ON THE DISTRIBUTION AND CONTROL OF SCHISTOSOMIASIS MANSONI IN MANIEMA, ZAIRE

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Introduction

Many millions of people in Africa, South America and Asia are infected with schistosomiasis. This observation, along with the notion that the infection may cause serious disease, justifies intense and basic research into the biology of this parasite as well as into the possibilities to control the adverse effects of its presence in man. Now, schistosomiasis is one of the parasitic diseases at which most scientific attention is directed. Attention in terms of research on the role of immunity, on the possibilities of vaccination, on methods of biological control, and on the production of new and better drugs. In the future the results of these research efforts might lead to more effective ways of control.

However, even at present many tools to control the disease are available already and though they are by no means perfect, they can be used. Numerous attempts to control schistosomiasis that have been made during the past decades have demonstrated that the intensities of the efforts and the expectations of their effects have often been out of balance. It is not clear how drastic control efforts should be to achieve a certain degree of success. The population biology of the parasite and the dynamics of transmission are insufficiently understood to arrive at an optimal use of the available methods of control and elementary questions which are of vital importance to any hospital or health centre in endemic areas remain unanswered. One of these basic questions is: What should a doctor in a small rural hospital do when schistosome's eggs are found in his patient's stool? When the patient is living in an endemic area he will be re-exposed and re-infected soon after treatment.

Some components of this question could be formulated as follows:

- With what reliability can the most seriously infected subjects in a population be recognized with the use of simple commonly used diagnostic procedures?
- How soon will re-infection occur after treatment and consequently, at what frequency should treatment be given?

- Even if re-infection occurs, does the patient benefit from an occasional reduction of his worm burden and are the prospects of developing serious disease in a later stage reduced?
- How effective, how safe and how expensive are the drugs to be used?

It is evident that the answers on these questions depend on many local variables and that no generalized answers can be expected, but even when the local conditions are well circumscribed and when the budgets which are available are properly determined, the questions cannot easily be answered.

In the present report the effect of treatment of groups of individuals in Maniema, Zaire, is discussed. Attempts to analyse the effects of measures taken to reduce transmission to a smaller or larger extent and the feasibility of control and prevention of transmission will be briefly discussed.

Description of the area and the distribution of schistosomiasis

In Maniema, Kivu Province, communities of several hundreds to a few thousands of inhabitants are living in the middle of the rain forest of Eastern Zaire. There, tin ore (cassiterite) is exploited in open cast tin mines. In the past, the alluvial cassiterite containing deposits in the beds of the rivers were exploited and no additional water was required but later, after ± 1950, exploitation was intensified and extended to cassiterite deposits at a greater distance from the river beds. For the acquisition of sufficient quantities of water, man-made lakes and canals to transport the water from the lakes into the mines, had to be constructed. It is only since those days that schistosomiasis established in the area. Now, the infested areas contain a variety of different and extensive transmission sites. The intermediate host, *Biomphalaria pfeifferi*, is found in the man-made lakes and in the canals but also in marshes which arose from filled old mines and from natural drainage systems which were blocked by debris of abandoned ones.

Amazingly, the parasite did not establish in some of the labourers' villages although it did in many others. This would seem to be caused by the great differences in the characteristics of the soil. Long ago, the mineralization of tin occurred, characteristically, along the border of granite outcrops and the surrounding schists. Stagnant water in the granite rocks proves too poor in nutrients to harbour the intermediate host snail while on the other side of the border line, in the schists, the surface water is slightly richer in minerals. There, snails survive and extensive populations established. In those places, the introduction of schistosomiasis has followed the development of mining activities (Polderman et al., in preparation).

Schistosomiasis in Maniema is a typical example of a man made disease. Economic development, mining activities, the production of (hydro)-electricity and the creation of fish ponds out of old abandoned mines have all

attributed to changing parts of Maniema's rain forest in which no schistosomiasis was found until ±1956, into favourable habitats for *B. pfeifferi*. Other ways of exploitation could possibly have reduced the extent of transmission and in theory, some sort of environmental control should be possible in this area. It remains very doubtful, however, whether other ways of exploitation remain profitable from an economic point of view and whether they are compatible with present day economic way of life in Zaire. Efficient control of schistosomiasis in Maniema is unlikely te be achieved through environmental measures, for the time being.

