OCULAR ONCHOCERCIASIS IN NORTHERN GHANA*

A TREATMENT SURVEY

BY

CHARLES M. McLEAN

Darwin, Australia

DURING the years 1953–1955, the Medical Field Units of the Ministry of Health, Gold Coast (now Ghana), attempted to control ocular onchocerciasis in the Northern Territories by means of Antrypol (Suramin). A series of weekly injections of 1 g. was given to infested subjects for 5 weeks, with the object of eliminating the adult onchocerae. This scheme of treatment was initiated by Dr. B. B. Waddy, who was at that time Specialist Epidemiologist in charge of the Medical Field Units. However, in 1956, reports of alarming reactions to the treatment, in the form of generalized oedema or of exfoliative dermatitis, became so numerous that Dr. Waddy's successor, Dr. D. Scott, decided that it would be unwise to continue mass therapy until it could be determined:

- (a) whether the treatment was effective,
- (b) if it was effective, whether continuation of treatment was justified in view of the possible toxic effects of the drug.

It was therefore decided to conduct a treatment survey in a known infested area, in an attempt to elucidate these problems, and, if possible, to find a safe and effective method of treatment which could be carried out by the unqualified field assistants of the Medical Field Units.

A survey team of three, consisting of the writer, a qualified male nurse, and a laboratory assistant, was formed, and headquarters were set up in Bolgatanga at the beginning of February, 1957. The equipment included a slit lamp capable of operating from a 12-volt car battery, and the main drugs provided were Antrypol (Suramin), Banocide (diethylcarbamazine), and Anthisan (mepyramine maleate). Two regions, the Navronga district and the Nangodi–Sekoti district, which were known centres of infestation and were each situated about 20 miles from Bolgatanga, were chosen as suitable areas, and the treatment survey was carried out there during the following 15 weeks.

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Diagnostic Signs

The diagnosis of onchocerciasis was decided by the presence of one or more of the following:

- (a) Positive skin snip;
- (b) Palpable nodules;
- (c) Skin changes;
- (d) Microfilariae in the anterior chamber;
- (e) Ocular signs.

Conjunctival snips were not performed, as previous experience had shown that patients tended to resent this procedure, and, when positive, microfilariae could be seen in the anterior chamber on slit-lamp examination.

Of the total number diagnosed, 43.4 per cent. had positive skin snips, 65.6 per cent. had palpable nodules, 75 per cent. had skin changes, 38.6 per cent. had microfilariae in the anterior chamber, and 84.5 per cent. had ocular signs.

It became obvious, at a very early stage in the survey, that skin-snipping was completely unreliable as the sole method of diagnosing onchocerciasis. Many patients with negative snips showed gross evidence of the disease.

It is probable that all onchocerciasis patients have nodules, but these may not always be palpable. The distribution of those discovered by the survey team was interesting:

	<i>Site</i>					<i>Percentage</i>
Chest	..	..	..	..	..	55
Anterior iliac crest	..	..	..	..	..	21
Knee	..	..	..	..	..	10
Buttock	..	..	..	..	..	8.6
Hip	..	..	..	..	..	7.8
Thigh	..	..	..	..	..	6.2
Scapula	..	..	..	..	..	5.5
Sacrum, Scalp	..	..	..	..	..	4.7
Abdominal wall, Elbow	..	..	..	..	..	3
Groin, Shoulder, Forearm, Leg, Sternum	..	..	..	..	..	2
Axilla, Upper arm	..	..	..	..	..	1.5
Foot	..	..	..	..	..	1

As all these patients also had ocular signs, this does not support the common belief that the nearer the nodules are to the eye, the greater is the liability to ocular complications. Many of the patients had several nodules, variously distributed; none had more than six.

The skin changes, which Hughes (1949) has aptly termed "presbyderma", consisted of wrinkling and fissuring, and the commonest sites for these were the thighs, buttocks, and lumbar region, although in the most severe cases the whole trunk and the arms were also affected.

The presence of microfilariae in the anterior chamber was the least common diagnostic sign, although on occasion it was the only one. In one case, a living microfilaria was seen in the substantia propria of the cornea. None was detected in the vitreous.

