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A pilot control trial of schistosomiasis in Central Liberia by mass chemotherapy of target populations, combined with focal application of molluscicide[4]

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Summary

In an area of high transmission of *Schistosoma haematobium* and *S. mansoni* in Central Liberia, populations of five villages and intermediate host snails were surveyed for two years. In three of these villages focal application of molluscicide (niclosamide) in the main transmission sites was combined with mass chemotherapy of a target population representing 76 to 90% of the contamination index. In the two other villages, which served as control, the prevalence indexes remained stable or increased a little during the period of this study. A three dose metrifonate mass treatment was applied in one village with only *S. haematobium* infections. The compliance was very poor for the second and third dose but the quantity of eggs eliminated by the whole population present before and after mass treatment was reduced by 50%. No snails were found after molluscicide applications but as the incidence remained unchanged it is suspected that inhabitants have been reinfected by going to their fields.

Concurrent metrifonate and niridazole mass treatment in one dose was applied in another village with only *S. haematobium* infections. Molluscicide applications reduced the snail population by 80% but did not affect the transmission. Prevalence indexes were almost the same before and after this intervention.

In the last village, praziquantel (40 mg/kg in 1 dose) was used because both *S. haematobium* and *S. mansoni* infections were present. Molluscicide applications reduced the snail population by 99% and 87% for *Bulinus globosus* and *Biomphalaria pfeifferi*, respectively. This intervention stopped the transmission

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of *S. haematobium* for at least one year and reduced the prevalence from 21% to 4.6%. On the contrary for *S. mansoni* infections, the incidence remained very high (50%) and the prevalence was unchanged after one year follow-up. This could be explained by lower efficacy of praziquantel against *S. mansoni* (cure rate: 53%) and of molluscicide application against *B. pfeifferi*, which are highly susceptible to *S. mansoni* (infection rate 44%).

The importance of migration in these villages is emphasized. Prevalence indexes were largely influenced by the arrival of newcomers who played a more important role in the maintenance of transmission after target mass chemotherapy than the infected persons excluded from this treatment.

The costs per capita protected were 3.33 US$ for metrifonate, 1.53 for metrifonate and niridazole combined and 1.67 US$ for praziquantel. These figures do not include costs for parasitological examinations.

It is concluded that in such a region of low morbidity and pronounced migrations, schistosomiasis control is reasonable only if based on an adequate network of primary health care services.

Key words: schistosomiasis mansoni; schistosomiasis haematobium; control; targeted mass chemotherapy; metrifonate; niridazole; praziquantel; snail control; bayluscide; Liberia.

Introduction

Epidemiological data on the occurrence of schistosomiasis and its intermediate hosts in Liberia have been collected by several authors, including Maas (1927, 1930), Vogel (1932, 1958), Miller (1957) and Sodeman (1973, 1979). Our previous study (Saladin et al., 1980) confirmed that no transmission of schistosomiasis occurs in the coastal belt of about 100 km in width. In the adjacent zone of the next 50 km in Bong County only the transmission of *Schistosoma haematobium* takes place. Further north the transmission of *Schistosoma mansoni* also occurs.

In Liberia the only intermediate hosts of *S. mansoni* and *S. haematobium* are *Biomphalaria pfeifferi* and *Bulinus globosus*, respectively. More precise epidemiological data about schistosomiasis in Liberia are presented elsewhere (Dennis, 1983). The purpose of the present study, carried out from 1979–1981, was to evaluate the impact of mass chemotherapy of a target group, combined with simultaneous application of molluscicide to the known water contact sites, on schistosomal infection rates in five communities of Bong County. The approach presented here was chosen to reduce the costs of schistosomiasis control by finding a method that permits the omission of expensive and time consuming parasitological examinations prior to control measures.

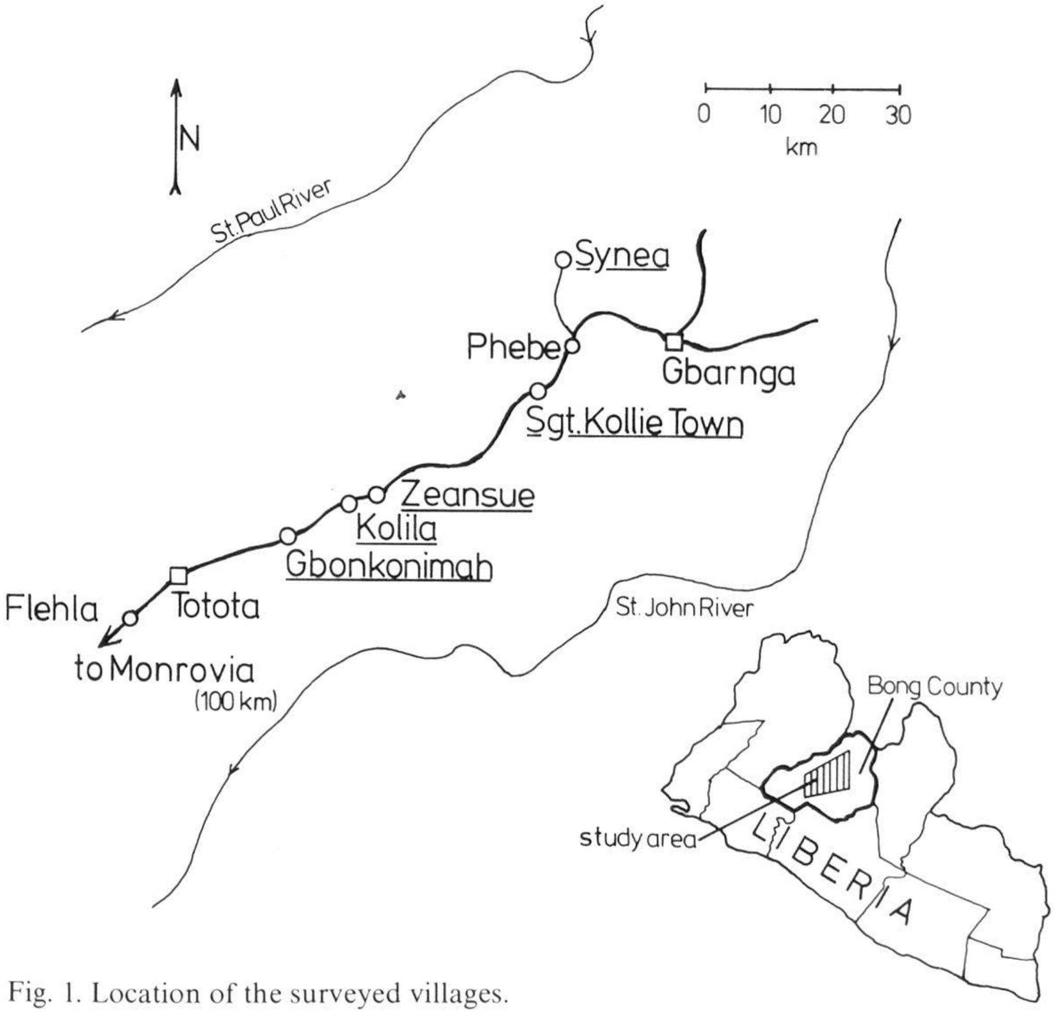

Fig. 1. Location of the surveyed villages.

Bong County was selected because of its high prevalence of schistosomiasis in an area of high human population density (Dennis, 1983), together with agricultural development projects financed by the World Bank and the Liberian Government. This trial was combined with a morbidity study (Holzer et al., 1983) and should help the Liberian Government as well as the Liberian agricultural development projects to estimate priorities and possibilities.