Control and evaluation of control

In view of the fairly poor results that have been obtained so far with the use of molluscicides in other than rigidly organized environments (Sturrock, 1974, Warren, 1976), it would seem logical to focus attention primarily on treatment of the final host when the infested water bodies are numerous and when the human population is comparatively small. Such a situation exists in Maniema and this approach of control using chemotherapy as the principal tool, has been adopted for Maniema's tin-mining district.

The effect of treatment could be evaluated in three different ways. To what extent is there:

1. a parasitological improvement (i.e. does a large proportion of the treated subjects stop excreting eggs, and is the mean egg output of those who continue to excrete eggs considerably reduced after treatment)?
2. an objective clinical improvement?
3. a subjective amelioration of the patient's feeling of well being?

The first parameter is frequently used in control programs. The worm load and correspondingly the intensity of infection and severity of the prognosis is supposedly reflected by the egg output. The egg output can be checked at regular intervals following treatment (Cook et al., 1977; Katz et al., 1978; Polderman and Manshande, 1981; Sleigh et al., 1981).

The second type of parameters is more difficult to define. The most commonly used clinical signs of infection are hepatomegaly and hepato-splenomegaly. When malaria is endemic in the area, the presence of splenomegaly should be interpreted with great care.

The third type of parameter, the degree of contentment of the treated population is generally ignored in the evaluation of control programs. The outcome of inquiries into the contentment of the people reflects much more than the medical efficacy of the control measures. Sometimes this might be an advantage rather than a disadvantage!

Control through chemotherapy

When attempts to control schistosomiasis with the use of chemotherapy are started, the obvious first question to be solved is: who should be treated and who not? In systematic well supervised control programs, this decision is normally based on quantitative stool examination techniques, the most commonly used method being the Kato method. In rural and provincial hospitals, on the other hand, the decision who will be treated is normally based on the examination of a simple direct smear. When assessing the impact of the rural hospital's treatment of patients, it should at first be evaluated to what extent a simple direct smear is likely to recognize those patients who excrete the highest numbers of eggs. This is analysed in table 1 for one particular community in Maniema (Makundju).

Table 1 shows that the intensity of infection is high in Makundju: 22 out of 48 randomly selected persons excrete more than 1200 eggs per gram. Table 1B shows that out of the 35 persons excreting more than 600 epg, only 21 were recognized using a single direct smear. Using a single Kato, 24-26 out of the 35 heavily infected persons were recognized (1B-C), but using a combination of 2 Kato-smears from 2 different stool samples 31 of them were recognized and only 4 "false negative" results were obtained (1E). It can be concluded that only on repeated examination of a person's faeces a fair selection can be achieved of the most seriously infected subjects. The results of one single Kato smear are hardly better than those of one direct smear. It should be noted, however, that the sensitivity of the direct smear is low, and a very high fraction of persons excreting more than for instance 200 eggs, would be missed if diagnosis would depend on direct smears. Returning to this paragraph's question: is a simple direct smear an acceptable tool to select the most seriously infected persons, the answer should be: yes, if the threshold is chosen sufficiently high, and probably mainly so if the results of more than one examination are combined.

The results of control through chemotherapy of infected individuals depend first of all on the quality of the drugs used. Several good drugs for treatment of *S. mansoni* are existing nowadays, the most important being Oxamniquine and Praziquantel. The cure rates are high, the side effects are unimportant, and they are easily (orally) administered. No further attention will be paid to this aspect here. In Maniema both Oxamniquine and – to a lesser extent – Praziquantel have been used.

If transmission is not effectively changed, how long does it take until reinfection of the treated subjects is so serious that a second round of treatments should be given? In two communities (Tshamaka and Tshonka) the rate of re-appearance of eggs was recorded one year after treatment (table 2). It can be concluded that in this particular area, re-appearance of eggs, interpreted as re-infection, is very quick. Chemotherapy of infected subjects only, would

Table 1. *The capacity of a Kato-smear, a Kato smear on two stoolspecimens, and a simple direct smear, to recognize the heavily infected subjects in a population.*