Ocular lesions formed the most common diagnostic sign of onchocerciasis, and fell into the following categories:

<i>Lesions</i>	<i>Percentage</i>
Corneal opacities	69
Optic atrophy	48
Choroido-retinal degeneration	41.5
Posterior synechiae	20
Iris atrophy	17
Keratic precipitates	15
Complicated cataract	14
Cupped discs	2.4
Phthisis bulbi	1.8

The corneal opacities, in the milder cases, consisted of nummular infiltrates in the substantia propria; in more severe cases, these coalesced to form a dense opacity (sometimes pigmented) covering most or all of the cornea, and in those most severely affected superficial vascularization spread over this from the limbus.

The optic atrophy was mainly of the consecutive type and associated with choroido-retinal degeneration, but in a few cases the atrophy was primary, and in these no choroido-retinal lesions were found, but positive skin snips, nodules, and/or corneal lesions were present.

In the majority of cases with choroido-retinal degeneration, the changes corresponded with those described by Hissette (1937) and Ridley (1945). Of these cases 25 per cent. showed marked perivascular sheathing. In one case, the changes closely resembled those of "retinitis punctata albescens".

Most of the patients with posterior synechiae showed keratic precipitates and a fine aqueous flare, but a few were old cases in which the iridocyclitis had evidently subsided. All showed other signs of onchocerciasis. Patches of iris atrophy were found in some cases of active iridocyclitis, but in others there was no other evidence of iris involvement, although corneal opacities or choroido-retinal degeneration were present. All cases showing keratic precipitates had active iridocyclitis, but this was never of the severe, exudative type. The patients with complicated cataract had other signs of present or past iridocyclitis. In the patients with cupping of the optic discs, the tension was either normal or only slightly raised, and other ocular signs of onchocerciasis were present. In those with phthisis bulbi, one eye only was affected, and the other eye showed signs of onchocerciasis.

No cases of "acute ocular onchocerciasis", as described by Rodger (1957), were seen, although several cases of phlyctenular kerato-conjunctivitis, limbal vernal conjunctivitis, and leprotic interstitial keratitis were observed.

Nearly all the patients seen were grossly emaciated, but this is a common finding in the Northern Territories, and not confined to onchocerciasis areas. There is no doubt that the diet of the inhabitants of this region is deficient in protein and in vitamins A and B complex, but an adequate nutritional survey of the area has not yet been undertaken. Until this is done, it will be impossible to say whether dietary deficiencies may play a part in producing the severe ocular manifestations of onchocerciasis, but the writer has noticed that in Ashanti, where there is a fairly

high incidence of the disease, the inhabitants are better nourished and the eye lesions are less severe. Many of the onchocerciasis patients in the Northern Territories also suffered from bilharzia, and several had endemic goitre.

Scheme of Treatment

The patients selected for treatment were divided into three groups:

- (a) Those receiving Antrypol plus Banocide (Course A);
- (b) Those receiving Antrypol only (Course B);
- (c) Those receiving Banocide only (Course C).

As will be seen later, this programme had to be modified, owing to the number of patients who developed reactions to Antrypol.

Experience in Accra had shown that combined treatment with Antrypol and Banocide over a period of 8 weeks offered a reasonable chance of eradicating the infestation. It was realized, however, that the number of cases seen there was comparatively small, consisting mainly of migrants from infested areas in the Northern Territories and lower Volta regions, who were now employed in the vicinity of Accra and whose nutritional standard was, in consequence, fairly high. In addition, they were no longer subject to the hazard of re-infestation, as the environs of the capital are free from *Simulium damnosum*. The routine treatment of these cases consisted of the intravenous injection of 1 g. Antrypol at weekly intervals for 8 weeks; during the first 2 weeks, one tablet (0.05 g.) of Banocide was taken orally three times daily, two tablets three times daily for the next 2 weeks, and three tablets three times daily for the final 4 weeks, making a total course of 8 g. Antrypol and 378 tablets Banocide. With this dosage, forty patients, followed-up for a period of one year, became free of symptoms and signs, apart from irreversible changes such as choroido-retinal degeneration and optic atrophy. Throughout the post-treatment period they showed negative skin snips and absence of microfilariae from the anterior chambers. Approximately 50 per cent. complained of skin irritation during the first week or two of treatment, but this was easily controlled by the administration of an antihistamine (Anthisan). Only two patients had severe abdominal discomfort, which ceased on the temporary withdrawal of Antrypol, and none showed albuminuria, oedema, or exfoliative dermatitis.

