with 3×20 mg/kg and 31 with 1×50 mg/kg; 33 and 22 patients respectively were found to be cured after six months, and most of them remained free from infection after one year. Two groups totalling 82 and 42 patients infected with *S. japonicum* were treated with 3×20 mg/kg and 1×50 mg/kg respectively. After six months, 60 (80%) of 75 examined in the first group and 29 (71%) of 41 examined in the second group were found to be negative for eggs. After one year the corresponding figures were 25 (76%) of 31 and 14 (54%) of 26 examined in the two groups respectively. Egg output reductions in all those still positive were 95% and 58% in the two groups. No clinically significant changes occurred in ECGs of the treated persons; haematological and biochemical tests indicated that the patients were clinically normal. Some paired electroencephalographic recordings taken before and after treatment of patients with *S. mansoni* or *S. japonicum* infections showed abnormalities and further evaluation is now in progress. Tolerance was generally good, with mild to moderate side-effects mostly of short duration. The most frequent were colicky abdominal pain, sweating, and pyrexia. A coordinated programme of extended trials is nearing completion and field studies can be expected shortly.

Amoscanate, a new isothiocyanate that has undergone limited clinical trials, is experimentally effective against all three species of

schistosomes pathogenic for man after oral administration in a single dose to various animal models—mouse, hamster, Mongolian jird *(Meriones unguiculatus)*, dog, and monkey (*Cercopithecus aethiops* and *Cebus appella*). In man it has proven activity against *S. mansoni* and *S. japonicum* but is of doubtful efficacy against *S. haematobium*, possibly owing to imperfect pharmaceutical formulation and consequently poor absorption. In clinical trials in Brazil, Costa Rica, India, and the United Republic of Tanzania it has been shown to be effective against *Necator americanus* and *Ancylostoma duodenale*. Macro- and microfilaricidal activities have also been observed against *Litomosoides carinii, Dipetalonema witeae*, and *Brugia pahangi* in the multimammate rat *(Mastomys natalensis)* and the Mongolian jird *(Meriones unguiculatus)*. There is experimental evidence that a marked increase of activity may be achieved by improving the pharmaceutical formulation; intensive investigations as well as toxicity studies with new formulations are now in progress.

Ro 11–0761 [3-(3,5 dinitro-2-thienyl)thiazolidine] is at a relatively early stage of development and very few clinical studies have been carried out. It is experimentally effective against *S. mansoni, S. haematobium*, and *S. japonicum* in mice, hamsters, and monkeys. It is twice as active against *S. japonicum* as against *S. mansoni* after an oral 5-day treatment. Furthermore, the compound shows chemotherapeutic activity against *Leishmania donovani* in hamsters and against *L. tropica* in mice. So far 24 patients with *S. haematobium* and 5 patients with *S. mansoni* infections have been treated with different dosages. Cure was obtained in *S. haematobium* in infections with 3×10 mg/kg/day for 6–7 days (total dose 3.6–4.2 g). Out of the 5 patients infected with *S. mansoni* only 2 could be cured with a dosage schedule of 10–12 mg/kg per day, given on 6 consecutive days.

Ro 11–3128 [(+)-5-*o*-chlorophenyl)-1,3-dihydro-3-methyl-7-nitro-2H-1,4-benzo-diazepin-2-one)] has been suggested for pilot clinical trials on the basis of its pronounced laboratory antischistosomal activity. It showed marked curative activity against *S. mansoni* and *S. haematobium* infections in mice, hamsters, monkeys *(Cebus appella)*, and baboons (*Papio* spp.). A dose of as low as 25 mg/kg was curative against *S. mansoni* and *S. haematobium* while no effect against *S. japonicum* was observed. Besides the activity against sexually mature schistosomes, the compound proved to be effective against all stages of immature *S. mansoni* in mice after a single oral dose. Pilot clinical trials against *S. mansoni* and *S. haematobium* are envisaged.

The Committee noted that major advances in antischistosomal therapy had been achieved in recent years with respect to simpler treatment, better tolerance, and readier acceptance.

2.3.2 *Snail control*

Snail control by molluscicides is a rapid and effective means of reducing transmission. Its efficiency is likely to be enhanced if it is combined with other methods of control. There are now substantial scientifically acceptable data to show that incidence, prevalence, and intensity of infection are greatly reduced when molluscicide is used in combination with other methods in schistosomiasis control programmes. The data show that molluscicide is most cost-effective where the volume of water to be treated per person at risk is small. It is therefore well suited to arid areas where transmission is seasonal and confined to relatively small habitats. It may, however, be less suitable in large rivers and lakes unless transmission is focal in distribution. In areas where population density is high and the amount of water available per person is consequently low, molluscicide may be the most cost-effective method of schistosomiasis control, although the total volume of water may be large. Irrigation schemes, in which controlled water-management is practised and where population density is high, are well suited to cost-effective chemical molluscicide.

A review of the available and candidate molluscicides shows that, with the exception of nicotinanilide group of compounds, there are no new compounds to be added to the list of molluscicides presented in the report of the WHO Expert Committee on Schistosomiasis Control (*1*). Unfortunately the chemical industry has been reluctant to undertake the complex work needed to develop new compounds, in view of the high costs and uncertain returns—a situation caused in part by the considerable legislative pressure on pesticides.