Population, Study Area, Material and Methods

1. Description of the study area

The five villages selected for the trial after preliminary investigations (Saladin et al., 1980) are all situated in a main focus of transmission of schistosomiasis in Liberia, in Upper Bong County (see Fig. 1). Three settlements, Gbonkonimah, Kolila and Zeansue are located in the area where only transmission of *S. haematobium* occurs, and two villages, Sgt. Kollie Town and Synea, are situated in the transmission area of urinary as well as intestinal schistosomiasis. Even though Bong County lies within the West African rain forest belt the study area represents the driest part of Liberia, with an average yearly rainfall of 2000 mm. The rainy season lasts from May to October, interrupted by a short dry period in August. The average population density in Bong County is 150/km^2. Along the tarred road, the only connection between the coast and the interior of the country, the population has become denser. About 60% of the population of Bong County belong to the Kpelle tribe and 30% are Mandingoes. The sanitary facilities are similar in all five villages. Each one is equipped with at least one hand water pump. Only about 10% of the housholds have a toilet (pit latrine), and these are located at the periphery of the settlements and locked by the owners. Malaria is holoendemic in the study area, the prevalence of onchocerciasis is high (Holzer et al., 1983) and intestinal helminthiases are frequent (Saladin et al., 1980). Most of the land around the villages is cultivated with rubber trees, swamp rice and other crops (tropical subsistence farming).

2. Description of individual watersites

All the transmission sites of the research area are located in the catchment area of the St. John River (see Fig. 1). During the whole year water is available in natural bodies of water around the settlements. Even though the different water areas around the villages would be used separately for different purposes, by tradition the nearest water site serves as bathing and washing place as well as a toilet and occasionally for drinking. For most people, especially for the younger, frequent water contact is unavoidable.

Gbonkonimah is surrounded by swamps occasionally used for swamp rice cultivation. These are fed by small creeks. No intermediate host-snails could be found in the immediate vicinity of the village. The nearest bodies of water harbouring *B. globosus* are located about 5 km south of the settlement near Blanta. These sites are frequented by the inhabitants of Gbonkonimah, mainly for fishing.

Kolila Town is situated near the Kolila, a fast running river, the side arms of which occasionally harbour *B. globosus*. Fono Creek is south of the village and is the main transmission site for Kolila Town. It is used by the people of the village for bathing and fishing. Four places are easily accessible by footpaths.

Zeansue is located by the Yaale, a fast running, sandy river, where no intermediate hosts could ever be found. Zeansue Creek joins the main river, splitting the village into two parts and harbours *B. globosus*. It is accessible by footpaths at seven places and is used for washing, bathing and fishing. Drinking water is also fetched from the river.

Sgt. Kollie Town is enclosed by two streams, the big Gbalang River in the north-east and Gbaia Creek in the west and south. The latter forms a transmission site, where *B. globosus* and *B. pfeifferi* are abundant and where a footpath leads all along the shore and several footbridges cross the water. The Gbaia is used for all daily needs, including bathing, washing, fishing and as a latrine. The rice irrigation system of the Central Agricultural Research Institute also harbours the snail hosts, but is not accessible to the public. The stream feeding these swamps passes behind the schoolhouse and is densly populated with *B. globosus* and *B. pfeifferi*.

Synea is surrounded by swamps where rice is cultivated. Neither *B. globosus* nor *B. pfeifferi* was found in these swamps. The two species could be collected in a stream crossing the road to Balama, about 4 km north of Synea, as well as on the road to Garlain, 500 m east of Synea in a place called the women's bath. The main transmission area, however, is a creek near Garlain, 5 km east of Synea, which was not accessible during the time of the survey, since it was occupied by a society bush school.

3. Census and population sampling

Each house in all five villages was marked with a number, and all the inhabitants of each house were registered by name, age, sex and tribe. In Sgt. Kollie Town and Synea, each with a known population exceeding 1000 persons, random samples of 500 individuals were selected for examination. This sampling was made by selecting house numbers with a random number generator (Texas Instruments 59) which produced numbers of homogenous distribution. The same houses were selected for all the following examinations. The people living in these selected houses were, however, not always the same during the whole period of the study. In the smaller villages (Gbonkonimah, Kolila and Zeansue) the whole population was expected to participate in the study.

4. Collection and examination of stool and urine samples

In Sgt. Kollie Town and Synea stool and urine samples were collected in plastic containers. In Gbonkonimah, Kolila and Zeansue only urine specimens were collected. Samples were obtained at any time during the day, depending on the presence of the people. Fresh urine samples were filtered as described by Olivier (1973), using Whatman filters No. 1 and stained with Lugol solution. Microscopic examination was carried out in the villages and the results were expressed as number of eggs per 10 ml of urine. Portions of one gram of stool were transferred to 10% formol-saline-solution and processed in the laboratory by the modified Ritchie formol-ether concentration method, described by Knight et al. (1976). *S. mansoni* eggs were counted and recorded as number per gram of stool. The presence of other helminth eggs was also recorded. These results are not presented here.

The results of the quantitative egg counts were expressed as geometric means (geom. $\bar{m}$) for all examinations before treatment, as well as geometric means of the actual egg count + 1 [geom. $\bar{m}$ $(x+1)$] for posttherapeutic controls, to include the non-infected subjects (Lewis and Taylor, 1967). The 1 added to the egg counts was not substracted later, so that the 1-level represents the zero-line. The Mann-Whitney U-Test was used to demonstrate statistically significant differences between egg counts before and after treatment. The statistical significance in differences of prevalences was tested by the χ^2-test, including the Yates' correction.

5. Mass treatment of the target population

The target groups were determined on the basis of the results of the first parasitological examination in 1979. A preliminary study carried out on 69 persons according to the method described by Davis (1968) showed the percentage of hatching miracidia to be statistically not different in all age groups (80–95%).

For the determination of the contamination index (CI) of each age group from each village the following formula was used:

CI = population of age group × prevalence × geom. mean of egg count

Similar indexes have been used earlier by Jordan and Webbe (1969) (Transmission Index), Jordan et al. (1980) (Index of Potential Contamination) and Upatham et al. (1976) (Contamination Potential).

The age groups making up about 80% of the CI of the whole village were considered as the target group. Everybody belonging to the target group, whether infected or not, was scheduled for the treatment according to Table 1. Gbonkonimah and Synea served as control villages for the *S. haematobium* and the *S. haematobium* plus *S. mansoni* transmission areas, respectively. The population outside the target groups as well as that in the control villages received polyvitamins or mebendazole to assure cooperation. The drugs had to be taken by each person individually on the spot and under medical supervision. Pregnant women were excluded from treatment. Only side effects brought to our attention were recorded.

6. Timing of the parasitological examinations and of the mass treatments

1. Examination (one year before treatment)	June/July 1979
Examination of Zeansue only (one month before treatment)	May 1980
Treatment of target groups (three months after application of molluscicide)	June/July 1980
2. Examination (3 months after treatment)	Oct./Nov. 1980
3. Examination (one year after treatment)	Aug./Sep. 1981

7. Snail surveys and snail control

The surveys were carried out monthly for one year before and one year after the applications of molluscicide. Snails were collected manually by five men searching for 10 minutes and the findings were reported as number of snails per man per 10 minutes.

Patent trematode infections in *B. globosus* and *B. pfeifferi* were detected by exposing the snails, in test tubes, to sunlight for at least two hours, taking care that no overheating occurred. The snails were returned to the habitats on the same day. The water in the test tubes was carefully examined, and the cercariae of mammalian schistosomes were identified the following day under a dissecting microscope after storage at 4° C.