Experimental design

In Makundju 48 subjects have been examined 7-9 times over a period of 2 years. The ages of the subjects were between 6 and 60 years. On each occasion, 2 Kato smears (25 mg each) were made of each stool sample. One smear was examined by microscopist A, the other by W. From the second stool sample also a direct smear was made and examined by microscopist B. The arithmetric mean egg count over the 7-9 samples of each individual is supposed to stand for "the" egg count of that person. The frequency distribution of the mean egg counts of the 48 subjects is as follows:

Mean number of eggs per 25 mg of faeces (=in one Kato smear)	Number of eggs per gram (epg)	n
less than 7.5	less than 300	7
7.5- 14.9	300- 599	6
15.0- 29.9	600-1199	13
30.0- 59.9	1200-2399	11
60.0-119.9	2400-4799	9
120.0 and more	4800 and more	2

How many of the seriously infected persons, excreting many eggs, will be detected with one single Kato smear (chosen randomly from the set of 7-9 samples), one particular Kato smear (second stool sample), one direct smear (again from the second stool sample), and with a combination of 2 randomly chosen Kato smears from 2 different stool samples?

"The" mean egg counts were determined by calculating the mean of 7-9 slides A, examined by microscopist A. For the evaluation of the capacity of one or 2 Kato smears, the other slides, examined by microscopist B were used. The thresholds for "heavily infected" were arbitrarily chosen 600 and at 1200 epg.

	Randomly chosen single Kato		One single Kato, second sample		Direct smear second sample		Two randomly chosen Kato smears	
	<15 eggs/ 25 mg	⩾15 eggs/ 25 mg	<15 eggs/ 25 mg	⩾15 eggs/ 25 mg	no eggs	eggs present	<30 eggs/ 50 mg	⩾30 eggs/ 50 mg
<600	11	2	12	1	10	3	13	0
⩾600	9	26	11	24	14	21	4	31
	<30 eggs/ 25 mg	⩾30 eggs/ 25 mg	<30 eggs/ 25 mg	⩾30 eggs/ 25 mg	no eggs	eggs present	<60 eggs/ 50 mg	⩾60 eggs/ 50 mg
<1200	20	6	22	4	15	11	26	0
⩾1200	10	12	9	13	5	17	4	18

Table 2. *The percentage of subjects excreting more than 600 eggs per gram before, and one year after treatment. Chemotherapy only. No additional measures taken (Tshonka and Tshamaka).*

Age class (in years)	TSHAMAKA percentage excreting over 600 epg		TSHONKA percentage excreting over 600 epg	
	before treatment	1 year after treatment	before treatment	1 year after treatment
1- 5	26	29	8	28
6-10	57	42	52	34
11-20	61	71	76	42
21-40	29	29	43	21
41-60	24	18	39	11

Explanatory notes.

1. The table refers to two communities, Tshonka and Tshamaka, in which no attempts were made to control transmission (no snail control).
2. Treatment was done with Oxamniquine, either 15 or 40 mg/kg. Apart from pregnant women, subjects presenting contraindications, very young children, everybody was treated. A small group treated with Placebo-Oxamniquine is left out of consideration in this table.
3. The pre-treatment egg counts refer to the mean of two surveys (46-161 persons per age class, per survey). The post-treatment data refer to one survey only (40-92 persons per age class in Tshamaka; 28-53 in Tshonka).

seem insufficient to control schistosomiasis to an "acceptable" degree in Maniema, and additional measures to reduce the intensity of transmission, and therefore the rate of re-infection, are to be taken.

Other measures of control in addition to chemotherapy

Thorough snail control around the mining villages of Maniema is not easily to achieve due to the diversity and dimensions of the infested water bodies. Yet, an attempt was made in one community (Makundju) to arrive at a proper snail control in all transmission foci in the immediate surroundings of the village. Following an intensive search for these foci and a system for regular application of molluscicides (Bayluscide) was developed. On a two-monthly basis the molluscicide was applied, and the results in terms of presence of snails were good: no snails were found any more. The results in terms of rates of re-appearance of eggs following treatment of the population of Makundju are presented in table 3. It can be concluded that a considerable re-appearance of eggs occurred, predominantly in the older children. Apparently, we did not succeed in killing all snails in all transmission sites. It is likely that an important part of transmission occurred beyond the immediate surroundings of the village. Mollusciciding of an even wider area around the village would require too

Table 3. *The percentage of subjects excreting more than 600 eggs per gram before, and one year after treatment. Chemotherapy plus intensive snail control (Makundju).*

Age class (in years)	Percentage excreting over 600 epg.	
	before treatment	1 year after treatment
1- 5	40	3
6-10	65	27
11-20	65	37
21-40	50	13
41-60	40	6

Explanatory notes.