The two compounds that are of major interest are niclosamide and trifenmorph; the former is now more widely used than the latter. The use of trifenmorph, despite its high efficacy even at very low concentrations, is diminishing and the compound is no longer readily available. While sufficiently large orders may still be considered by the manufacturers, delays in delivery can be expected.

The molluscicide compounds worthy of interest are listed in Table 4. Niclosamide and trifenmorph were adequately discussed in the report of the WHO Expert Committee on Schistosomiasis

Table 4. Properties of some available and candidate molluscicides

	Niclosamide	Trifenmorph	Sodium pentachlorophenate	Copper sulfate	Nicotinanilide (candidate compound)
Physical properties					
Form of technical material	crystalline solid	crystalline solid	crystalline solid	crystalline solid	crystalline solid
Solubility in water	230 mg/l (pH dependent)	0.02 mg/l	330 g/l	316 g/l	not known
Toxicity					
Snail, LC_{90} (mg/l × h) [a]	3–8	0.5–4	20–100	20–100	5
Snail eggs, LC_{90} (mg/l × h) [a]	2–4	240	3–30	50–100	20–50
Cercaria, LC_{90} (mg/l)	0.3	no effect	not known	no effect at molluscicidal concentrations	not known
Fish, LC_{90} (mg/l)	0.05–0.3 (LC_{50})	2–4	not known	toxic [b]	>30
Rats, LD_{50} (mg/kg given orally)	>5000	1400	40–250	300	>2000 (mice)
Herbicidal activity	none	none	phytotoxic	phytotoxic	unknown
Formulations	700 g/kg wettable powder 250 ml/l emulsion concentrate	165 ml/l emulsion concentrate 40 g/kg granules	750 g/kg flakes 800 g/kg pellets 800 g/kg briquettes	980 g/kg pentahydrate crystals	not yet formulated
Field dosage					
Aquatic snails (mg/l × h) [a]	4–8	1–2	50–80	20–30	not known
Amphibious snails (g/m^2)	0.2	ineffective	0.4–10	ineffective	not known

[a] The term "mg/l × h" indicates that the figures given are the product of the concentration and the number of hours of exposure.
[b] Toxicity depends very much on the species of fish and on the water quality.

Control in 1973; additional notes in the present report are, therefore, only on copper compounds, the nicotinanilides, and molluscicides of plant origin. Recent trends in molluscicide usage have been towards improved cost-effectiveness and reduction in environmental damage. Efforts have been made in this direction through new or improved delivery systems and the development of more target-specific compounds.

Whenever possible, it is suggested that the local manufacture of molluscicides should be explored. This approach may not only stimulate a local industry but may alleviate inherent difficulties encountered in transport and importation. In Egypt, for example, the production of 2,5-dichloro-4′-nitrosalicylanilide started as a result of such an approach.

Copper compounds. Copper salts have the advantage of being continuously available and a large amount of literature exists on their use. Research should be continued on ways and means of improving their utility.

Organotins. In the light of available toxicological information on organotins, and in particular on bis(tributyltin) oxide and in the absence of adequate data on their potential long-term cumulative effects on the aquatic environment, it is considered that the use of such compounds as molluscicides or larvicides cannot be recommended at the present time (*19*).

Nicotinanilides. Nicotinanilide and its 3′- and 4′-chloro- analogues have been reported to have effective molluscicidal activity at concentrations in water of approximately 0.2 mg/l. Ovicidal activity is somewhat disappointing; nicotinanilide is the most active compound of the three against maturing egg masses, but none of the three compounds has been shown to have any useful activity against one-day-old eggs. Later studies have shown, however, that many eggs surviving treatments were either undeveloped or abnormal and that, if these individuals were included, the LC_{50} was 0.8 mg/l.

When the three compounds were applied at dosages of 2-5 mg/l to fish ponds, no visible effect could be seen on fish, tadpoles, frogs, or water weeds. Similarly, 4′-chloronicotinanilide has been shown to have no acute toxicity to adults of the tropical food fish *Sarotherodon mossambicus* in laboratory tests employing doses 200 times that of the LC_{50} to *Biomphalaria glabrata.* The compounds do not affect goldfish or *Daphnia* at molluscicidal concentration. Mice tolerate 2 g/kg given

internally and rabbits respond minimally in skin and eye irritation tests. Nicotinanilide and 4′-chloronicotinanilide have no toxicity to third-instar larvae of *Aedes aegypti* exposed to 5 mg/l for 24 hours. The half-life in water of a solution of 4′-chloronicotinanilide is 10 days. These compounds now offer the possibility of truly selective control of snails. Their future development will involve laboratory and field trials of slow-release formulations, investigation of field methods for analysis of low concentrations in water, and feasible routes for commercial synthesis.

Molluscicides of plant origin. Endod (*Phytolacca dodecandra*) remains the most thoroughly studied example of a molluscicide of plant origin. Although endod has been found to be somewhat less cost-effective than niclosamide, its use can obviate importation of synthetic chemicals since the substance does not require industrial synthesis and can be easily produced locally. The material has some advantages for self-help schemes, but the toxicology requires further investigation. Being a saponin, endod is not target-specific. Its widescale use would depend either on well-organized harvesting of the native bush for local use or commercial growing. The latter has never been successfully undertaken. A number of other molluscicides of plant origin have been reported in the literature but further research on their toxicology and cost-effectiveness is required.

