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THE CONTROL OF SCHISTOSOMIASIS: EPIDEMIOLOGICAL ASPECTS OF REINFECTION

by

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Current strategies for schistosomiasis control rely heavily on drug treatment intended to reduce morbidity and disease to an insignificant level of public health importance. This approach reduces but rarely, if ever, eliminates transmission. Indeed, infection rates may be little altered snail chemotherapy. Reinfection is inevitable. The mean community prevalence usually returns rapidly to precontrol levels but the mean intensity of infection takes much longer, distorting the general relationship between the two. Because of the focality of schistosomiasis transmission, retreatment based on mean population prevalence is often too late to protect people living near active transmission sites. However, if suitable methods can be developed to examine man after treatment, they should simplify the detection of the main transmission sites, allowing the employment of alternative, focal control measures to consolidate the beneficial effects of mass chemotherapy,

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The whole approach to community control of schistosomiasis changed two decades ago with the arrival of drugs 'safe' enough for widespread field use (WHO,1985). Previously, molluscicides had been the sole weapon available (WHO,1965), and then only for relatively small, circumscribed habitats, such as medium-sized, irrigation schemes (Fenwick, 1972) or isolated natural water sheds (Sturrock et al., 1974; Barbosa & Costa, 1981). Environmental modifications are essential to mount effective public health education programmes against schistosomiasis. Improved sanitation and safe water supplies should control urban transmission, but, realistically, cannot be provided purely for schistosomiasis control in rural areas. It was tacitly assumed that, as the economies of developing countries grew, such environmental improvements would eventually come and control a range of water-borne and water-related diseases.

Today, therefore, schistosomiasis control is based almost exclusively on different forms of population-based chemotherapy, aimed at reducing morbidity to a level where it is not a major public health problem (WHO, 1985). The problems of reinfection have rarely been considered; nor have strategies been developed to deal with them. Before doing so, though, it is necessary to understand what is happening before trying to produce a solution, and such an analysis could be described as studying the "epidemiology of reinfection with schistosomiasis".

#### BASIC CONCEPTS IN THE EPIDEMIOLOGY OF SCHISTOSOMIASIS.

The transmission of schistosomiasis involves three different animals sharing a common habitat — a water body — for at least part of their existence. The parasite moves back and forth through the water body between man and the snail in the course of its life cycle. The intermediate host, the snail, acts as a passive bystander and man, if anyone, is the vector of the parasite. Human behaviour relating to water bodies is immensely important in transmission (Dalton & Pole, 1978), but will not be pursued further here.

In an endemic area, there are five possible combinations for man, snails and water bodies. Transmission of the parasite occurs only where all three overlap (A), which may be quite extensive for a highly endemic area as shown in Figure 1a. Even

#### (Insert Figure 1 hereabouts)

so, some people may have contact restricted to water free of snails (B) or no water contact at all (C). Equally, there can be snail-infested and snail-free water-bodies with which man has no contact (D & E). The ideal control programme should eliminate combination A by whatever means available, but, in practice, minimizes rather than eliminates it (Fig. 1b).

Note, too, that contact includes two processes: contamination and exposure. At one extreme, most people contaminating a site differ from those exposed in it, allowing transmission of the parasite from one person to another (Fig. 1c). At the other extreme, people contaminate and are exposed in the same site, leading to superinfection without extending transmission (Fig. 1d).

Control measures aimed at one sector will not affect parasite stages already in other sectors. Thus, even if chemotherapy eradicates adult worms in man, larval stages in snails are unaffected. Experience, though, has shown that even true mass chemotherapy rarely achieves a 100% cure rate in man (Anderson & Medley, 1987). Some worms, possibly at the prepatent stage, survive treatment, or escape it in untreated people (pregnant women, very young children and patients with other diseases) and in people who refuse treatment. Where treatment is targetted at a specific group of people, parasites will still survive in undiagnosed cases within that group, as well as in infected people in non-target groups (Lehman et al., 1976; Katz et al., 1978; Sleigh et al., 1981; Butterworth et Jordan, 1985; Mahmoud et al., 1987; Kloetzel & Schuster, 1987; King et al., 1988). Population movements further confuse the issue: 'cured' residents reinfected elsewhere and immigrants can reintroduce the parasite to a successfully treated For these various reasons, transmission, albeit at a reduced rate at first, persists after even the most successful chemotherapy programmes and reinfections are inevitable.