Table 1. Type of treatment, number of persons in the target groups and compliance

Village/ transmission	Drug/dosage	Target group (No. of persons)	Compliance
Kolila *S. haematobium*	metrifonate 12.5 mg/kg × 3 with interval of 3 weeks	male 0–15 y. female 0–25 y. (198)	1 dose only 29% 2 doses only 21% 3 doses 24% total 74% at least 1 dose
Zeansue *S. haematobium*	single dose of metrifonate (12.5 mg/kg) + niridazole (30 mg/kg)	male 6–15 y. female 6–15 y. (294)	74%
Sgt. Kollie Town *S. haematobium* *S. mansoni*	praziquantel 40 mg/kg single dose	male 0–20 y. female 6–30 y. (1,120)	86%

After thorough questioning of the local people about fishing and washing places, "where the water makes your skin itch", and after extended exploration of the surroundings of the villages, application of molluscicide to the water contact sites harbouring the transmitting snails was scheduled for January 1980, when the water levels reach a minimum and the snail population is increasing. Due to difficulties in supply of the molluscicide, the first application could, however, only be carried out in April 1980. The application of molluscicide was repeated in early January 1981, when the snails began to reappear.

Niclosamide (WP-70, Bayluscide R) was used. Different methods of applications were tried: either spraying with flower cans with simultaneous stirring of the water (in 1980), or drip-feeding (in 1981). The concentration of the molluscicide was previously calculated to be about 1 ppm. No concentration test was made, but snails were exposed in cages to demonstrate the effect of the molluscicide.

Fono Creek, south of *Kolila*, was treated in 1980 for 3 km upstream.

In *Zeansue* the creek (Zeansue Creek) was treated with molluscicide as far as 1 km upstream, including all the ponds and side arms as well as a small stream joining Zeansue Creek from the western side (length about 500 m). The application of molluscicide was carried out in 1980 and repeated in 1981.

Gbaia Creek in *Sgt. Kollie Town* was treated with molluscicide in 1980 and again in 1981 for 3 km. In addition to the Gbaia, the stream behind the schoolhouse, which feeds the Government rice fields, was treated with molluscicide in April 1980 as far upstream as the water was stagnant about 2 km.

8. Cost analysis

The cost analysis was based on the local salaries of a physician, a principal investigator and four trained assistants. It includes the time used for the mass chemotherapy and the molluscicide treatment, as well as the costs of the drugs (metrifonate: US$ 0.27/treatment/60 kg; metrifonate + niridazole: US$ 1.27/treatment/60 kg; and praziquantel: US$ 4.25/treatment/60 kg) and the molluscicide. The time invested in the parasitological examinations was not considered, since the present trial was carried out to show possibilities for control measures without preliminary parasitological investigations.

Table 2. Number of persons registered in 1979-census (C), sample size (S) and participation in the three examinations: I = 1979 (one year before treatment), II = 1980 (three months after treatment) and III = 1981 (one year after treatment), % f = % females

	Gbonkonimah		Kolila		Zeansue		Sgt. Kollie		Synea	
	No.	% f	No.	% f	No.	% f	No.	% f	No.	% f
C	413	54.0	284	56.7	649	50.8	1976	49.2	1385	50.3
S							500	48.6	610	51.1
I	284	52.5	239	59.0	477	50.0	418	53.1	391	56.0
II	266	50.4	153	46.4	288	59.7	304	50.3	239	60.3
III	165	50.3	167	55.1	437	45.8	201	53.2	197	60.4

Results

1. Census, population sampling and compliance

The number of persons registered in the 1979 census, the sample size and the participation of the population in the three examinations during 1979 (one year before treatment), 1980 (three months after treatment) and 1981 (one year after treatment) are shown in Table 2. In the two villages where a sample of the population was examined the age and sex distribution of the sample showed no difference from that of the total population (χ^2-test). The age and sex distribution of the participating persons at each of the examinations was representative of the total population (test of homogeneity). At Zeansue (about 40) as well as in Synea (an unknown number of) boys aged between 10 and 15 years were attending the society bush school and therefore were not present at the time of the 1979-census, the first and second examination or for the treatment, but they showed up one year later for the last examination.

Compliance to treatment is reported in Table 1.

2. Parasitological findings and results of treatments

The evaluation was carried out for two purposes: first to check the efficacy of specific treatment on treated people, and secondly to evaluate the impact of the control measures on the whole community.

The efficacy of specific treatment could only be evaluated for persons who attended the first examination in 1979, were treated in 1980 and were followed up three months later. For the calculation of the egg reduction, the geometric mean of the egg counts was used. The results are presented in Table 3.

The efficacy of the targeted mass treatment on the transmission of schistosomiasis in the five villages is summarized in Tables 4 and 5 and Fig. 2. The results are subsequently analysed separately for each village.

Table 3. Egg reduction and cure rates in the 3 villages treated

Village/drug	No. treated and followed-up	Cure rate	Egg reduction rate
Kolila Metrifonate	38*	60.8%	96.4%
Zeansue Metrifonate + Niridazole	53*	11.1%	70.7%
Sgt. Kollie Town Praziquantel	67* 65**	100.0% 52.7%	100.0% 98.3%

* *S. haematobium* infections
** *S. mansoni* infections

a) *Gbonkonimah* (Control village for *S. haematobium* infection, see Table 4a). The total population was 413 persons (1979 census) but 430 were registered for the first examination. Of these 103 were never examined during the whole study. Before the second examination 144 newcomers were registered and examined at the second or third examination. At the third examination 39 newcomers were surveyed. Thus, at least 44% of the population had changed from June 1979 to September 1981.

Within the three years of examination, the prevalence of *S. haematobium* fluctuated from 16.6 to 23.7% (χ^2-test, $p<0.05$) and to 18.8%. These fluctuations can, however, be explained by the introduction of newcomers with higher prevalence (26.6%) at the second examination and with lower prevalence (10.3%) than the residents at the third examination. Statistically, the difference is significant between prevalence in June 1979 and prevalence in September 1980 among newcomers (χ^2-test, $p<0.01$) but not among people who had already been examined in 1979.

The prevalence between the male and the female population showed no difference in any of the examinations.

The incidence was 7% (9.7% in age-group 6–15 years) among 139 persons examined only in 1979 and 1980 and 16.7% (15.6% for age-group 6–15 years) among 89 persons examined only in 1980 and 1981. These low incidence rates confirm that the source of infection is far from the village.

The fluctuations observed in the geometric means (x + 1) of egg counts (see Fig. 2) are also explained by the introduction of infected immigrants.

b) *Kolila* (Metrifonate treatment for *S. haematobium*, see Table 4b). The total population was 284 persons (1979 census) but 295 were registered for the first examination. Of these 18 were never examined or treated during the whole study. 105 newcomers were registered for the mass treatment, but only 29 were present at either the second or the third examination. 63 newcomers appeared after the treatment and were surveyed at the second or third examinations. 80 newcomers were examined only at the third examination.

The prevalence of *S. haematobium* in 1979 was 43.5%, with no difference between males and females.

The target group contained 83% of the contamination index and was formed by the age-group 0–15 years for the males and 0–25 years for the females. However, small children who were not yet walking were excluded from the treatment. 74% of persons in the target group took at least one dose of metrifonate, representing 51% of the total population (see Table 1).

Only minor side-effects were reported. Itching skin and nausea being the most frequent complaints but only reported in 2% of cases treated.