Focal and area-wide application of molluscicides. Snail control based upon the identification of foci and seasonal variations of transmission is an approach which can be applied in many endemic situations, and even in large impounded habitats it may permit cost-effective mollusciciding regimens. It should be emphasized, however, that such delivery mechanisms will depend on surveillance procedures, and these may not be feasible in large irrigated areas where population density is high and human water-contact patterns are diffuse. In these habitats area-wide chemical control, based on water-management procedures, will offer the most cost-effective approach.

2.3.3 *Biological control of snails*

In the last decade, concern over the environmental effects of some chemical pesticides, and their escalating costs, has stimulated searches for alternative snail control methods including many wide-ranging studies on biological control. Several hundred species

(including fish, fungi, parasites, and pathogens) have been proposed as potential competitors or predators, but their efficacy has rarely been tested outside laboratory model systems. Of the many species of predators listed, only two groups, fish and insects, have been studied in sufficient detail to merit consideration, but rigorous evaluation of their efficiency in field situations is still lacking. Similarly, the phenomenon of inter-larval trematode antagonism and predation has been investigated intensively in recent years, but the findings of limited field trials have failed to substantiate the encouraging results of earlier laboratory tests.

Of all biological control mechanisms intermolluscan competition and predation is perhaps the most attractive at present. The introduction of possible competitive species of snails (*Marisa cornuarietis, Helisoma duryi, Pomacea haustrum, Potamopyrgus jenkinsi, Physa* spp., etc.) has received considerable attention. Of these species *Marisa* has been most extensively studied in Puerto Rico, where its effectiveness has been demonstrated in certain types of habitats, such as permanent ponds, but not in sites with dense vegetation or in swamps and streams. As with molluscicide, persistence of effort was needed to maintain *Marisa* in the habitats, but the cost was about one-third the cost of applying the best molluscicide. In addition to *Marisa, Helisoma duryi* appears to have interesting possibilities as an effective competitor. However, further well designed laboratory studies and, in particular, carefully controlled field trials of the efficacy of this species, in a range of simulated habitats against several snail host species, are desirable.

In 1975, a scheme for the rational screening and evaluation of the most promising organisms for biological control was proposed by the WHO Expert Committee on Insecticides (*20*). For obvious reasons this scheme stressed that due attention must be paid to the safety of the agents for man in particular, and for nontarget organisms in general, under a wide range of environmental situations. In this connexion, the Committee considered it appropriate to quote from the report of the Expert Committee on Schistosomiasis Control: "Under no circumstances should such an agent be introduced into an exotic geographical area before exhaustive testing of its potential capacity to compete with, or destroy, animals or plants of economic importance. Furthermore, the Committee strongly recommended that a snail intermediate host from one endemic region should not be transferred to or maintained in the laboratory of another endemic region for any purpose whatsoever"(*1*). The present Committee

deplored the fact that, in spite of the latter recommendation, *B. glabrata* continues to be maintained in some laboratories, for example, in Africa. Moreover, the deliberate or accidental transfer of snail hosts from one tropical area to another (e.g., the discovery of *B. straminea* in Hong Kong) or into potential transmission sites where they did not previously exist remains a problem which public health authorities should not underestimate.

While the screening and evaluation scheme proposed in 1975 in the report of the WHO Expert Committee on Insecticides (*20*) was devised with the biological control of insect vectors in mind, its relevance to biological control of snail intermediate hosts is evident. Most studies on biological control of snails are still in Stages I and II (laboratory findings), very few have reached Stage III (preliminary field trials), fewer still have advanced to Stage IV (nontarget impact studies), and none has achieved Stage V (large-scale field trials).

Finally, while it was considered that the role of biological control in schistosomiasis suppression would in most cases be minor and supportive rather than dominant, the Committee fully commended support for carefully designed research programmes, especially those concerned with field testing and impact on nontarget species, as well as the search for effective pathogens.

2.3.4 *Control by environmental modification*

The advantage of control by environmental modification is that permanent changes can be made that have a lower maintenance cost than other methods of control. This offers the potential for considerable reductions in the cost of control in the long term.

Socioeconomic development may markedly affect transmission, both favourably as in Venezuela and adversely as in many new irrigation areas. The object of specific control measures is to anticipate and promote favourable changes and to forestall the potential disadvantages of development.

Both in St Lucia and in Lake Volta in Ghana, it was demonstrated that provision of domestic water supply supported by health education reduced human contact with water and this reduced schistosomiasis transmission. The installation of water supply systems can be a relatively expensive control method, since in one project an estimate of the cost of installation was US $10 per capita served and in 1975 the maintenance cost was US $4.95 per capita. However, the cost should not be wholly attributed to schistosomiasis control in

view of the other benefits conferred by water supplies. On the other hand, whether a control programme using water supply would be cheaper than snail control depends on local epidemiology. Field trials have been started in St Lucia on the cost and effectiveness of a new type of latrine for controlling the dissemination of faeces in order to prevent *S. mansoni* transmission.