# EPIDEMIOLOGICAL STUDIES ON SCHISTOSOMIASIS

Epidemiological terms - Epidemiology is often a loosely used term. Epidemiological studies must consider the entire population, both susceptible, uninfected normals as well as infected cases and, possibly, immunes (subjects who have been infected but who are no longer susceptible). A peculiar complication in helminthic diseases is that non-immune cases continue to acquire additional parasites after their initial exposure, accumulating progressively increasing worm burdens.

The basic measurements widely used in schistosomiasis are:

- Prevalence: the proportion or percentage of a population infected at a given time;
- Incidence: the rate at which uninfected normals acquire infection over a defined time period, usually expressed as a percentage or proportion per time unit, and
- Intensity: the number of parasites present within the entire population (or cases) at a given time.

Schistosome epidemiology in man — For man, these epidemiological measurements are conventionally obtained by parasitological methods detecting eggs in faeces (epg) or urine (eggs per 10 ml of urine) (Jordan & Webbe, 1981). Intensity is a quantitative measurement in as far as increasing egg loads reflect increasing worm burdens. Some confusion is caused by the inconsistent reporting of results: mean intensities may be for the entire population or only the cases, and may be simple arithmetic means or geometric means. The latter eliminate distortions due to a few, heavily infected outliers in the skewed, often log normal distribution of egg counts within the whole population or any part of it.

Both prevalence and incidence are qualitative measurements giving no direct information about intensities among cases. Even so, prevalence, within its upper limit of 100%, has a general, direct relationship with intensity: the higher the prevalence, the greater the intensity. In man, both age-specific schistosome prevalence and intensity curves are almost universally convex, rising to peaks at some time in the second decade of life. Consequently, inferences can be made about mean intensities from prevalence surveys, especially if supported by incidence data.

Thus, qualitative serodiagnosis for antibodies appears to offer an attractive alternative to egg counting for prevalence surveys. Alas, this really only applies to untreated populations at present because antibody detection is not widely considered appropriate for monitoring the effects of treatment. anti-egg antibodies persist for months after successful treatment eliminates egg excretion (Mott & Dixon, 1982). antibodies are little better. Their levels sometimes rise with the release of antigen from dying worms or, because many schistosomular and adult worm antigens cross react, persist unchanged due to continued stimulation by schistosomula during re-exposure after treatment, even in immunes (Butterworth et al., 1984, 1985). In theory, quantitative antigen detection could overcome these problems but, so far, no technique suitable for routine field use has yet been developed, despite considerable effort to this end (De Jonge et al., 1989; Doenhoff et al., 1989).

Morbidity and pathology, whose reduction is the primary goal of current chemotherapy programmes, are also related to the intensity of infection (WHO, 1985). In general terms, the the higher the egg count the greater the risk that a person will develop disease. However, one of the mysteries of schistosomiasis is that not all people with high egg counts develop schistosomal disease and it also sometimes develops in people with low counts. Consequently the results of morbidity and intensity surveys often correlate rather poorly (Cook et al., 1974; Warren et al., 1974; Lehman et al., 1976; Andrade & Bina, 1985; Gryseels & Polderman, 1987). A confounding factor is that the most common signs of schistosomal morbidity (e.g.

hepatomegaly, splenomegaly and hepatosplenomegaly, diarrhoea and abdominal pain) may have other aetiologies. Possibly, the field use of ultrasonography, if properly standardized, will help clarify this somewhat confusing picture (Homeida et al., 1988; King et al., 1988; Abdel-Wahab et al., 1989).

Schistosome epidemiology in snails — Most epidemiological studies of snails have focussed on prevalence, obtained by examining collections of field snails for cercarial shedding, or by crushing snails to detect both cercariae and sporocysts (Olivier, 1973). Intensity has little meaning in snail epidemiology because the parasite is undergoing rapid, asexual multiplication. However, a snail's daily output can be measured directly (Chu & Dawood, 1970). Supplementary information can be obtained either by cercariometric methods, which recover cercariae directly in water samples taken from transmission sites (Theron, 1979), or indirectly by animal exposures (Webbe, 1966; Sturrock, 1973).

Surprisingly little attention has been given to the incidence of infection in snails. As they have a much shorter lifespan relative to either man or adult schistosomes, incidences have to be measured over a period of days or weeks rather than years. Estimates from age prevalence curves of field snails derived by catalytic model analyses (Sturrock & Webbe, 1971) agreed surprisingly well with direct estimates obtained by exposing uninfected, laboratory-bred snails in transmission sites (Sturrock et al., 1974; Woolhouse & Chandiwana, 1989).

