

Reinfections with *Onchocerca volvulus* in Cured Patients Exposed to Continuing Transmission

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In drug trials reported by Duke,^a patients infected with the West African forest strain of *Onchocerca volvulus* were treated with suramin or with stibocaptate (TWSb) in doses sufficient to eliminate their load of *O. volvulus* parasites. During and after treatment the patients remained in their villages, where they were exposed to continuing transmission at presumably much the same intensity as that to which they had been exposed since birth. Some of them were re-examined at intervals of 4–9 years after completing a course of curative treatment, and the intensities of the reinfections that had developed in them were compared with those of their initial infections.

Materials and methods

Twenty-one adult male Africans (aged between 20 and 50 years), living in the Cameroon forest village of Bombe on the Mungo River, where transmission of *O. volvulus* is thought to be moderately heavy, were examined by the method of multiple skin snips.^b Weighed snips were taken from their right and left calves and buttocks and the counts of microfilariae per milligram (mf/mg) in them were recorded. The patients were then treated with suramin (a course of 4.5 g–9.5 g total dosage in 20 patients) or with TWSb (at a total dosage of 2.4 g in one patient). Re-examinations by the same methods were made at intervals of up to 2 years after the conclusion of treatment, and these showed that, for all practical purposes, the patients' infections with *O. volvulus* had been eliminated. They were then followed up after further intervals of 4 years (15 patients) and 7 years (16 patients), the patients having received no further filarial medication.

Another 15 male patients (aged between 20 and 50 years), living in the villages of Bolo and Weme

on the upper tributaries of the Mungo River, where transmission of *O. volvulus* is known to be very heavy,^c were examined in a similar manner and were treated with at a total dosage of 4.1 g–6.1 g. Re-examinations made at intervals up to 18 months after the conclusion of treatment indicated that their infections had been eliminated. They were examined again 2½ years later, i.e., 4 years after the conclusion of treatment with suramin.

Results

The table shows, separately for the 21 Bombe patients and for the 15 Bolo/Weme patients, the total microfilarial counts (mf/mg) found in 4 snips taken before treatment. The corresponding figures for the nearly negative examinations made 2 years (Bombe) and 18 months (Bolo/Weme) after the end of treatment are then given, together with those obtained at the follow-up examinations made 6 years and 9 years after treatment at Bombe and 4 years after treatment at Bolo/Weme. For each patient the values obtained at the post-treatment examinations are also expressed as percentages of the pretreatment figure, and the means of the percentages so obtained from all patients at each examination are given.

The figure shows the percentage values from the table plotted graphically for (A) Bombe patients and (B) Bolo/Weme patients. The mean percentages are indicated for each group at each examination.

Discussion

The treatment with suramin (or, in one case, TWSb) was considered to have killed all the adult *O. volvulus* worms in both series of patients, this being evidenced by the decline in microfilarial

^a See the papers on pages 137, 147 and 157 of this issue.

^b See the paper on page 137 of this issue.

^c Duke, B. O. L. (1968) *Ann. trop. Med. Parasit.*, 62 (in press).

DEVELOPMENT OF MICROFILARIAL CONCENTRATIONS FROM REINFECTIONS IN CURED PATIENTS EXPOSED TO MODERATE AND HEAVY TRANSMISSION ^a

(A) BOMBE VILLAGE (Moderate transmission)

Microfilariae (total mf/mg in 4 skin snips)			
Before treatment	After treatment ^b		
	2 years	6 years	9 years
831	0 (0)	65 (8)	657 (79)
696	1.6 (0.2)	14 (2)	—
642	1.6 (0.2)	225 (35)	—
384	4.6 (1.2)	222 (58)	435 (113)
368	2.5 (0.7)	80 (22)	528 (144)
346	0.8 (0.2)	253 (73)	—
300	3 (1)	168 (56)	802 (267)
260	0.4 (0.2)	57 (22)	275 (106)
204	0.3 (0.1)	137 (67)	441 (216)
195	1 (0.5)	105 (54)	166 (85)
144	1 (0.7)	146 (101)	—
135	0 (0)	49 (36)	49 (36)
114	3 (2.6)	114 (100)	430 (377)
79	5 (6.3)	162 (205)	—
57	0.5 (0.9)	35 (61)	261 (458)
621	0 (0)	—	986 (159)
347	0 (0)	—	378 (109)
240	1 (0.4)	—	711 (296)
165	0.5 (0.3)	—	342 (207)
123	3 (2.4)	—	430 (350)
113	0 (0)	—	428 (379)
Arithmetic mean of percentages	0.9	60	212