In view of the reports from the Medical Field Units of the reactions to Antrypol injections in the Northern Territories, it was thought advisable to modify the dosage of this drug in the treatment survey, and it was decided that those patients selected to receive it (whether combined with Banocide or alone) would be given 0.25 g. in the first week, 0.5 g. in the second and third weeks, 0.75 g. in the fourth and fifth weeks, and 1 g. in the remaining three weeks (making a total of 5.75 g.). Patients receiving Banocide were to receive a total of 378 tablets, as in Accra.

Results of Treatment

In all, 374 patients received treatment. Of these 192 received Course A (Antrypol plus Banocide), 68 received Course B (Antrypol only), and 114 received Course C (Banocide only).

Patients showing albuminuria before beginning treatment were given Course C—the majority of these were found to be suffering from bilharzia. Only thirty (15·6 per cent.) of those receiving Course A completed the full course of treatment; the remainder had to stop Antrypol because of reactions, and completed the course with Banocide only. No patient receiving Course B completed his full course of Antrypol, and treatment was switched to Banocide when reactions occurred. Patients on Course C were able to complete their full course of treatment.

Of the 374 patients treated, 308 (82 per cent.) developed reactions. Those due to Antrypol were albuminuria, headache, nausea and vomiting, oedema of feet and legs, and giddiness, in the following order of frequency:

<i>Antrypol Reactions</i>	<i>Percentage</i>
Albuminuria	82
Headache	20
Nausea and vomiting	14
Oedema of feet and legs	8
Giddiness	6

Antrypol treatment was stopped immediately a patient produced albuminuria, and further treatment was continued with Banocide. Those patients who developed oedema of the feet and legs showed albumin in their urine. The majority of patients receiving Antrypol developed albuminuria between the fifth and eighth weeks of treatment, *i.e.* after receiving between 2·75 and 4·75 g. In general, the more emaciated the patient, the earlier the albuminuria appeared. In view of the known toxic effect of Antrypol on the kidneys, it was considered unjustified to continue this form of therapy once this sign was detected, and some anxiety was felt lest other signs of renal insufficiency should appear, but only two patients required to be admitted to hospital, and these were free of symptoms and signs after 2 weeks of treatment consisting mainly of rest and withdrawal of the drug. No cases of exfoliative dermatitis were seen.

Banocide reactions were skin irritation, muscle and joint pains, papular rash, abdominal discomfort, and headache, in the following order of frequency:

<i>Banocide Reactions</i>	<i>Percentage</i>
Skin irritation	74
Muscle and joint pains	62
Papular rash	50
Abdominal discomfort	24
Headache	22

These were all controlled by the administration of Anthisan, and treatment did not require to be interrupted. Skin irritation and papular rash appeared within the first 2 weeks; the other reactions tended to occur between the third and sixth weeks.

108 patients (28·8 per cent.) showed some improvement in vision at the end of treatment. All had negative skin snips and anterior chambers clear of microfilariae when the course was completed. The visual improvement was mainly due to clearing of the corneal opacities; several patients whose corneae were unaffected but who had choroido-retinal changes also showed improved vision. No case with optic atrophy was improved. The results of this survey showed that both Antrypol and Banocide produced an improvement in visual acuity where corneal opacities were the main cause of defective vision. Typical cases are illustrated in Appendix 1.

As previously mentioned, no patient with definite optic atrophy showed any visual improvement, but there was an improvement in visual acuity in some who had choroido-retinal degeneration. With the facilities at our disposal it was impossible to arrive at a logical explanation for this, and all one can do is record the fact. Some of these cases are illustrated in Appendix 2.

In addition a small number of cases *appeared* to show slight improvement in visual acuity, through increasing familiarity with Snellen's illiterate chart and by using eccentric fixation.

At the end of the period of treatment and observation, nodulectomy was performed on a few cases. It had been hoped that most of the patients would submit to this procedure, which would have given some indication as to the efficacy of treatment in eradicating the adult worms, but evidently previous experience of this, carried out by other teams, had left an unfavourable impression, and it was impossible to persuade many to undergo this minor operation. The results showed that, in those receiving Antrypol (either alone or combined with Banocide) the adult worms invariably showed signs of degeneration; whereas, in those receiving Banocide only, less than 30 per cent. showed degenerative changes. The numbers involved were too small for us to arrive at a definite conclusion, but, allowing for the fact that degeneration is liable to occur in long-standing nodules, the impression formed was that Antrypol had a lethal effect on the adult worm, while Banocide had none.