1. The table refers to the community of Makundju. All transmission sites known to the authors were treated regularly with molluscicides from approximately one month prior to treatment onwards.
2. Treatment was done with Oxamniquine (15 or 40 mg/kg) or Praziquantel (30 or 40 mg/kg). Apart from pregnant women, subjects presenting contra-indications, and very young children, everybody was treated. The small group treated with Placebo is left out of consideration in this table.
3. The pre-treatment egg counts refer to the mean of three surveys (42-98 persons per age class per survey). Treatments were given immediately after the third survey. The post-treatment data refer to one survey in which no less than 40 persons were examined.

great an effort to determine possible transmission sites and too great a quantity of molluscicides to be feasible. It should be admitted that our efforts to properly control snails in the surroundings of Makundju failed and that, under the prevailing conditions, such an approach is unlikely to be more successful in a next attempt.

Often, the majority of contacts of man with infested water can be pinpointed to occur in a few spots which can fairly easily be identified. In another community (Kakota) regular focal mollusciciding of the man-made canal flowing through the centre of this village was added to the usual chemotherapeutic approach. The village of Kakota is located close to Tshamaka (± 5 km) and the pretreatment infection rates and intensities of infection were very similar in both villages. The results of this measure, in terms of re-appearance of eggs one year later are presented in table 4. It can be concluded from this table that in the older age classes the rate of re-appearance of eggs would seem to be slower in Kakota as compared to Tshamaka, where no molluscicides were applied.

Although it is dangerous to compare the rates of re-appearance of eggs, and the percentages of subjects requiring renewed treatment (e.g. those excreting more than 600 epg) after one year, since transmission characteristics might change dramatically from one spot to the other, we do not believe this factor to

Table 4. *The percentage of subjects excreting more than 600 eggs per gram before, and one year after treatment. Chemotherapy plus focal snail control in the main transmission site only (Kakota).*

Age class (in years)	Percentage excreting over 600 epg	
	before treatment	1 year after treatment
1- 5	23	30
6-10	54	53
11-20	57	50
21-40	39	4
41-60	34	6

Explanatory notes

1. The table refers to the community of Kakota, a few kilometers from Tshamaka. The "race" crossing the centre of Kakota was treated at regular intervals with Bayluscide but it was not attempted to control *B. pfeifferi* in the numerous other transmission foci in the area.
2. Treatment was as in Tshamaka and Tshonka. Only Oxamniquine was used in two different dosages and treatment was given immediately after the second pre-treatment survey to everybody except to pregnant women, subjects presenting contra-indications, and very young children. Again, the placebo-treated group was left out of consideration in this table.
3. The pre-treatment egg counts refer to the means of two surveys (36-91 persons per age class, per survey). The post-treatment data refer to one survey with groups of 11-33 persons per age class.

be very important while comparing Tshamaka, Kakota and Makundju. (Only in Tshonka, where the transmission foci are somewhat different from the other communities). We believe it can be concluded that the most complete and most expensive type of intervention (as practised in Makundju) has been hardly more efficient than the less ambitious and much cheaper type of intervention: chemotherapy with additional focal molluscicide, as performed in Kakota.

Clinical parameters in the evaluation of control

Returning to the question whether it is useful to treat individual patients in whose stools schistosome eggs were found, and who will probably get re-exposed, it is of great importance, not only to assess the degree of parasitological success of treatment, but also to determine the extent of clinical improvement. It has been shown repeatedly in the literature that patients with schistosomal periportal fibrosis show a clinical improvement which is measurable as a regression of hepatomegaly. These observations refer to clinical situations in which individual patients were examined, treated and followed up after treatment. To what extent, however, is the effect of treatment on the morbidity of treated groups of subjects recognizable in field situations, and to what extent can clinical parameters be used to assess the effect of control measures? Only

little literature exists on this type of assessment of control (e.g. Cook et al., 1974).