(B) BOLO/WEME (Heavy transmission)

Microfilariae (total mf/mg in 4 skin snips)		
Before treatment	After treatment ^b	
	18 months	4 years
549	52 (9.5)	421 (77)
492	43 (8.7)	431 (88)
405	7 (1.7)	536 (132)
390	3 (0.8)	340 (87)
375	7 (1.9)	101 (27)
355	22 (6.2)	268 (75)
354	0.4 (0.1)	388 (110)
340	12 (3.5)	248 (73)
235	0.4 (0.2)	149 (63)
234	0.5 (0.2)	191 (82)
191	1.5 (0.8)	101 (53)
95	0 (0)	16 (17)
77	2 (2.6)	257 (334)
65	0 (0)	22 (34)
55	0.4 (0.7)	62 (113)
Arithmetic mean of percentages	2.5	90

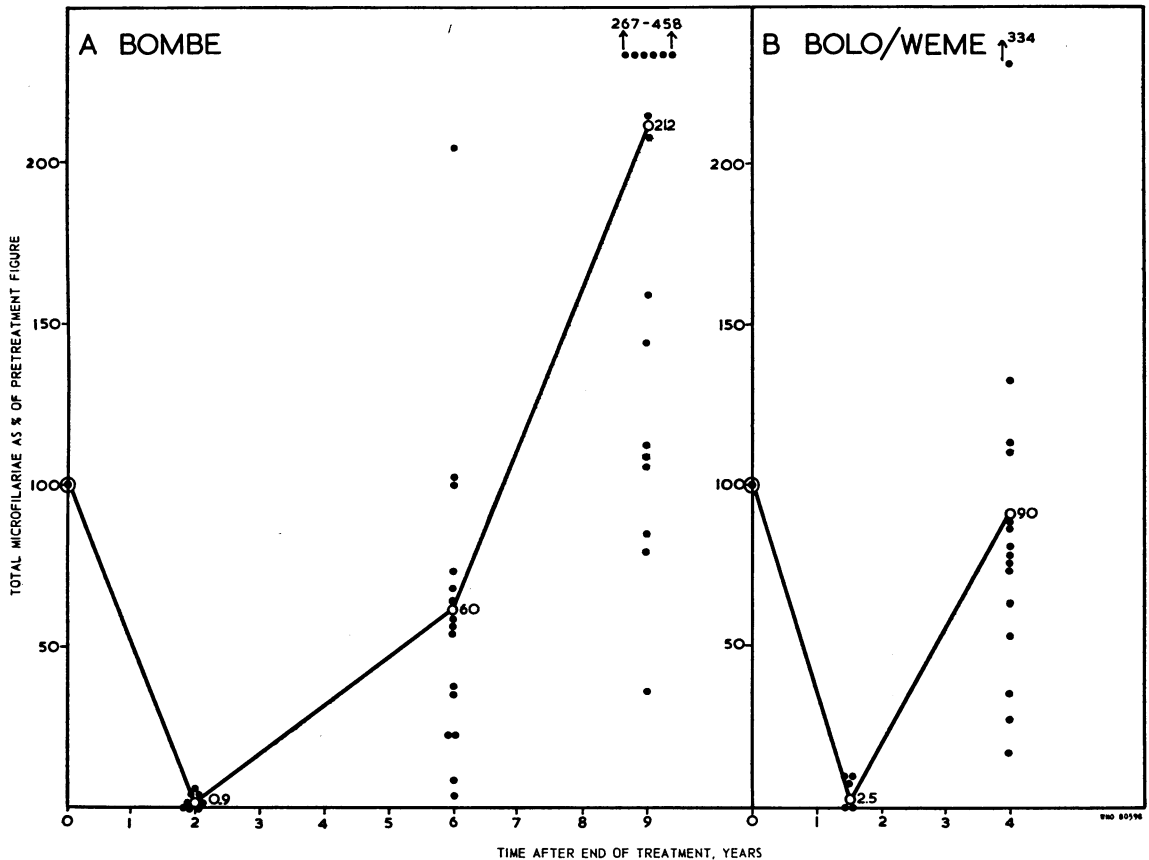
^a Each line of the table refers to an individual patient.