### EPIDEMIOLOGICAL MONITORING OF A CHEMOTHERAPY PROGRAMME

Conventionally, the success or otherwise of chemotherapy-based control programmes is assessed primarily by their effect on mean prevalence, sometimes with information on intensity and incidence, either for the whole community or broken down by age (and sex). Figure 2 shows the results for a single

#### (Insert Figure 2 hereabouts)

treatment programme against Schistosoma mansoni in Kenyan school children. The limitations of prevalence as an indicator are evident. Pretreatment age-specific prevalences (dark towers) follow the typical convex curve. After treatment in 1985, prevalences dipped briefly in the target age groups, but had returned almost to pretreatment levels within two years.

In contrast, intensity in these groups dropped much more dramatically, and rose more slowly in the face of reinfection. The general relationship between intensity and prevalence was weakened, if not entirely destroyed. Moreover, there was some differential effect: the rise in intensity was less pronounced in the oldest target group and there was some evidence of a decline

in the untreated adults. Does resistance to reinfection develop during the second decade of life and are adults immune to reinfection?

The extensive summary of mean population data included in figure 2 hints at this possibility, but observations must be focussed on individual subjects and transmission sites within the study area to obtain more conclusive evidence (Butterworth et al., 1985). Even then, the relationships are by no means easy to to unravel. As shown in Table I, long term snail studies in this

#### (Insert Table I hereabouts)

area revealed substantial variations in the presence and abundance of Biomphalaria pfeifferi snails, both infected and uninfected, from site to site and from year to year. Although the prevalence in snails dropped in the year after treatment, it oscillated violently in subsequent years. Moreover, the overall snail populations, which were relatively stable in the first three years, dropped substantially in years 4 and 5.

#### FOCALITY OF TRANSMISSION

i. Spatial relationships — Its focal nature is perhaps the most important feature of schistosomiasis transmission. A number of studies have shown that both prevalence, intensity and incidence of human infections diminish with distance from a known transmission site (Lehman et al., 1976; Sturrock et al., 1983; Jordan, 1985). This is illustrated in a simplified form in Figure 3a by a series of concentric circles, equivalent to contours on a

## (Insert Figure 3 hereabouts)

map, drawn on the horizontal plane with high, medium and low prevalences (or intensities) centered on the transmission site (X). Plotting prevalence (or intensity) on a vertical axis produces a series of concentric cones as illustrated (Fig. 3a), representing a "volcano" of prevalence erupting from the transmission site. A chemotherapy programme would shrink this "volcano" but it would remain centered over the transmission site (Fig. 3b). Without further intervention, continuing transmission would allow it to regrow to its original size.

In most endemic areas, transmission is rarely confined to a single site. The previous model can be extended to adjacent sites whose catchment areas overlap. If, for simplicity, it is assumed that the effect is additive where the prevalence bands overlap (i.e. low + low = medium; low + medium = high etc.), then the 'contours' shown on figure 4 would represent a complicated,

(Insert Figure 4 hereabouts)

triple-peaked volcanic range. Before any treatment programme, it would not be clear if it represented a single large and complex area of transmission, or several separate transmission sites. This is the problem facing public health epidemiologists planning control measures when they plot precontrol prevalences on maps of an endemic area. Only after a chemotherapy programme would it be possible to see that there were in fact but two localised transmission sites.

ii. Temporal (seasonal) relationships — The two preceding examples assumed that transmission was continuous at each site. Studies in many countries have shown, with a few notable exceptions, that this is rarely the case (Sturrock, 1973; Woolhouse & Chandiwana, 1989). Seasonal changes related to climate affect both the human and, especially, snail populations (Sturrock, 1984; 1986). During heavy rainfall, people have reduced contact with transmission sites: the water becomes too muddy for clothes washing and clean water can be collected around the home for domestic use. Heavy rainfall also dislodges snails from rivers and streams although it may be beneficial for populations in pools, lakes and marshes. Conversely, snail habitats may dry up during droughts, killing most snails and halting transmission.