Other general environmental modifications have been shown to be effective—for example, weed control in Lake Volta and the filling and drainage of snail habitats in Iran have successfully reduced snail populations. A historical analysis of three sugar cane irrigation systems in Puerto Rico showed that simple improvements in design prevented increases in transmission. A slightly higher rate of flow of water in canals, the lining of canals with cement, the elimination of night storage ponds, and improved drainage systems appeared to prevent transmission completely in an irrigation system on the north coast of Puerto Rico; however, in a similar system on the south coast there was an outbreak of the disease in spite of these improvements.

2.3.5 *Health education*

Human attitudes towards water and waterborne disease transmission frequently need to be modified, particularly in areas with endemic schistosomiasis.

Health education should be the responsibility of all health workers and should be based on a clear understanding of the people's perception of disease and its relation to the environment. Efforts should be directed towards those groups that are at greatest risk and most involved in transmission—usually young children. It is recommended that, whenever possible, efforts be positive rather than negative in orientation. In other words, it is better to encourage children to refrain from initially polluting water sources than to try to prevent water contact. Infection is likely to be associated with certain types of water-contact behaviour which will vary in different transmission situations. If a link is established between specific activities and schistosomiasis transmission, then these activities should be discouraged.

An effective health education programme should promote active community participation. Such participation may range from a community installing its own water supply to a community simply cooperating with the health authorities in reducing contact with unsafe water bodies.

There is an urgent need to recruit social scientists to study the behavioural aspects associated with schistosomiasis transmission and control.

2.3.6 *Community participation*

Community participation must be considered as an essential element of any schistosomiasis control programme.

National interest should be promoted once the schistosomiasis problem is considered to be a serious public health problem. Governments or communities implementing schistosomiasis control programmes have the responsibility of organizing national or local efforts through mechanisms acceptable to the communities concerned.

Recognition of the problem by the local population and its awareness of the risks and possible consequences of infection must be the basis of its cooperation. To this end, the advice should be prepared in a clear, simple and convincing form, and presented in the most suitable style. Simple, inexpensive, and appropriate technology must be carefully selected and transmitted to those members of the community most involved in schistosomiasis control.

Community participation must be organized as an integral part of basic health care activities and the primary health workers must be prepared to assume their responsibilities at the local level.

2.4 Factors influencing the choice of control methods in schistosomiasis

There are considerable differences between the various ecosystems involved in the transmission of schistosomiasis. The particular ecological requirements of the parasitological cycle vary with different species of schistosome and their respective intermediate snail host (or hosts) as well as with the customs and habits of the human population in the endemic areas. Ecosystems may change under the influence of environmental variations due to natural factors such as geoclimatic conditions or factors related to human activities particularly those resulting from human environmental modification or developmental activities; these changes may have an effect on transmission.

Control methods must be adapted to meet individual situations. They must therefore be selected carefully for each particular case and sometimes even for each separate site in order to obtain optimum results for the least cost.

From an operational viewpoint there are two essential objectives:

(1) control of transmission (which according to individual circumstances may mean either interruption of transmission or at least a marked reduction in the transmission rate) and

(2) control of disease and a marked reduction of prevalence of human infection.

The first objective is generally attempted through snail control, provision of satisfactory sanitary facilities and water supply, and health education; the second objective may be achieved through chemotherapy.

2.4.1 *Intermediate snail hosts*

Control methods for aquatic *Biomphalaria* and *Bulinus* species are quite different from those for the amphibian *Oncomelania* species of intermediate snail hosts.

If environmental control or biological tools are to be used effectively, and if molluscicide is to be conducted with maximum efficacy at minimum cost, it is essential to know a great deal about the biology of each transmitting snail species and also about the ecology of each habitat occupied by these species.

2.4.2 *Geoclimatic conditions*

Geographical and climatic factors form a complex and cannot be considered separately because the abundance or scarcity of water, the distribution of fresh water, and the various types of water collections, all of which have a great influence on snail distribution and abundance, are the product of both these factors. Frequently, geographical and climatic conditions induce periodic variations in the distribution and abundance of the snails. Geoclimatic conditions favour the feasibility of environmental control work, such as the drainage of swamps and ponds, flood control, and the economic application of molluscicides, if the volume of water is not too great;

on the other hand, if large water bodies are involved, in areas that are difficult to reach, environmental control methods become so expensive that their practical value is reduced.

Transmission may be reduced by a limited rainfall, by a hard winter that reduces snail populations, by a reduced human contact with water, or by the timing of agricultural activities. The seasonal nature of transmission can be used in determining the best means of operational intervention for the control of schistosomiasis.

2.4.3 *Schistosomiasis in arid areas*

Schistosomiasis transmission is always a focal ecological phenomenon, particularly in arid or desert lands, where it occurs in oases or fertile valleys. The most important ecological characteristics of such areas are the limited volume of water found in each oasis and the fact that water frequently emerges from a single or a limited number of sources (springs or artesian wells) and is then distributed throughout the irrigated areas. These circumstances are particularly favourable to snail control by molluscicide and can lead to the eradication of the intermediate snail host, as in southern Tunisia.