^b Figures in parentheses are percentages of total treatment microfilariae counts.

counts to near zero over the first 18 months to 2 years after the conclusion of treatment. The small numbers of microfilariae found at the 18-month and 2-year examinations may have been a residuum from the patients' original infections—for suramin does not kill all the microfilariae in the skin—or they may have been the earliest arrivals reaching the skin from reinfections with adult worms acquired after treatment had been concluded. After this near-negative condition, which was reached 18 months to 2 years after treatment, reinvasion of the skin by microfilariae stemming from newly acquired adult worms began to take place. At Bolo/Weme, where transmission was known to be very heavy, the mean value of the total microfilarial count had reached 90% of the pretreatment figure by the fourth year after the conclusion of treatment, i.e., 2½ years after the last negative skin examination. In individual patients the figures ranged from 17% to 334%. At Bombe, where transmission is thought to have been rather less intense, mean figures of 60% (range 2%–205%) and of 212% (range 36%–458%) were reached at the sixth and ninth years after the conclusion of treatment, i.e., 4–7 years after the last negative skin examination. It appears, therefore, that among patients who have received curative macrofilaricidal treatment sufficient to eliminate their whole load of adult *O. volvulus*, together with virtually all their microfilariae, continued exposure to reinfection in a forest environment may result in the re-establishment of infections of pretreatment intensity within 4–9 years.

Among cured adults at Bolo/Weme, the restoration of microfilarial concentrations to around their pretreatment levels took some 4 years only, the build-up taking place much more quickly than is normal in children born into the same environment. Duke & Moore,^d working in the same villages, found that children below the age of 10 years showed generally low microfilarial concentrations. The first marked rise in concentrations was seen in the 11–15 years age-group and the level usual in adults was not reached until the 16–20-years age-group. The rapid re-establishment of microfilarial concentrations in cured adult males, as compared with the normal development of infections in untreated children in the same environment, may result from the greater degree to which adults are exposed to the bites of *S. damnosum*. On the other hand, it may be that curative treatment in adults interferes with some

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process of premunity and, by returning them to a non-immune state while they are still exposed to very heavy transmission, may render them more susceptible to the rapid development of intense infections.

In areas of heavy transmission there is a tendency toward the formation of a plateau in microfilarial concentrations in adults aged 20 years and over.^{d, e, f} This of itself suggests that in untreated persons some mechanism of premunity may be operating, which prevents superinfections from

increasing microfilarial concentrations beyond a certain level. Whether such a mechanism is associated with the death of microfilariae and, consequently, with the production of pathological lesions, or whether it acts by eliminating superinfecting worms before they reach maturity, is not known. However, in endemic areas where transmission is not interrupted by control measures, it should be borne in mind that the advantages of treating individual patients in order to reduce their microfilarial loads for a period of perhaps 2-4 years may have to be weighed against the possible disadvantages of reinfections producing even higher microfilarial concentrations and more serious pathological lesions later on. If transmission cannot be controlled at the same time, it may be necessary to give repeated courses of treatment at intervals of 2-3 years.

^d Duke, B. O. L. & Moore, P. J. (1967) *Trans. roy. Soc. trop. Med. Hyg.*, **62**, 22.

^e Woodruff, A. W., Barnley, G. R., Holland, J. T., Jones, D. E., McCrae, A. W. R. & McLaren, D. S. (1963) *Trans. roy. Soc. trop. Med. Hyg.*, **57**, 50.

^f Woodruff, A. W., Choyce, D. P., Pringle, G., Laing, A. B. G., Hills, M. & Wesega, P. (1966) *Trans. roy. Soc. trop. Med. Hyg.*, **60**, 695.