The situation in Maniema is particularly suited to evaluate the results of control in terms of clinical parameters. Due to the existance of heavily infested and non-infested communities in the same area it was at first recognized that the hepatomegaly rate in the infested communities was much higher than in the non-infested communities. This is illustrated in figure 1. Subsequently it could be shown that within the infected communities the hepatomegaly rates were highest for the high egg-excreters and lowest for those who were uninfected. This appeared to be true for each of the age classes when analysed separately (Polderman et al., unpublished data). Since simple determination of the hepatomegaly rates on population level appeared to be sufficiently sensitive to recognize these patterns, it was believed that the effect of treatment might be similarly recognized in treated populations. The results of two measurements of the degree of hepatomegaly before treatment and one after

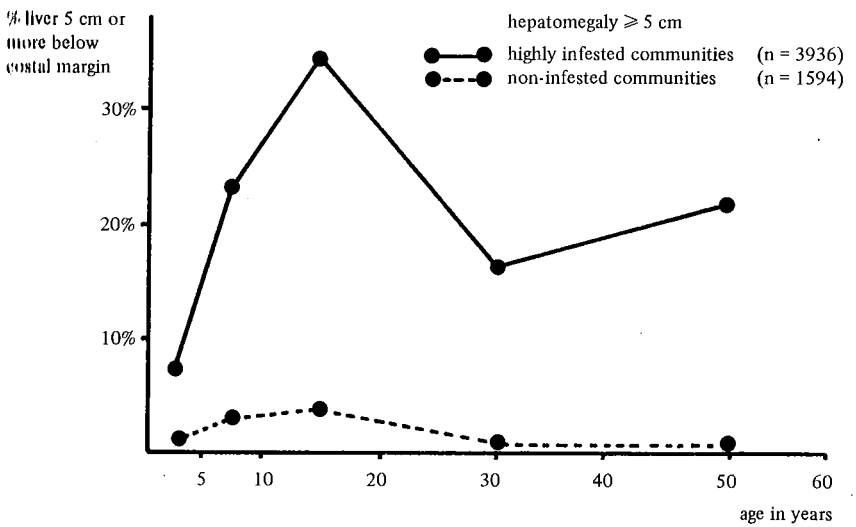

Figure 1. The age-specific hepatomegaly rates (liver 5 cm or more below costal margin), in a number of heavily infested and in a number of uninfested communities in Maniema's mining district.

Explanations to the figure:
1. In the infested communities the overall prevalence was always higher than 80%. In the uninfested communities, the prevalence was lower than 20% while there, the intensities of infection were normally low.
2. The data all refer to one single physical examination.
3. It should be noted that the data are liable to a certain bias. One is inclined to over-estimate the liver size in a village known to be severely infested and to underestimate in an uninfested community. This was not easy to avoid.

treatment among the Oxamniquine-treated populations of Tshonka and Tshamaka are summarized in table 5. It can be concluded that no effect can be seen. The implications are that either the measurements are too rough to register the relatively small changes in liver size or that re-infection has been too rapid to result in clinical improvement in terms of regression of liver size. The period after which the hepatomegalies were measured after treatment (8 months) might have been too short, but later the effect of re-infection would have been even more pronounced. Moreover, the Placebo-treated group had to be treated at 8 months which would have complicated the interpretation of the data at a later stage.

Table 5. *Changes in liver size among subjects from Tshonka and Tshamaka. In groups of individual patients the liver size was determined to the nearest 2 cm during four different surveys: 7 months before treatment, on the day of treatment, and 8 months after treatment.*

Age (in years)	Liver size	On the day of treatment as compared to 7 months prior to treatment			Eight months after treatment as compared to the day of treatment		
		Pl	Ox 15	Ox 40	Pl	Ox 15	Ox40
	increase	6	8	10	5	13	7
6-10	decrease	3	13	10	9	9	11
	unchanged	15	28	11	10	27	13
	total	*24*	*49*	*31*	*24*	*49*	*31*
	increase	5	8	3	3	2	0
11-20	decrease	6	7	6	10	13	10
	unchanged	5	8	12	3	8	11
	total	*16*	*23*	*21*	*16*	*23*	*21*
	increase	2	10	4	1	3	1
21-40	decrease	4	3	5	8	8	8
	unchanged	23	31	31	20	33	31
	total	*29*	*44*	*40*	*29*	*44*	*40*
	increase	5	9	8	2	6	2
41-60	decrease	8	17	19	8	11	14
	unchanged	26	45	33	29	54	44
	total	*39*	*71*	*60*	*39*	*71*	*60*
	increase	18	35	25	11	24	10
total of all	decrease	21	40	40	35	41	43
age-groups	unchanged	69	112	87	62	122	99
	total	*108*	*187*	*152*	*108*	*187*	*152*

N.B. "Pl" stands for: Placebo; "Ox 15" stands for: Oxamniquine 15 mg/kg; "Ox 40" stands for: Oxamniquine 40 mg/kg.