At the end of treatment, and for a period of at least 4 weeks afterwards, skin snips were negative and the anterior chambers were free of microfilariae in all patients. It was concluded that both Antrypol and Banocide had a lethal effect on the microfilariae. It was intended that the survey team should follow up these cases at intervals of 6 months, but circumstances arose which prevented this.

Conclusions

The following conclusions were drawn from this survey:

- (1) That Antrypol has too toxic an effect to be used in mass treatment,

particularly where this is being carried out in the field by assistants with little medical training, and where there are no adequate hospital facilities;

(2) That Banocide is a reasonably safe drug for use in mass therapy; reactions are not severe, and are quickly controlled by antihistamines;

(3) That both Antrypol and Banocide produce an improvement in visual acuity in cases in which the ocular manifestations of onchocerciasis are mainly corneal;

(4) That both Antrypol and Banocide have a microfilaricidal action.

Summary

- (1) The objects of a treatment survey in Northern Ghana are outlined.
- (2) The diagnostic criteria used in the survey are stated.
- (3) The scheme of treatment is described, and the results reported.
- (4) The conclusions arrived at are enumerated.

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APPENDIX I
THIRTY TYPICAL CASES SHOWING IMPROVEMENT IN VISUAL ACUITY

Case No.	Age (yrs)	Sex	Eye Lesions at Beginning of Treatment		Treatment		Visual Acuity				Eye Lesions at End of Treatment
							At Beginning of Treatment		At End of Treatment		
			Right	Left	Antrypol (g.)	Banocide (tabs)	Right	Left	Right	Left	
27	11	M	Central nummular opacities	Lateral nummular opacities	2.75	378	6/18	6/6	6/6	6/6	Faint corneal opacities remain
28	65	M	Central nummular opacity	—	5	378	6/12	6/6	6/6	6/6	Corneae clear
30	30	M	Numerous nummular opacities in both corneae Those in centre of left cornea confluent		2	378	6/18	1/60	6/6	6/60	Right: very faint opacities Left: opacities less dense
36	30	M	Numerous nummular opacities	—	3.75	378	6/24	6/6	6/6	6/6	Right: faint opacities
38	24	F	Nummular opacities		4.75	378	6/12	6/9	6/6	6/6	Corneae clear
46	48	M	Confluent opacities with superficial vascularization		4.75	378	Hand movements	3/60	1/60	6/60	Opacities less dense Vascularization less

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Case No.	Age (yrs)	Sex	Eye Lesions at Beginning of Treatment		Treatment		Visual Acuity				Eye Lesions at End of Treatment
							At Beginning of Treatment		At End of Treatment		
			Right	Left	Antrypol (g.)	Banocide (tabs)	Right	Left	Right	Left	
51	52	M	Nummular opacities Immature cataract		2.75	378	Counting fingers at 2 ft	Counting fingers at 2 ft	5/60	6/18	Faint corneal opacities remain Cataracts unchanged
83	46	M	Nummular opacities		3.75	378	6/12	6/24	6/6	6/6	Faint opacities remain
86	49	M	Numerous nummular opacities, some confluent Immature cataracts		3.75	378	Hand movements	Hand movements	1/60	2/60	Corneal opacities less Cataracts unchanged
90	40	M	Nummular opacities		1.25	378	6/36	6/36	6/9	6/9	Faint opacities remain
110	32	M	Nummular and confluent opacities		4.75	378	6/60	6/12	6/24	6/6	Right: opacities less dense Left: cornea clear
111	27	M	Nummular opacities		4.75	378	6/18	6/18	6/6	6/9	Corneae clear
113	28	M	Dense central opacities Complicated cataracts		3.75	378	Perception of light	2/60	4/60	4/60	Opacities less dense
118	37	M	Nummular opacities		2.75	378	6/12	6/6	6/6	6/6	Corneae clear
127	28	M	Numerous nummular opacities		4.75	378	Hand movements	6/60	6/12	6/9	Faint opacities remain
151	30	M	Dense central opacity	Optic disc pale	2.75	378	Hand movements	6/12	2/60	6/12	Right corneal opacity less dense
180	40	M	Dense opacities		2.75	—	Hand movements	Hand movements	3/60	1/60	Opacities less dense
187	22	M	Nummular opacities	Nummular opacities Optic atrophy Choroido-retinal degeneration	2.75	—	6/12	Perception of light	6/6	Hand movements	Faint opacities remain
202	37	F	Nummular opacities		3.75	—	6/12	6/9	6/6	6/6	Corneae clear
211	20	M	Numerous nummular opacities		2.75	—	1/60	1/60	6/60	6/24	Opacities less dense
235	36	M	Nummular opacities		—	378	6/18	6/24	6/6	6/12	Right cornea clear Left opacities fainter
248	38	M	Nummular opacities	Dense central leucoma	—	378	6/18	Perception of light	6/6	Perception of light	Right cornea clear Left cornea unchanged
273	57	M	Nummular opacities Mature cataract	Nummular opacities Immature cataract	—	378	Perception of light	1/60	Perception of light	5/60	Faint opacities remain Cataracts unchanged
278	40	M	Nummular opacities Immature cataracts		—	378	Hand movements	1/60	5/60	5/60	Faint opacities remain Cataracts unchanged
301	35	M	Central leucoma	Nummular opacities	—	378	Perception of light	4/60	2/60	6/24	Opacities less dense