Temperature also plays a role. High temperatures <30 C speed snail growth and breeding, as well as the rate of development of the intramolluscan schistosome stages (Foster, 1964; Pfluger, 1981). They also encourage increased human water contact, especially among children. Low temperatures slow the rate of development of snail populations and their larval schistosomes, and discourage human water contact. Average climatic figures show clearcut seasonal patterns, but the actual figures vary considerably from year to year making it difficult to predict what will actually happen.

iii. Human and snail mobility - The importance of human population movements has already been touched on. Snails, though not renowned for their speed, are also mobile, complicating studies on their part in schistosome transmission. When adverse conditions produce catastrophic population declines, surviving in protected sites (refuges or reservoirs) can reinvade and repopulate adjacent areas with surprising rapidity (Sturrock, 1973). Much, though not all, snail movement is passive, with snails carried from one place to another by flowing water, either free or on floating vegetation. However, it is often a matter of chance whether they reach any particular site. It is relatively easy, with practice, visually to identify potential transmission sites in the field, but it is impossible to be sure that they are currently active without repeated, direct snail or cercariometry observations, or to predict accurately what may happen in the future. The earlier analogy likening transmission sites to volcanoes is still appropriate: transmission through the snails is as irregular, unpredictable and violent as the eruptions of a volcano.

#### IMPLICATIONS OF REINFECTION AFTER CHENOTHERAPY.

Epidemiological studies before any treatment campaign in an endemic area usually show a confusing spatial pattern of human infection in terms of prevalence and intensity. Long-term human and snail studies are needed to identify actual and potential transmission sites (Butterworth et al., 1984; Sturrock, 1986). While such studies are feasible in small-scale projects, they are impractible in large scale control programmes. Consequently, the strategy of morbidity and disease control using selective, targetted, population-based chemotherapy is usually applied after the minimum of precontrol studies focussed almost entirely on man (Machado, 1982). Although treatment rapidly lowers mean population prevalence and intensity, this approach has the inherent weakness that transmission is, at best, halted temporarily: reinfections are inevitable. What, then, should be the next step?

So far, the most popular choice has been to retreat at some later stage, often using the same criteria as for the initial treatment campaign. Alternative approaches include case detection and retreatment, although this is only applicable in relatively small schemes (Jordan, 1985), or to rely on self diagnosis by heavily infected people presenting themselves at clinics for retreatment (WHO, 1985). These approaches have important defects. First, they may encourage the development of drug resistance, as has already been documented for oxamniquine and hycanthone in Brazil, though not for praziquantel so far (Diaz et al., 1982; Foster, 1987). Secondly, where a simple overall mean prevalence level is used as the indicator for retreatment, it may no longer reflect intensity accurately but may mask focal pockets of high intensity around the major transmission sites, especially if it is diluted by data from resistant or immune adults (Butterworth et al., 1985; Wilkins et al., 1987). At this point, one might despair of ever controlling schistosomiasis but I would like to finish on a more optimistic note.

If suitable techniques can be devised to screen populations 6 to 12 months after treatment, plotting post treatment human prevalence and intensity could assist the location of the main transmission sites, and alternative measures for snail control could then be applied to these especially dangerous sites. This approach should consolidate the beneficial effects of one or two rounds of chemotherapy. It may not be easy, as teams will have to be trained for the purpose, and an appropriate administration set up to make them effective and to monitor their performance. This approach may appear to increase the complexity and cost of control programmes, but it could prove cheaper and more effective

in the long run than eternal rounds of human diagnosis and treatment.

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Table I.

Total annual snail recoveries from 12 sites over a 5-year period. Schistosoma mansoni percentage infection rates shown in parentheses.

(NB. Chemotherapy targetted at all infected schoolchildren was given at the end of year 1 - see Figure 1.)