Three months after treatment the prevalence dropped significantly in the male population from 51 to 31.7% (χ^2-test, $p<0.05$), but for the total population the decline was not significant (see Table 4b).

Taking into account the migrations, the results look different (see Fig. 2). At the third examination, the geometric mean $(x+1)$ of egg counts was 2.6 and 6.8, respectively, for the group present before mass treatment and the newcomers. The difference is highly significant (U-test, $p<0.01$). Statistically, no difference can be observed between the egg counts 3 months and 1 year after treatment among those people that were present at the mass treatment. For the residents the transmission was stabilized for one year at least after treatment but the impact of the control measures can be misinterpreted by the arrival of infected newcomers.

The incidence could be calculated at 10 month intervals after mass treatment among 53 persons. With a level of 29% (40% for age-group 6 to 15 years) it shows that transmission was far from being interrupted by focal mollusciciding.

c) *Zeansue* (single dose metrifonate and niridazole treatment for *S. haematobium*, see Table 4c). The 1979 census showed a population of 649 persons but 670 were registered for the first examination. Of these 96 (14%) were never examined or treated during the whole study and should be considered to have emigrated. 190 newcomers (28%) were registered at the second examination, just before mass treatment, and at least treated or examined once later. 278 newcomers (41%) arrived after the mass treatment and were present only at the third and/or fourth examinations. One has to consider that more than 50% of the population changed during the period of the study (1979–1981).

The prevalence of *S. haematobium* was 47.9% and 61.4%, respectively, in 1979 and 1980. During the same period, the overall incidence was 38% (150 persons) but 80% and 85%, respectively, for the age groups 0–4 and 5–15 years.

The target group, covering 81% of the contamination index, included males and females from 6 to 15 years old. 74% of the children of the target group received the treatment, representing 33% of the total population present at this time.

Table 4. Prevalence (P), geometric means, geometric means (x + 1) and contamination indexes (CI) at the time of the parasitological examinations in 1979, 1980 and 1981 (the contamination index found in 1979 was assumed 100% in all villages)

Table 4a. Control villages: Gbonkonimah *(S. haematobium)* and Synea *(S. haematobium* and *S. mansoni)*

Census 1979	1979				1980			1981		
No. of pers.	No. examined	P %	Eggcounts		No. examined	P %	Egg-counts $\bar{m}$ (x + 1)	No. examined	P %	Egg-counts $\bar{m}$ (x + 1)
			geom. $\bar{m}$	geom. $\bar{m}$ (x + 1)						
Gbonkonimah *(S. haematobium)*										
413	284	16.6	11.7	1.6	266	23.7	2.3	165	18.8	1.8
	CI = 802 (100%)				CI = 3,141 (392%)			CI = 1,495 (182%)		
Synea *(S. haematobium)*										
1,385	391	30.9	14.7	2.4	239	37.7	3.4	197	36.5	3.2
	CI = 6,291 (100%)				CI = 11,173 (177%)			CI = 11,829 (188%)		
Synea *(S. mansoni)*										
1,385	373	44.0	13.8	3.3	217	51.6	4.7	200	59.0	5.8
	CI = 8,409 (100%)				CI = 11,363 (135%)			CI = 14,218 (169%)		

Table 4b. Kolila (*S. haematobium* treated with metrifonate). Target groups: males (m) 0–15 years, females (f) 0–25 years

Age-groups (years)	June 1979					mass treatment of target group June/July 1980	Nov. 1980			Sept. 1981		
	Census 1979 No. of pers.	No. examined	P %	Eggcounts geom. m̄	Eggcounts geom. m̄ (x+1)		No. examined	P %	Egg-counts geom. m̄ (x+1)	No. examined	P %	Egg-counts geom. m̄ (x+1)
0– 5	62	52	38.5	30.2	3.8		31	22.6	2.0	30	33.3	3.6
6–10	22	22	50.0	84.7	9.5		28	42.9	3.9	37	40.5	4.4
11–15	27	21	85.7	58.6	35.3		33	63.6	8.4	37	62.2	15.6
16–20 m	13	11	54.5	59.5	9.6		7	42.9	3.7	4	50.0	15.6
16–20 f	14	12	58.3	22.0	6.7		5	60.0	6.5	8	50.0	3.4
21–25 m	11	6	66.7	8.9	4.8		1	0	1.0	1	0	1.0
21–25 f	23	20	40.0	130.9	7.1		11	18.2	2.2	7	28.6	3.6
26–30	21	18	22.2	21.4	2.0		8	12.5	1.4	14	28.6	2.4
>30	91	77	29.9	23.2	2.6		29	27.6	2.4	29	13.8	1.4
Total	284	239	43.5	37.8	5.1		153	37.3	3.3	167	39.5	4.4
	CI = 4,669 (100%)						CI = 2,312 (50%)			CI = 4,375 (94%)		

Table 4c. Zeansue (*S. haematobium* treated with metrifonate + niridazole). Target groups: males and females 6–15 years

Age-groups (years)	June 1979					May 1980					Oct. 1980			Aug. 1981		
	Census 1979 No. of pers.	No. examined	P %	Eggcounts geom. m̄	Eggcounts geom. m̄ (x+1)	No. examined	P %	Eggcounts geom. m̄	Eggcounts geom. m̄ (x+1)	mass treatment June 1980	No. examined	P %	Egg-counts geom. m̄ (x+1)	No. examined	P %	Egg-counts geom. m̄ (x+1)
0– 5	109	71	21.1	35.3	2.2	51	45.1	74.9	7.2		53	52.8	8.2	84	51.2	6.8
6–10	105	78	70.5	98.5	26.2	58	84.5	145.9	69.5		49	63.3	17.1	101	72.3	22.9
11–15	102	82	79.3	123.3	46.2	62	83.9	84.2	44.3		45	73.3	26.2	87	66.7	11.7
16–20	64	41	68.3	24.4	9.4	15	60.0	11.6	4.9		29	58.6	14.3	28	67.9	8.9
21–25	36	28	50.0	30.3	5.8	13	53.8	10.2	4.0		25	48.0	10.5	20	40.0	5.9
26–30	61	46	32.6	34.3	3.2	23	43.5	18.8	3.7		26	42.3	5.1	28	32.1	3.1
>30	172	132	28.0	28.7	2.6	56	37.5	30.2	3.8		61	42.6	4.2	89	32.6	2.7
Total	649	478	47.9	58.9	7.3	278	61.4	65.4	13.7		288	54.9	10.2	437	54.8	8.0
	CI = 18.310 (100%)					CI = 26.060 (142%)					CI = 22.660 (123%)			CI = 14.546 (79%)		

Table 4d. Sgt. Kollie Town (*S. haematobium* and *S. mansoni:* treated with praziquantel). Target groups: males (m) 0–20 years; females (f) 6–30 years