2.4.4 *Schistosomiasis in relatively dry areas*

In areas such as the north-central part of Venezuela, with permanent rivers and lakes, the reduced volume of these water bodies during most of the year makes snail control economically feasible. The drainage and desiccation of swamps, found along the higher courses of the rivers, are also favoured by geoclimatic factors for control since they tend to eliminate important residual habitats in which snails might otherwise survive.

2.4.5 *Schistosomiasis in rainy and intensively irrigated areas*

Difficulties in control in rainy and intensively irrigated areas may frequently be anticipated, particularly when there is a dense population relying on the use of water for land cultivation. Examples can be found in the Nile Delta of Egypt and in the Gezira region of the Sudan. In general a combination of all control methods will be necessary. Whether emphasis is placed on initial molluscicide followed by recurrent chemotherapy or whether chemotherapy will be the main tool with molluscicide used as a seasonal or focal

adjunct will depend on local transmission and disease patterns. In all control programmes, the provision of adequate community water supplies and environmental sanitary facilities with a supporting health education programme should be encouraged.

2.4.6 *Types of snail habitats*

Usually the intermediate snail hosts do not occupy the whole habitat but exist mainly in suitable microhabitats within a larger environment. Consequently, special measures (e.g., elimination of aquatic vegetation) directed against these microhabitats can prove to be very efficient in snail control.

The possibility of combining land reclamation and agricultural development of waste land with snail control offers a permanent solution to the problem of schistosomiasis control and may contribute greatly to the reduction of long-term engineering costs.

In water resources development schemes, such as irrigation and the creation of lakes, adequate preliminary epidemiological and biological studies, good water management practices, careful maintenance of the canals, and improved agricultural methods may prevent snail proliferation and facilitate chemical control of snails.

Man-made lakes require complex surveillance services and continuous measures to maintain the quality of water and to avoid eutrophication and snail proliferation. The best use of land and the judicious planning of human settlements are major factors to consider in preventing schistosomiasis and other health problems.

2.4.7 *Economic, social, and cultural factors*

In most instances the national authorities prefer to direct all available financial resources (national as well as external) to economically important development projects such as irrigation schemes and man-made lakes. While these activities are of extreme national importance, it must be borne in mind that unless adequate provisions are made for transmission control and unless ecological studies are first carried out, the development efforts may not turn out to be a sound investment. In many countries, owing to the lack of foreign exchange, the authorities prefer to spend public funds on local manpower rather than on importing chemicals, drugs, and

equipment. This approach makes environmental control of snails a more acceptable proposition than recurrent molluscicide.

In endemic areas where fish are the local source of protein, the use of molluscicides that may harm the fish may have to be limited. It has been suggested that in such areas large-scale fish farms should be established in order to provide the population with low-cost protein and to minimize individual local fishing—thus reducing human contact with water.

A critical review of past experience in schistosomiasis control indicates that long-term intervention measures such as local environmental improvements and health education of the population at risk are unlikely to be successful without active community participation. However, impediments to community participation may be encountered and may be of a strength sufficient to arrest the progress of control programmes. Some of these impediments are: high illiteracy rates in some rural populations, leading to irrational concepts of disease and its origin; hostility between rural dwellers and local authorities; and the absence of trained personnel in a community or the incapacity of the person in charge to appreciate the value of community participation.

Of major importance is the national political decision on the degree of priority to be attributed to the control of schistosomiasis. This will influence the budget and hence the control policy adopted. The subsequent progress of control and the methodology to be used will ultimately depend on this decision.

It may be said that during the past 50 years of schistosomiasis control, the expenditure on control has been disproportionally high in relation to the results achieved. One reason for this negative balance is the limited life of most control projects and the short duration of the benefits gained after control measures have been abandoned. Yet the realization of the importance of combined control measures, the accurate delineation of the total ecology of an area, and the advent of safe and effective drugs make it probable that major advances in the control of schistosomiasis will soon be attainable.

2.4.8 *Special factors influencing the control of* S. japonicum

The methods of control of *S. japonicum* infection, while superficially similar to those used in the control of *S. mansoni* and *S. haematobium* infection, differ markedly in the emphasis placed on

the various measures applied. The application of control measures in *S. japonicum* endemic areas is often complicated by the biology of the parasite and its intermediate snail hosts.

(1) *Environmental modifications to alter or eliminate snail habitats.* Experience in a pilot project in Leyte, the Philippines, and control programmes in China and Japan have shown that alterations of snail habitats should be permanent and, where this is not possible, control efforts should be sustained in order to reduce snail populations to the minimum since *Oncomelania* as a general rule multiplies rapidly.

Japan was able to afford the large capital expenditure and recurrent expenses to sustain the control programmes, and could also procure active community support; as a result, schistosomiasis has been completely eliminated from humans.

In China, the sociopolitical structure made it possible to implement the necessary environmental changes and sustain control efforts without resorting to large capital outlay, thus achieving a considerable reduction in prevalence. However, in other areas of Asia increased community participation would be desirable to ensure the success of control programmes.

(2) *Molluscicidiṅg.* In earlier programmes molluscicidiṅg played a minor role in the control of *Oncomelania.*The amphibious nature of these snails requires application of molluscicides to adjacent moist areas in addition to direct application in water. The operculum of *Oncomelania* snails enables them to escape the effects of molluscicides and because they are small they often remain protected under objects such as rocks and leaves. In general, application of the molluscicides is carried out after environmental modification.