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Case No.	Age (yrs)	Sex	Eye Lesions at Beginning of Treatment		Treatment		Visual Acuity				Eye Lesions at End of Treatment
			Right	Left	Antrypol (g.)	Banocide (tabs)	At Beginning of Treatment		At End of Treatment		
							Right	Left	Right	Left	
314	30	M	Dense opacities		—	378	Perception of light	Hand movements	5/60	6/60	Opacities less dense
328	16	F	Numerous nummular opacities		—	378	Perception of light	Perception of light	5/60	3/60	Opacities less dense
337	42	M	Nummular opacities		—	378	6/18	6/60	6/6	6/6	Corneae clear
342	25	M	Nummular opacities Complicated cataracts		—	378	Hand movements	Perception of light	4/60	Hand movements	Corneae clear
369	20	M	Nummular opacities	—	—	378	6/12	6/6	6/6	6/6	Corneae clear

APPENDIX 2

TEN TYPICAL CASES WITH CHOROIDO-RETINAL DEGENERATION SHOWING IMPROVEMENT IN VISUAL ACUITY

Case No.	Age (yrs)	Sex	Eye Lesions at Beginning of Treatment	Treatment		Visual Acuity				Eye Lesions at End of Treatment
						At Beginning of Treatment		At End of Treatment		
				Antrypol (g.)	Banocide (tabs)	Right	Left	Right	Left	
3	42	M	Choroido-retinal degeneration in both maculae	3.75	378	1/60	3/60	6/9	6/9	Fundi unchanged
114	38	M	Widespread choroido-retinal degeneration in both fundi	5.75	378	3/60	2/60	6/60	6/60	Fundi unchanged
167	32	F	Widespread choroido-retinal degeneration in both fundi	2.75	378	Perception of light	3/60	Hand movements	6/36	Fundi unchanged
174	35	M	Widespread choroido-retinal degeneration in both fundi	2.75	378	Hand movements	Counting fingers at 2 ft	1/60	3/60	Fundi unchanged
221	27	F	Choroido-retinal degeneration in left macula	—	378	6/6	6/18	6/6	6/9	Left fundus unchanged
249	36	M	"Retinitis punctata albens" in both fundi	—	378	6/6	6/24	6/6	6/6	White spots less numerous
252	50	M	Choroido-retinal degeneration in both maculae	—	378	6/60	6/60	6/12	6/24	Fundi unchanged
284	55	M	Right: Widespread choroido-retinal degeneration Left: Phthisis bulbi	—	378	2/60	No perception of light	6/36	No perception of light	Right fundus unchanged
317	30	M	Widespread choroido-retinal degeneration in both fundi Optic atrophy of left eye	—	378	6/36	No Perception of light	6/12	No perception of light	Fundi unchanged
370	45	M	Widespread choroido-retinal degeneration in both fundi	—	378	Perception of light	Hand movements	1/60	2/60	Fundi unchanged