Age-groups (years)	June 1979						Nov. 1980			Sept. 1981		
	Census 1979 No. of pers.	No. exam-ined	P %	Eggcounts geom. $\bar{m}$	Eggcounts geom. $\bar{m}$ (x + 1)		No. exam-ined	P %	Egg-counts geom. $\bar{m}$ (x + 1)	No. exam-ined	P %	Egg-counts geom. $\bar{m}$ (x + 1)
S. haematobium						mass treatment of target group June 1980						
0– 5 m	173	41	9.8	32.0	1.4		34	2.9	1.2	27	11.1	1.5
0– 5 f	184	36	5.6	6.2	1.1		35	2.9	1.0	27	0	–
6–10	288	72	30.6	29.8	2.9		63	3.2	1.2	48	16.7	1.8
11–15	240	52	30.8	46.1	3.3		35	2.9	1.2	19	36.8	5.2
16–20	213	39	38.5	64.7	5.1		31	12.9	1.6	11	9.1	1.5
21–25 m	104	16	18.8	12.3	1.6		7	0	–	5	0	–
21–25 f	110	25	28.0	11.4	2.1		15	0	–	10	20.0	2.1
26–30 m	82	13	15.4	5.7	1.4		14	0	–	6	0	–
26–30 f	100	18	16.7	5.8	1.4		11	0	–	10	0	–
>30	482	106	12.3	15.8	1.4		58	8.6	1.3	38	5.3	1.1
Total	1,976	418	20.8	26.5	2.0		303	4.6	1.2	201	11.4	1.5
	CI = 10,891 (100%)						CI = 2,972 (27%)			CI = 8,132 (75%)		
S. mansoni												
0– 5 m	173	41	24.4	20.5	2.1		34	11.8	1.2	22	13.6	1.2
0– 5 f	184	38	28.9	19.1	2.4		36	13.9	1.3	30	46.7	4.9
6–10	288	73	63.0	17.0	6.5		64	10.9	1.3	49	59.2	4.9
11–15	240	49	65.3	38.7	11.5		33	30.3	2.3	19	68.4	8.6
16–20	213	36	47.2	37.3	5.7		28	42.9	3.6	11	54.5	4.2
21–25 m	104	14	50.0	6.6	2.9		5	40.0	1.7	5	20.0	2.0
21–25 f	110	23	52.2	12.7	4.2		14	28.6	1.7	9	22.2	2.7
26–30 m	82	9	55.6	12.2	4.3		15	26.7	2.4	6	50.0	5.0
26–30 f	100	17	35.3	25.6	3.3		11	27.3	2.2	10	70.0	5.2
>30	482	99	44.4	21.8	4.2		57	42.1	2.8	35	40.0	2.7
Total	1,976	399	47.6	22.6	4.6		297	25.3	1.9	196	46.9	3.5
	CI = 21,257 (100%)						CI = 4,899 (23%)			CI = 11,584 (54%)		

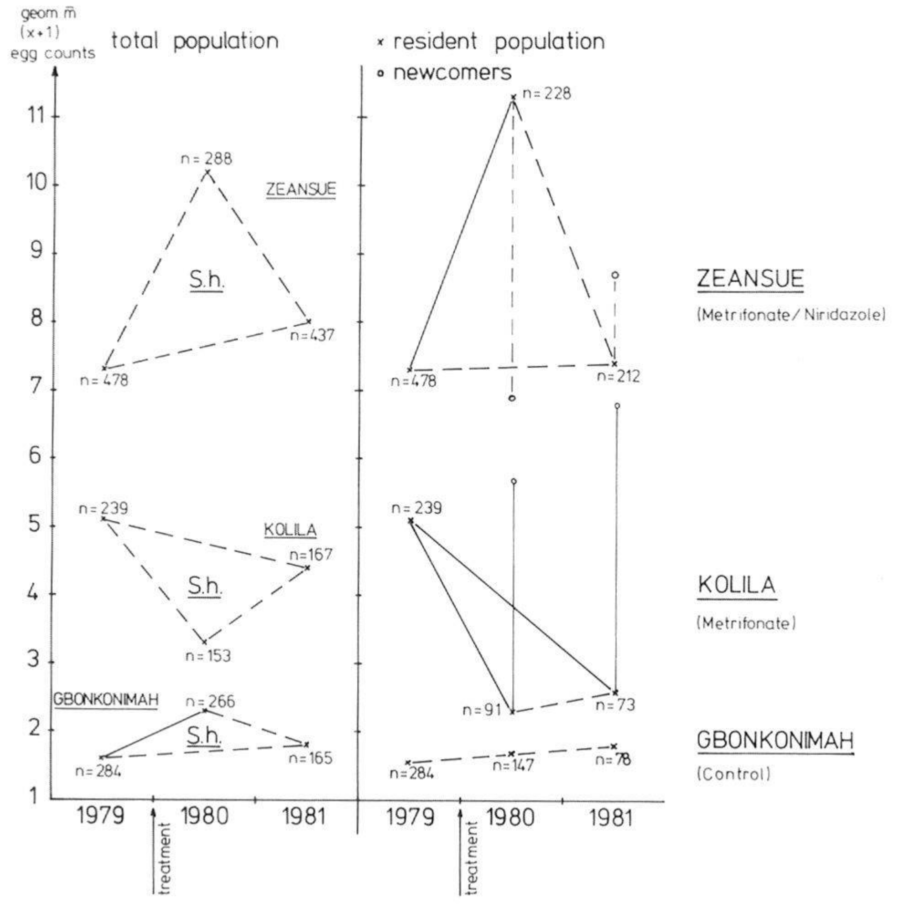

Fig. 2a

Fig. 2b

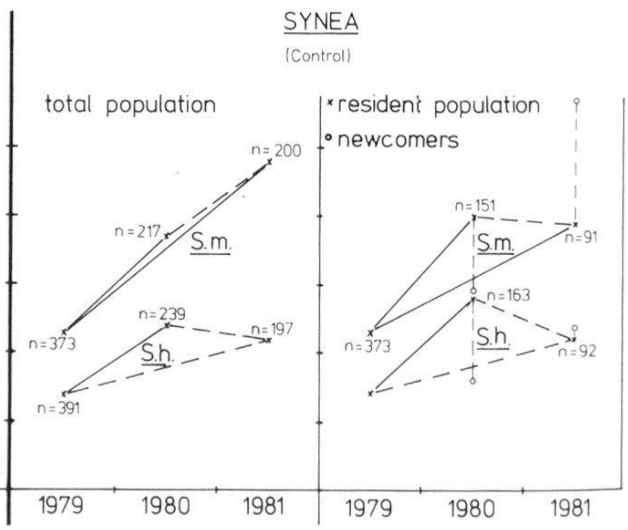

Fig. 2c

Fig. 2a–c. Effect of the mass treatment on eggcounts in *Schistosoma haematobium (S. h.)* and *Schistosoma mansoni (S. m.)* infections. ——— = significant difference ($p < 0.05$) (U-Test); - - - - = difference not significant.