(3) *Chemotherapy.* Most of the currently available chemotherapeutic agents, although effective against *S. mansoni* or *S. haematobium* or both, are ineffective or minimally effective against *S. japonicum* and therefore are not recommended. In view of this, chemotherapy has not yet played a significant role in the control of *S. japonicum* infection. Praziquantel offers promise as a future control tool, and other drugs currently under development are expected to become reliable chemotherapeutic agents in the future.

(4) *Reduction of pollution in water courses.* Cows, buffaloes, dogs, pigs, cats, rodents, and other mammals are reservoir hosts of *S. japonicum,* and the disease should also be controlled in these

animals if contamination of water courses is to be totally prevented. The role of these animals in the transmission of the disease may become more important as levels of transmission are lowered.

2.5 Evaluation of control

While in research-oriented control projects extensive evaluation techniques should be employed, in public health schemes evaluation need not be as detailed. However, it is essential to monitor the effects of intervention in pilot areas which should be selected carefully and changed periodically in order to avoid bias. Preferably, the staff undertaking evaluation should be different from the control programme staff. Evaluation should be carried out in more than the restricted areas, so as to detect any breakdown in control efficacy at an early stage. Annual examination of 6–7-year-old schoolchildren has been shown to be useful in this respect.

2.5.1 *Epidemiological measurements*

Recent epidemiological studies have clarified the meaning and interpretation of many epidemiological measurements and of their implications in control programmes. Measurements of prevalence, incidence, and intensity of infection are all needed to determine the effectiveness of intervention.

The methods for measurement of prevalence, especially of changes in prevalence with time, need to be carefully defined and the results of these measurements require critical analysis. The prevalence of infection in a population examined varies directly with the sensitivity of the diagnostic technique. In the analysis of prevalence, a standard presentation of data by age and sex subgroups is recommended although the overall population prevalence remains a valuable index of infection. It is essential to distinguish between the changes in prevalence in the same individuals examined at two or more points in time and those in a specified age-group examined in the same way. Failure to recognize the difference in these two measures of prevalence is a well-known pitfall.

Incidence is an essential measurement of transmission in large communities but relatively little work has been published on this important subject. In recent years the conversions (from negative to positive stool examinations), reversions (from positive to negative

stool examinations), and the ratios of the two have been employed as an additional measure of the effects of intervention on transmission. Evaluation of the several available alternative techniques for measuring incidence will be required to determine which of them are most suitable in field studies and in the assessment of control programmes.

There are difficulties in the measurement of intensity of infection in populations. The sensitivity of the parasitological technique used will influence the geometric mean egg output of the infected individuals in a community. With the sensitive formol-ether technique, using 1 mg of faeces, the lowest possible egg count may be 1 egg per gram of stool. In a 20-mg thick-smear stool examination, the results are multiplied by a factor of 50 to convert the egg count to an egg-per-gram basis. Consequently, the lowest possible count would be 50 eggs per gram of stool.

Although changes in the intensity of infection may be useful in assessing the effects of intervention in control programmes, it is necessary, as with prevalence, to distinguish between changes in a cohort (same individuals) and changes in an index group (different individuals).

The advent of new techniques or improvements of older methods can be expected to give more precision to epidemiological measurements. The recent introduction of quality control procedures in parasitological laboratories engaged in research and control will improve the performance of technicians. Quantitative techniques of stool examination now include modifications of the Kato method (i.e., the quick Kato method and the Kato-Katz method) but further studies are needed to determine their accuracy compared with that of other quantitative parasitological techniques. Developments in immunodiagnosis, in particular the radioimmunoassay and the enzyme-linked immunosorbent assay show promise, and their field evaluation is currently proceeding.

2.5.2 *Epidemiological surveillance procedures in control programmes*

Adequate supervision of all aspects of control methodology is essential. In pilot areas and in research-based control programmes, the annual incidence of new infection among children should be determined because this index of transmission is essential in control schemes employing chemotherapy. Ideally, the prevalence and intensity of infection in all age-groups should be measured.

While cross-sectional studies give useful information, repeated examinations of the same individuals (cohort studies) provide information on the status of transmission in the area, and results are uncomplicated by population movements.

From data obtained in cohort studies in areas where chemotherapy is not used, the ratio of new infections (conversions) to spontaneously lost infections (reversions) can be calculated; it is this ratio that determines changes in prevalence. When, among children, there are more conversions than reversions (ratio > 1), prevalence is increasing; on the other hand, when reversions exceed conversions, prevalence is decreasing and control of transmission has been obtained.

While examination of the human population is essential for reliable information on control status, complementary investigations may yield other indications of progress such as reduced snail populations, reduced infection rates in snails from index sites or from sentinel exposures, reduced cercarial levels in water, fewer observed human water contacts—where water supplies have been used to control exposure, and, in some areas, reduced infections in animal reservoir hosts.

2.5.3 *Surveillance of controlled areas*

When low rates of prevalence have been achieved, as is the case in some countries, surveillance becomes extremely important in order to detect trends in baseline endemicity.