The data in the table (age-specific and per type of treatment) compare the changes in liver size as the result of treatment with unspecific variations.

Treatment and subjective feeling of well-being

Again, the existance of highly infected as well as uninfected communities in the same area makes it possible to determine the population's subjective feeling of suffering from schistosomiasis. In an open questionnaire into the pattern of complaints in an infected and a non-infected community in Maniema (Makundju and Massimelo respectively), the complaints appeared to be altogether different (Gryseels et al., in preparation). Some results are summarized in table 6. This table illustrates that the local population is suffering from schistosomiasis or, at least, that it is aware of the presence of a disease which is generally said to be a serious disease. The results of a repetition of the inquiry 20 months after treatment are not yet available at this moment.

Conclusions

First of all it should be stressed that Maniema is by no means representative as an endemic area for *Schistosoma mansoni* in Africa. The intensities of infection are very high and the ecological conditions differ from most other endemic areas. The conclusions drawn from studies in this particular area may – therefore – not be generalized.

Table 6. *The frequencies of three different types of complaints of the populations of an infected and an uninfected community (Makundju and Massimelo respectively), as expressed during an inquiry.*

type of complaint	age	Makundju (infected)	Massimelo (non-infected)
	1- 5	49%	2%
	6-10	61%	4%
Intermittant diarrhoea,	11-20	55%	2%
(mostly with blood)	21-40	62%	1%
	41-60	55%	0%
	1- 5	51%	12%
	6-10	71%	31%
Abdominal Discomfort	11-20	68%	40%
	21-40	64%	26%
	41-60	68%	18%
	1- 5	29%	6%
	5-10	25%	7%
Fatigue	11-20	34%	8%
	21-40	43%	26%
	41-60	39%	33%

Note: In Makundju: 80-138 persons per age class and in Massimelo 53-96 persons per age class participated in the inquiry.

Schistosomiasis in Maniema is a man-made disease. It resulted from the great changes in man's way of life and from the subsequent ecological changes. Environmental control of schistosomiasis, if possible, would require another drastic change of man's way of life, a radical change in the way of cassiterite exploitation. The actual economic situation of Zaire as a whole and of Maniema in particular, is not such that these changes can be realized.

Systematic and comparatively ambitious control efforts in one particular community (Makundju) have not resulted in promising results. Apparently a great deal of transmission takes place outside the area that could be properly treated with molluscicides. The results obtained in another community, where only the most obvious transmission sites were regularly treated with small amounts of molluscicides (Kakota), were hardly worse. Moreover, the focal and regular mollusciciding of the canal in the centre of Kakota reduced the rate of re-infection as compared to the near-by Tshamaka where no additional measures were taken.

Finally, it was shown that the old-fashioned and insensitive direct smear method for detection of helminth ova, was not that bad as compared to a single standardized quantitative Kato slide, in detecting the heavily infected subjects.

It can be concluded that much more efforts ought to be paid to the systematic control of schistosomiasis in Maniema to render it successful, and to achieve a promising reduction of transmission. The great difference between hepatomegaly rates in the infected and uninfected villages should convince medically qualified personnel, and the high rate of specific complaints should convince the local populations themselves, that integrated efforts are required. Awaiting the results of such an integrated and more intense approach, it should be noted that the most simple diagnostic procedure does recognize a fair proportion of the high egg-excreters. To what extent the high egg-excreters benefit from an occasional treatment could not been clearly demonstrated in the present study. As integrated control efforts proved too ambitious, in Makundju, and focal mollusciciding in "the most obvious transmission sites" was hardly less effective, treatment of the seriously infected subjects supplemented by incomplete snail control in the most important water contact sites should be recommended, for the time being.

To find a scientifically sound answer to the most simple questions appeared – once again – most difficult!

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