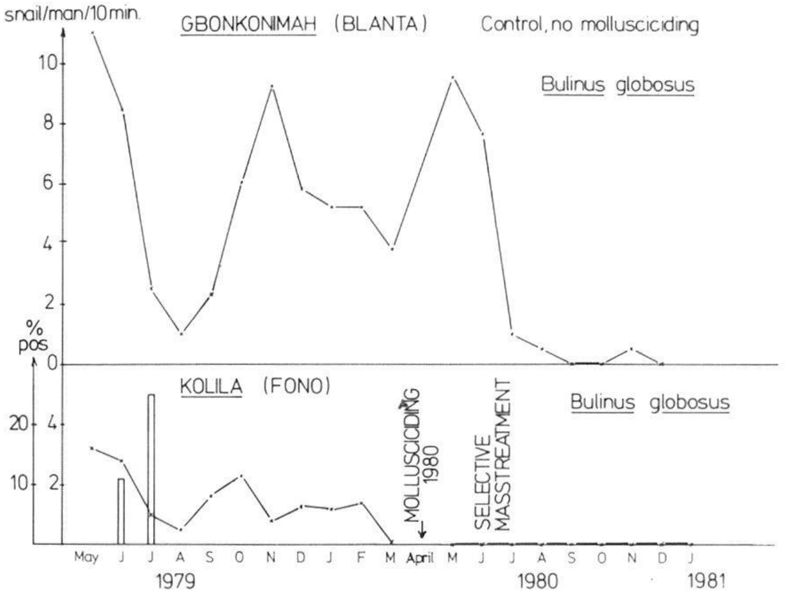

Fig. 3a

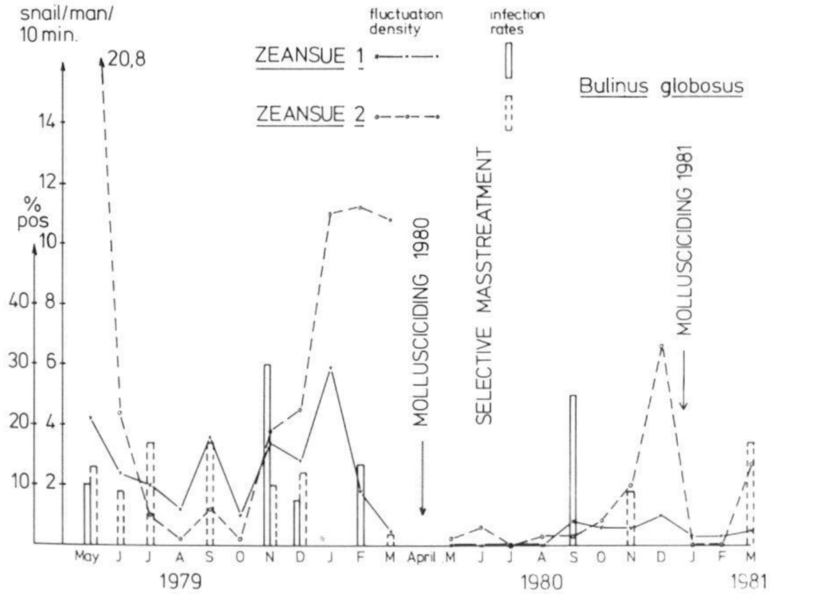

Fig. 3b

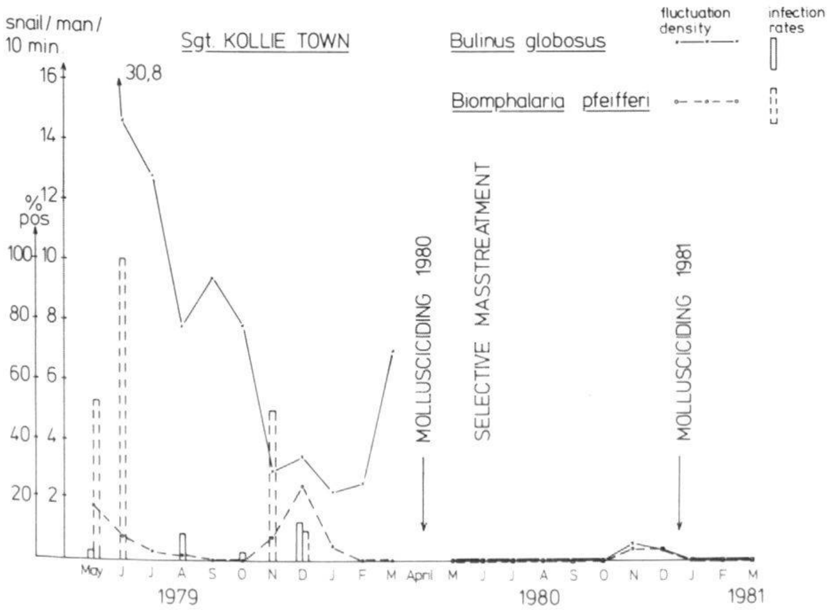

Fig. 3c

Fig. 3a–c. Snails fluctuation density (lines) and infection rates (histograms) of *Biomphalaria pfeifferi* and *Bulinus globosus* in the five observed water contact sites.

Only minor side effects of treatment were reported. 20% of the people complained of exhaustion. Itching eyes caused troubles for almost 5% of the persons treated.

The prevalence three months after treatment was within the normal deviation, compared with the examinations of 1979 and 1980, whereas the increase one year after treatment was significantly higher than in the 1979 (χ^2-test, $p<0.05$).

In this village, the migrations do not seem to have had much influence on the prevalence index because at the fourth examination this was 53.7% among persons present before mass treatment, whether treated or not, and 56% among the persons who had arrived after the mass treatment. In the same groups, the geometric mean $(x+1)$ of egg counts was respectively 7.4 and 8.7 (U-test $p<0.05$).

In 103 persons who were examined in October 1980 and in August 1981, the incidence was 39% (54.5% for age group 0–15). One can conclude that the transmission has not been much modified by the control measures applied here.

d) *Sgt. Kollie Town* (single dose praziquantel for *S. haematobium* and *S. mansoni* infections, see Table 4d). The 1979 census showed a total population of 1976. A total of 500 persons were living in the houses selected at random at the time of the first census, but 585 were already living in the same houses at the time of the first examination. 224 newcomers were registered in the sampled houses before mass treatment. After treatment, 55 and 142 newcomers were registered in these houses at the second and third examination, respectively.

The differences in infection rates between the sexes were insignificant for *S. haematobium* and *S. mansoni* in both pre- and post-control surveys. In 1979, the male population between 0 and 20 years and the females from 6 to 30 years represented 75.6% and 90% of the contamination index for *S. mansoni* and *S. haematobium* respectively. These age-groups were chosen for selective mass treatment.

963 persons, representing 85.7% of the target group and 48.7% of the total population, were treated. Side effects were minor and reported by less than 2% of the individuals treated. Only nausea and general weakness were encountered and mainly in women between 20 and 30 years of age.

Three months after treatment, a sample of 303 persons were examined and results showed a decrease in prevalence rates from 20.8 to 4.6% (χ^2-test, $p<0.01$) for *S. haematobium* and from 47.6 to 25.3% (χ^2-test, $p<0.01$) for *S. mansoni.*

One year after treatment, samples of urine from 201 individuals were examined. The prevalence of *S. haematobium* increased from 4.6 to 11.4%, but was still lower than before treatment (χ^2-test, $p<0.01$). The increase in prevalence was mainly due to the introduction of infected newcomers. Detailed evaluation of the sample showed that the geometric mean $(x+1)$ of egg counts among 99 persons who had arrived after the mass treatment was significantly higher (U-test, $p<0.05$) than that for those 102 persons who were present at the selective mass treatment. Among the latter group the geometric mean $(x+1)$ of egg counts did not increase during the year after the treatment (U-test, $p<0.01$) (see Fig. 2). The incidence of infection, calculated for 67 persons who were present at the second and third examinations, was 3.7%. These results show that transmission of *S. haematobium* was interrupted during this period.

One year after treatment the prevalence of *S. mansoni* reached the same level as it had before mass treatment and it was even higher (49.5%) among the persons who had already been examined before mass treatment than among newcomers (37%) who arrived after chemotherapy.

The incidence of infection, calculated for 62 persons who were present at the second and third examinations was 50% for all age group and 18.5% and 73% for age-groups 0–5 and 6–15 years, respectively.

For the *S. mansoni* egg counts the same variations as for prevalence were observed (see Table 4d). The geometric mean $(x+1)$ of egg counts of the persons who were present at the time of the treatment with praziquantel changed from 4.6 before treatment to 3.9 one year after. The newcomers are not responsible for the increase of egg counts during the year after the treatment (see Fig. 3).

The percentage of mixed infections is shown in Table 5.

e) *Synea* (Control village for mixed infections, see Table 4a). The 1979 census showed a total population of 1385 persons. In the sampled houses 610 persons were registered at the time of the first examination. For the second examination 112 and for the third examination another 101 newcomers where registered in the sampled houses.