Immunodiagnostic techniques that are currently being evaluated may be more sensitive than and preferable to parasitological methods of detecting light infections in children. If young children are found to be infected in controlled areas then attempts must be made to locate the source of infection so that appropriate intervention measures can be implemented.

3. TRAINING

The Committee recognized the efforts of WHO in developing training courses both in parasitology and in epidemiology in different regions, with special emphasis on the endemic parasitic diseases of each region. It was also noted that other programmes are being implemented through the Special Programme for Research and

Training in Tropical Diseases established by UNDP, WHO and the World Bank.

It was recommended that auxiliary health personnel engaged in control programmes should be trained at the regional and national levels—if possible in national control programmes and research areas. Technical manuals are needed for good training and national authorities are recommended to develop such manuals for local training programmes.

The Committee felt that parasitic diseases should be given more weight in medical curricula in both developing and developed countries.

4. CONCLUSIONS

The changes in the tools available for schistosomiasis control and the experience gained in their field use in different countries have been set out in this report. It will be necessary to see how they affect the future control of schistosomiasis. The Committee considered them to have major implications for the feasibility of control, the methodology of control, and long-term policy in relation to both control practice and research.

4.1 The feasibility of control

At the meeting in 1972 of the WHO Expert Committee on Schistosomiasis Control 25 projects, scattered throughout the world, were reviewed. Although they had been evaluated with varying rigour, they showed a general trend towards achieving some reduction in schistosomiasis by a variety of methods(*1*).

The chief change since then has been the emergence of several large-scale national programmes, some of which are noted in section 2.2. These have shown that in countries of patchy or limited endemicity and middle levels of national income, it is possible to reduce schistosomiasis to a level of little public health importance and even to contemplate prevention of further autochthonous cases.

More notable still have been the large control programmes launched by some countries with areas of high endemicity affected by one or more of the three major schistosomes. Examples include

Egypt and Brazil. The fact that these programmes have been undertaken at all shows that the tools are now adequate, given sufficient political determination, for launching national schistosomiasis control programmes; the results so far obtained from some programmes show that considerable reduction of infection has been achieved. Control costs have been at a more uniform level than in earlier campaigns despite adverse inflationary trends. Furthermore, a whole range of possible approaches can be used—from labour-intensive methods of environmental improvement to capital-intensive integrated control methods.

The Committee therefore considered that endemic countries should develop national schistosomiasis control programmes within the health care delivery systems.

4.2 The strategy of control

The 1960s can be thought of as the period when molluscicides were the only reliable approach to schistosomiasis control. However, with the widening of knowledge, in the present decade integrated control (using several approaches concurrently) has become the preferred way of controlling schistosomiasis.

Since the meeting of the WHO Expert Committee on Schistosomiasis Control in 1972, there have been improvements in drug efficacy and safety; another major change has been the increase in the cost of molluscicides. The Committee anticipated that the large-scale chemotherapy of infected persons will be a major component of control programmes over the next decade. Chemotherapy provides immediate relief to the infected person and helps in the control of transmission; it also permits the rapid reduction of prevalence and intensity of infection. Since the benefits of chemotherapy will be greatest in areas of highest prevalence and intensity of infection, it is likely that these areas would be the first to receive attention.

Once the control programme begins, reduction in infection occurs rapidly and the prevalence may fall below 10% after 3–4 years of determined effort, if population composition and compliance are satisfactory and immigration is not too great a problem. Thereafter, the policy will vary according to the size of the endemic area. When the area is small and circumstances are favourable, a considerable effort may be directed towards treating the residual cases; but, when the affected populations are extensive the programme may pass on to

a follow-up phase in which the goal is to keep the infection below the level at which it is of public health importance and at a lower cost than the initial intervention phase. There is limited experience on the minimum degree of control activity necessary to maintain infection at a low level of endemicity using the various available health infrastructures. A careful evaluation of the programmes in this phase of control should provide such data over the next few years.

Three main phases of control operations may now be distinguished:

Phase 1 is the period when the necessary collection of epidemiological data takes place, the goals of the control programme are defined in the light of the priority accorded to the problem, a feasible control strategy is designed, and appropriate resources are allocated to the programme.

Phase 2 is the period of active intervention; the chosen strategy is intensively applied and continuously evaluated. In this phase a substantial reduction in endemicity can be anticipated.

Phase 3 is likely to be a protracted follow-up period during which some maintenance measures will continue to be necessary in most situations; however, the applied inputs (finance, manpower, material, etc.) may be reduced by several orders of magnitude.

The Committee recognized that further research is necessary in relation to the follow-up phase in control operations and that the applied maintenance inputs during this phase must necessarily vary according to the achievements made during the phase of active intervention. In the follow-up phase the technology used should be appropriate to the needs of the transmission area and related to the available health infrastructure.

4.3 Control policies in the future

The Committee envisaged a great acceleration in control activities in affected countries in which chemotherapy would play a major part. There are two major topics to be considered if the benefits of such activities are to be made available to all endemic countries.

(1) The present cost of control will clearly make it very difficult for the poorer endemic countries to have effective programmes

within the constraints of their health budgets; therefore, much less expensive methods of control are needed. This requires research on a variety of approaches.