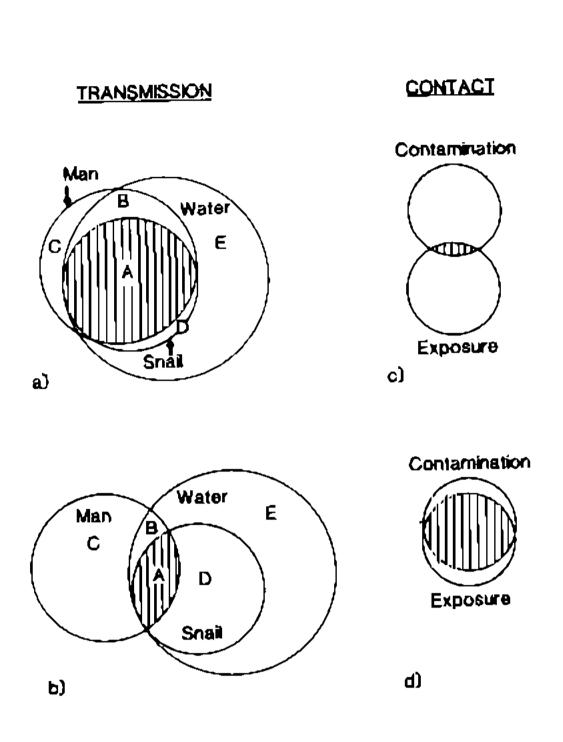
SITE	YEAR					SITE
	1	2	<u> </u>	4	5	TOTALS
1	710	951	1361	52	0	3074
	(9.4)	(0.4)	(1.3)	(0)	(0)	(2.9)
2	2657	1397	1332	806	1432	7624
	(1.1)	(1.4)	(1.5)	(1.4)	(0,4)	(1.2)
3	742	813	416	282	695	2948
	(16.9)	(1.7)	(O)	(O)	(Ŏ)	(4.7)
4	1817	743	356	58	12	2988
	(18.5)	(3.0)	(2.5)	(5.2)	(0)	(12.4)
5	171	406	<del>9</del> 8	0	0	675
	(5.3)	(1.2)	(¢)	(0)	(Ø)	(2.1)
6	0	713	348	329	48	1458
	(0)	(2.1)	(3.0)	(0.6)	(0)	(1.9)
7	270	1046	1203	261	6	2786
	(20.4)	(5.3)	(5.7)	(64.4)	(0)	(12.5)
8	1466	1286	1092	71	35	3950
	(19.2)	(11.1)	(10.2)	(11.3)	(2.9)	(13.8)
9	8	277	578	187	105	1157
	(Q)	(8.3)	(0.9)	(0.5)	(1.0)	(2.6)
10	0	72	<b>29</b> 3	29	7	401
	(O)	(36.1)	(6.1)	(0)	(Ŏ)	(11.0)
11	0	570	588	84	14	1256
	(0)	(タ.フ)	(6.1)	(16.7)	(0)	(8.4)
12	0	616	499	0	83	1198
	(Q)	(6,3)	(2.4)	(O)	(日.4)	(4.8)
YEAR	7843	8890	8184	2161	2437	29515
TOTALS	(11.5)	(4.8)	(3.8)	(9.6)	(O. 6)	(6.3)

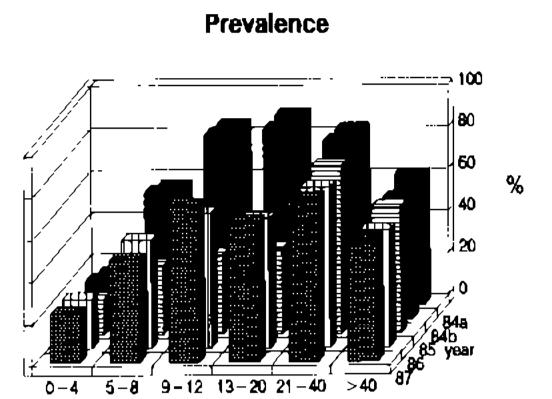
Captions for figures.

- Fig. 1. Venn diagrams showing the 5 combinations of snails, man and water bodies for schistosomiasis transmission (a) before and (b) after treatment; and that human contact with transmission sites comprises two processes, contamination and exposure, which may overlap only slightly (c) or almost completely (d).
- Fig. 2. Mean human Schistosoma mansoni age-specific prevalences and intensities before (dark towers) and for two years after a single treatment of school children.
- Fig. 3. Diagrammatic representation of spatial relationship between transmission sites and human prevalence and intensity a) before and b) after treatment of a single site.
- Fig. 4. Flots of human prevalence a) before and b) after control around two transmission sites.

FIG. 1

FIG. 2





AREA S(chools)

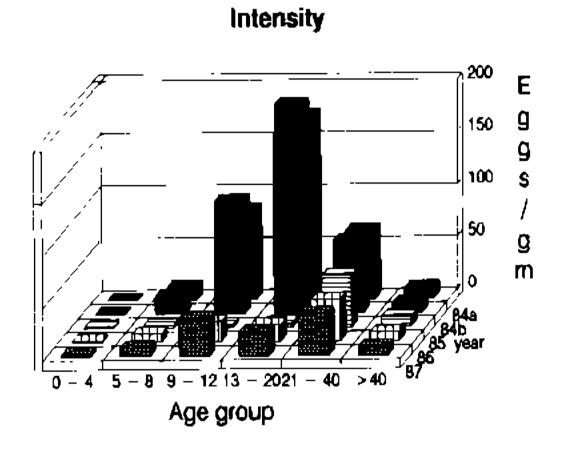


FIG. 3

FIG. 4