From a sample of 610 persons, only 373 stool and 391 urine specimens were collected for the first examination.

There was no difference in the number of males and females investigated in all examinations and the prevalence of *S. haematobium* was not different in all the three urine controls. The prevalence of *S. mansoni* increased from 44.0 to 59% between 1979 and 1981. At the third examination, the prevalence of *S. mansoni* was higher, but not significantly, among newcomers (62%) than among people who had already been registered in 1979 and/or 1980 (55%).

The incidences measured from 120 persons for *S. haematobium* and 98 persons for *S. mansoni* were respectively 26.8% and 45.8% for all age groups (33.3% and 52% for age group 6–15 years) between 1979 and 1980. From October 1980 to August 1981, the incidences were 23% for *S. haematobium* (54 persons) and 32% *S. mansoni* (53 persons). During these periods the proportion of persons who lost their infections of *S. haematobium* or *S. mansoni* were not statistically different from persons who developed an infection with the same parasites.

The percentage of mixed infections are shown in Table 5.

Table 5. Mixed infection rates (Pm) and percentages of persons with any *Schistosoma* species infection (Ps) in Sgt. Kollie Town (SKT) and Synea

	No.	Pm %	Ps %
SKT* 1979	418	13.9	56.6
1980	303	2.8	27.3
1981	201	5.8	53.1
Synea 1979	391	18.9	60.3
1980	239	24.9	70.5
1981	200	29.0	68.5

* with selective mass treatment in 1980

3. Snail control (see Fig. 3)

Kolila: In Fono Creek near Kolila, after 600 g niclosamide had been applied to the water in April 1980, no *B. globosus* could be found during the following year. 2.8% of the snails collected during the year before were positive for schistosome cercariae (total 71 snails).

Of the 78 snails exposed during the mollusciciding at 4 different spots in the creek, 8 were found living the following day.

Zeansue: The application of molluscicide to Zeansue Creek and to its sidearm in April 1980 suppressed the high population densities of *B. globosus*. The amount of molluscicide applied was 400 g and 200 g, respectively. At the two collection spots (Zeansue *1* and Zeansue *2*) the snail populations did not really recover until December 1980. The following application of molluscicide, carried out in January 1981, eliminated the peak of the dry season. 1.8 kg of niclosamide were applied by drip feeding at three different spots in Zeansue Creek and 200 g in the side-arm. However, snails with *Schistosoma* cercariae were rediscovered in both areas after the application of molluscicide.

6.2% (22) of the *B. globosus* collected during the year before the first application of molluscicide and 6.7% (9) collected the year after were found to be positive for *Schistosoma*. Comparing the total numbers of snails found the year before (481) with the number collected during the year after application of molluscicide (90), we can see that about 80% of the yearly snail population was eliminated by the control measure.

Of the 79 snails exposed at 4 different spots in Zeansue Creek during the application of molluscicide, only one was found to be alive the following day.

Sgt. Kollie Town: After the application of 400 g of niclosamide in Gbaia Creek in April 1980, no snail was found until November 1980, when *B. globosus* as well as *B. pfeifferi* reappeared. These few snails were all negative for schistosome cercariae. After repetition of the molluscicide application in January 1981 by drip-feeding at three different spots in Gbaia Creek using 3.8 kg of niclosamide, no snail was found again. Another 300 g of molluscicide was used to treat

Table 6. Cost analysis (in US$) of the selective treatment and mollusciciding in Kolila, Zeansue and Sgt. Kollie Town (SKT)

	Kolila	Zeansue	SKT
Manpower for treatment	1,152.– (3 × 3 days)	512.– (4 days)	896.– (7 days)
Manpower for mollusciciding	128.– (1 day)	384.– (3 days)	384.– (3 days)
Cost of drugs	39.42 (0.27 × 146)	371.– (1.70 × 218)	1,936.– (4.25 × 963)
Cost of molluscicide	12.– (600 g)	52.– (2.6 kg)	90.– (4.5 kg)
Total	1,331.42	1,319.–	3,306.–
Number of persons covered .	400	860	1,976
Cost per capita protected	*3.33*	*1.53*	*1.67*

stagnant waters along the creek. Three cages containing 20 *B. globosus* and 20 *B. pfeifferi* each were exposed at different places in the creek during the application of molluscicide. One cage was stolen. No snail in the remaining two cages was living the following day.

Comparing the number of snails collected the year before the application of molluscicide (*B. globosus*, 642; *B. pfeifferi*, 31) with the numbers found during the year after (*B. globosus*, 6; *B. pfeifferi*, 4), it can be seen that 99% of the *B. globosus* and 87% of the *B. pfeifferi* population was suppressed. Of the 642 *B. globosus* collected before the application of molluscicide 1.9% were positive for schistosome cercariae, whereas 44.2% of the 31 *B. pfeifferi* collected were harbouring these cercariae. No schistosome positive snails could be detected after the application of molluscicide.

Gbonkonimah: No molluscicide was used in the Blanta Creek, near Gbonkonimah. The *B. globosus* population from May to December 1980 was twice as large as in the same period in 1981. No schistosome positive snails was found in Blanta Creek.

In *Synea* no molluscicide was applied. The main transmission areas were occupied by the society bush school (Garlain) and therefore not accessible.

4. Cost analysis

The analysis of the total costs for the selective mass treatment together with application of molluscicide at the water contact sites is presented in Table 6.

Discussion

The area selected for this trial had the rare characteristic that it not only contained the highest endemicity of schistosomiasis in Liberia but at the same time foci of transmission of *S. haematobium* alone and of mixed infections with *S. mansoni* in close vicinity (Dennis et al., 1983). The patterns of age prevalence are classical and comparable with those found in many other endemic areas; however, the prevalence differs from village to village depending on snail-densities and on the location of the transmission-sites. Such observations are not uncommon (King et al., 1982) and make the planning of pilot control programs difficult.

It is well known that the excretion of *S. haematobium* eggs reaches a maximum around midday (Pugh, 1977), but at this time of the day most of the adults are on their farms. In order to get the highest possible cooperation of the whole population, we had to collect the specimens during the whole day. For this reason it can be assumed that the prevalences and especially the intensities of infection are underestimated. All investigations have, however, been made under the same conditions so that the results obtained are internally comparable.

The intensities of infection, recorded as number of eggs per 10 ml of urine and one gram of stool, respectively, correlate with the prevalences, but are relatively low compared with other highly endemic areas (Wilkins, 1977; Hiatt, 1976).

In Zeansue, where the prevalence of *S. haematobium* reaches 79% among the children between 11 and 15 years of age, 60% of the infected persons were passing less than 100 eggs/10 ml.

In Sgt. Kollie Town, where the prevalence of *S. mansoni* reaches 65% among the same age-group, 52% of the infected persons were excreting less than 20 eggs/gram of stool and only 19% more than 100 eggs/gram.

Different approaches to the control of schistosomiasis have been evaluated during the last few years and Jordan (1977) concludes that mass chemotherapy has proved to be effective in the short term, whereas improvement of domestic water supply is the solution in the long term. The implementation of both methods is expensive and requires the collaboration of the local population. According to the opinion of Jordan (1977), even if 80% of the schistosome eggs are eliminated, the remaining 20% are enough to maintain the transmission at a high level. On a large scale, control measures need a lot of qualified personnel, who might be bored and under-occupied during the long-term follow-up. In Brazil, such problems have been avoided by the systematic treatment of the whole population, infected and non-infected, of all the villages where the examination of a sample of school children showed a prevalence of 20% or more (Machado, 1982). At any rate the results obtained, although encouraging, are not yet sufficiant to persuade those who oppose these methods for ethical reasons. In an area with low morbidity, like the one we dealt with (Holzer et al., 1983), the schistosomiasis is not of sufficient importance to the population to ensure the necessary high compliance with the treatment, i.e. that no one excreting eggs escapes from treatment. Therefore a new outbreak of transmission is unavoidable if the follow-up does not include an expensive case detection program.