(2) Comparison with other endemic disease control programmes shows that programmes that relied exclusively on chemotherapy ran into difficulties after some years, either because of the development of drug resistance in the parasite or as a result of relaxation in vigilance once the incidence of disease had greatly fallen. The Committee therefore considered it of the greatest importance to encourage the use of other methods (environmental, behavioural, etc.) in programmes using chemotherapy on a large scale.

5. RECOMMENDATIONS

5.1 Technical recommendations

(1) Studies on the intermediate snail hosts of schistosomiasis should be directed towards the ecological requirements, the correlations between sites of water pollution and snail infection rates, and the bionomics and population dynamics relating to their role in transmission and pertinent to their control.

(2) Continuous evaluation of the effects of molluscicides on the biota in different localities should be made for a sufficient period to permit long-term assessment of any cumulative effects. The possible development of resistance in snails to molluscicides should also be investigated.

(3) More studies of the physiology and biochemistry of snails should be undertaken as a basis for a better understanding of the mode of action of molluscicides.

(4) Every effort should be made to encourage the development of new molluscicides with low toxicity for nontarget organisms, together with micro- and macro-analytical methods including ones suitable for field use.

(5) More research should be undertaken into the development of new slow-release formulations of molluscicides and matrices to be used with existing or newly developed compounds, particularly for focal transmission control.

(6) Every attempt should be made to devise more cost-effective methods of applying molluscicides in large-scale field operations.

(7) Carefully controlled field evaluation of potential biological control agents should be made together with a detailed analysis of costs.

(8) A snail intermediate host from one endemic region, and in particular *Biomphalaria glabrata*, should not be transferred to or maintained in the laboratory of another endemic region for any purpose whatsoever.

(9) With regard to *S. japonicum*, a more precise determination of the life-span should be obtained as well as information concerning egg production during the reproductive life of the worms and the proportion of eggs excreted.

(10) The development of regional guides for the identification of intermediate snail hosts should be encouraged, and this should proceed in parallel with a revision of the classification of snail hosts of the Neotropical Region.

(11) The use of the new antischistosomal drugs in control programmes is to be welcomed. Since these have a direct effect on prevalence and intensity of infection regardless of any reduction in transmission, it is necessary to evaluate, as fully as possible, the role of chemotherapy in control in the field.

(12) The accelerated migration of infected people from regions where *S. mansoni* strains are resistant to known drugs is a matter for concern. Diagnosis and treatment of these migrants must be pursued.

5.2 General recommendations

(1) In accordance with resolution WHA29.58 on schistosomiasis adopted in 1976 by the World Health Assembly(*21*), emphasis must once more be given to the importance of conducting planned epidemiological, biological, and ecological studies before the implementation of water development schemes in tropical areas in order to prevent, or at least minimize, adverse health effects, of which schistosomiasis is only one. WHO should emphasize these concepts to international and national lending agencies.

(2) Countries should consider introducing programmes for the control of schistosomiasis, since recent advances in the knowledge of control methods give additional reasons to expect success. Such control programmes will need to be set up on a long-term basis.

(3) WHO should draw the attention of national governments and of other agencies responsible for large-scale chemotherapy programmes in endemic areas to the advantages of regularly reporting severe reactions or deaths thought to be associated with antischistosomal agents. A monitoring programme would provide the information needed on the therapeutic risk associated with the various antischistosomal drugs in different areas. Drug registers, particularly of people given repeated doses of antischistosomal drugs, may be useful.

(4) In order to have a standard and unbiased evaluation of schistosomiasis projects, WHO should make its expertise in evaluation available to all governments requesting expert guidance in evaluation. However, it should be emphasized that governments should provide all the data required for evaluation purposes.

(5) While WHO has done valuable work in collaboration with Member States in the control of schistosomiasis in large man-made lakes, attention in endemic countries should also be directed to research on and the prevention of health problems arising from smaller reservoirs and irrigation schemes.

(6) There is a need for continuing research on both the field application and development of new tools, and special encouragement must be given to the continuing close liaison between actual control programmes and the field research and training aspects of the Special Programme for Research and Training in Tropical Diseases established by UNDP, WHO, and the World Bank.

(7) Community participation must be considered as a fundamental aspect of schistosomiasis control. Such participation may help to reduce costs and assure the maintenance of long-term intervention measures of surveillance of the epidemiological situation.

(8) In the Sahel area of Africa, following the recent drought, new rice irrigation schemes have been proposed, which are expected to increase schistosomiasis transmission in that area. Therefore, operational control projects, that would serve as core programmes for the

development of integrated control strategies and for training should be established in that region.

(9) WHO should give the maximum possible assistance to the national schistosomiasis control programmes recently established in classically endemic areas such as the Nile Valley, the Philippines, and Brazil, because these endemic areas contain most of the people in the world with severe infections.

(10) Since the shortage of adequately qualified personnel is a major limitation in many public health programmes for schistosomiasis control, career posts and specialized training programmes should be established at regional, national, and international levels. Emphasis should be placed not only on essential specialized techniques but also on inculcating the preventive attitude in all medical, technical, and auxiliary personnel in the application of preventive measures. Training programmes should include non-medical professional personnel such as behavioural scientists, engineers, and econometricians since these disciplines play a significant role in the control of schistosomiasis.

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