It seemed worth-while to us to evaluate the combination of the focal application of molluscicide to the known water contact sites with the mass chemotherapy of a target population, which is easy to reach and which contains the main egg excretors, with the aim of reducing transmission and worm-burden.

In regard to the control of schistosomiasis on a large scale, we restricted ourselves to the application of schistosomicides of good tolerability and easy administration, in order to make future distribution of the drugs possible by paramedical personnel. Metrifonate dosed 3× daily was chosen for its efficacy (Davis, 1968; Rugemalila et al., 1981; Feldmeier et al., 1982) and for its low price. The combination of metrifonate with niridazole in a single dose has been recently proposed (Pugh, 1978; Pugh et al., 1980; Teesdale et al., 1980) because it avoids inconvenient and costly retreatment. Praziquantel was also tested in spite of its higher price, because of its efficacy in a single dose against both *S. mansoni* and *S. haematobium* at the same time (Davis et al., 1979; Katz et al., 1981).

The compliance for the mass treatment was satisfactory (see Table 1). This, however, is due to a persistent and prolonged engagement of the team which conducted the treatment and which resulted in higher costs for the operation. The compliance obtained with the repeated treatment with metrifonate is comparable to that found by Rugemalila et al. in 1981. It confirms the difficulty in applying a 3× dose in a mass chemotherapy campaign. No serious side-effects were observed and among the minor complaints only the itching of the skin was not observed by Rugemalila (1981). Since this itching has only been observed with the treatment with metrifonate, it can be associated with the effect of the drug on *Onchocerca volvulus*, which is endemic in this area (Frenzel-Beyme, 1973; Holzer et al., 1983). This observation must be taken into consideration in zones where schistosomiasis occurs and where *Onchocerca* is abundant, because it might be another reason for the population to refuse the treatment.

The cure rates and the reduction of egg outputs by metrifonate are similar to those found by most other authors (Davis and Bailey, 1969; Reddy et al., 1975; Rugemalila and Eyakuze, 1981; Feldmeier et al., 1982) and to the results with praziquantel in *S. haematobium* infections (Davis et al., 1979; Diallo et al., 1981; Oyediran et al., 1981). For the combination metrifonate-niridazole the reductions of egg output are lower than described by Pugh (1978) and Teesdale et al. (1980). For *S. mansoni* infections the egg-reductions achieved with praziquantel are similar to those found by other authors, but the cure rates are less than those described by McMahon (1981) but similar to those found by Katz (1981) and Smith (1981).

If our results are analyzed as cross-sectional studies before and after the control measures they are disappointing, with the only exception being the effect of praziquantel on *S. haematobium* infections. The longitudinal analysis, however, moderates this impression and helps to define the reasons for the failure in regard to the prevalence values.

In the two control villages (Gbonkonimah and Synea) the contamination index, corroborated by the incidence, show that the transmission was about twice as high in 1981 as it was in 1979. In Gbonkonimah it seems to be evident that the contamination index takes into account the infected newcomers, since with an incidence of 7% from 1979 till 1980 the contamination index increased fourfold, whereas from 1980 till 1981 it decreased to less than half, with an incidence of 16.7%.

It is not contestable that incidence is the best index to estimate the effect of a control measure (Jordan, 1977). However, the evaluation is particularly problematic in the field because of migrations and most especially because the same people are to be examined in two consecutive years and may refuse to bring stool and urine samples twice. The contamination index, not including the newcomers, could be a realistic method, and more sensitive than the prevalence in judging the effect of a control measure. It has to be mentioned that at Synea the calculation of the incidences shows that the same number of persons loses their infections of *S. haematobium* and of *S. mansoni* as becomes infected.

The examination of the collected data shows the important role of the newcomers in certain villages (Gbonkonimah, Kolila and Sgt. Kollie Town for *S. haematobium*) (see Fig. 4). Since their infection rate is high newcomers represent a reservoir of egg-excretors of greater importance than the adults not included in the selective mass treatment. In Kolila for example they represented 59% of the index of contamination one year after treatment.

Even though the prevalence is practically unchanged because of the immigrants and the transmission has not been stopped one must nevertheless emphasize that, thanks to a cheap treatment which was limited to one target group, the incidence at Zeansue did not double like that at Gbonkonimah and that at Kolila the quantity of eggs eliminated by the people under mass treatment was reduced by 50%. One cannot doubt that this treatment, if repeated every year and with inclusion of the newcomers, would if not stop transmission at least considerably limit the incidence of disease.

At Zeansue the absence of interruption of transmission can largely be attributed to the failure of the focal application of molluscicide, which failed to eliminate more than 80% of the annual population of the intermediary hosts. On the other hand, at Kolila the application of molluscicide was apparently very effective (see Fig. 4) and the persistence of transmission can only be explained by the existence of transmission sites which were unknown to us. First class collaboration from the population in the identification of transmission sites is an essential for the success of the focal application of molluscicides. Even very limited contact with infected bodies of water can be enough to infect a large number of persons (Poldermann, 1979). In the case of Kolila, the inhabitants had sometimes to ford infected bodies of water to reach the fields, which could be several kilometres from the village. This could explain the failure to interrupt transmission by focal application of molluscicide near the village.

At Sgt. Kollie Town it was recorded that the newcomers increased the prevalence of *S. haematobium* and decreased that of *S. mansoni* after treatment. The efficacy of praziquantel against *S. haematobium* infections, together with the focal application of molluscicide and the low degree of infestation of *B. globosus,* explains the interruption of transmission in spite of the arrival of newcomers. Unlike at Kolila the inhabitants of Sgt. Kollie Town do not seem to frequent bodies of water infected with *S. haematobium* apart from those which were treated with niclosamide. For *S. mansoni* the situation is reversed. In spite of a considerable reduction in the quantity of eggs excreted, *B. pfeifferi* which showed a 44% infection rate before the application of molluscicide, remained in sufficient numbers to ensure that transmission remained at practically the same level as that before the mass treatment. Infections outside the village are nevertheless not excluded.

The role of migrants in the epidemiology and control of schistosomiasis, although known (Bella et al., 1980; Degrémont, 1973), has still been very inadequately studied. In Bong County the pattern of migration is very different from that observed by Bella et al. (1980) in the Sudan. Moreover, in Liberia, as in many other countries where schistosomiasis is endemic, the inhabitants frequently change their names and sometimes even refuse to admit to this, because of taboos, in spite of every evidence to the contrary. Even though we have talked of emigration and immigration (newcomers) we cannot for this reason totally exclude the possibility that a number of the so called migrants are people who changed their names.

With the exception of *S. haematobium* in Sgt. Kollie Town, and allowing for the low morbidity from schistosomiasis in this region (Holzer et al., 1983), the cost of the control measures per person protected is still too high in relation to the disposable local resources and the results obtained.

In conclusion, this pilot study convincingly demonstrated in our opinion that at least in regions of low morbidity and pronounced migration the long term success and profitability of measures for the control of the schistosomiases must be based on an adequate network of health services and that village health workers have to play an important role.

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