

# DIETHYLCARBAMAZINE CONTROL OF BANCROFTIAN FILARIASIS

## FOLLOW-UP OF A FIELD TRIAL IN WEST AFRICA

BY

IAN A. MCGREGOR, L.R.C.P.&S.Ed., D.T.M.&H.

AND

H. M. GILLES, M.D., B.Sc., D.T.M.&H.

Medical Research Council Laboratories, Gambia, B.W.A.

In February, 1951, the available population of Keneba, a village in the West Kiang District of the Gambia Protectorate, were examined and those infected with *Wuchereria bancrofti* recorded. As many as possible of these carriers were treated in the same month with diethylcarbamazine ("hetrazan"), each person who completed the prescribed course receiving 25 mg. of hetrazan base per kg. of body weight. Nine months later, in December, 1951, the population were again examined to determine the results of treatment. These results have already been described (McGregor *et al.*, 1952). This paper records the results of a third survey of Keneba, November, 1954, conducted three years and nine months after administration of the drug.

**Methods.**—Techniques identical to those of the earlier surveys were employed. Blood for the enumeration of microfilariae was taken by finger-prick between the hours of 9 p.m. and midnight. This blood, estimated by previous measurement to be approximately 20 c.mm., was spread uniformly over a measured area of slide marked by grease pencil. It is to this volume of approximately 20 c.mm. that all microfilaria counts in this paper are referred. The thick films were dehaemoglobinized, fixed in methyl alcohol, and stained with haemalum.

### Results

In 1954, 390 villagers who had been examined in the surveys of 1951 were again examined. Table I gives the breakdown of this number into groups pertinent to this paper.

TABLE I

A. Persons found infected in 1951 and treated with diethylcarbamazine base (25 mg./kg.)	122
B. Persons found infected in 1951 but not treated	46
C. Persons found uninfected in 1951	222
<b>Total persons examined</b>	<b>390</b>

**A. Treated Group.**—Of 122 persons who were treated with diethylcarbamazine base (25 mg. per kg. of body weight) in February, 1951, and who were re-examined in November, 1954, 32 were found to be infected. In Table II the results obtained in this group at all three surveys are contrasted. When the December, 1951, and November, 1954, figures are compared it will be noted that, although microfilaria density has increased in the persistently infected cases, the overall number of infected patients has decreased. This latter observation might suggest that 11 of the 43 subjects found infected ten months after treatment achieved total recovery three years and nine months after treatment. Our results, however, revealed that this was not the case. Of the 122 patients treated in February, 1951, 43 still harboured parasites in December, 1951, and 79 showed no evidence of infection. By November, 1954, only 15 of the 43 cases still showed microfilariae in the blood, but parasites had reappeared in 17 of the 79 negative cases. Thus, while the former group may be described as persistent infections, the possibility of either fresh inoculation or relapse in the latter group must be considered.

TABLE II.—Results in Three Surveys

	Before Treatment	After Treatment	
	February, 1951	December, 1951	November, 1954
No. in group	122	122	122
No. infected	122	43	32
Recovery rate	—	64.7%	73.8%
Sum of microfilariae in all positive films	3,931	229	478
Reduction in total microfilaria density	—	94.2%	87.8%

**B. Untreated Group.**—Forty-six persons recorded as microfilaria carriers in the surveys of 1951 were again examined in November, 1954. Forty-four were found still to be infected. Table III shows in contrast the 1951 and 1954 findings in this group. It will be noted that, whereas 4.3% of untreated patients recovered, an increase in microfilaria density occurred in those who remained infected.

TABLE III

	1951	1954
No. in group	46	46
.. infected	46	44
.. uninfected	—	2
Recovery rate	—	4.3%
Sum of microfilariae in all positive films	2,031	2,682
Increase in microfilaria density	—	32%

**C. Untreated Uninfected Group.**—Of 222 persons showing no evidence of infection in 1951, 11 were found to harbour parasites in 1954. If these cases are regarded as fresh infections, a village filariasis infection rate of 4.9% over the period of observation is calculated.

TABLE IV.—Recovery Rates

	December, 1951	November, 1954
<b>A. Treated group (43 persons):</b>		
No. infected	43	15
.. cleared	—	28
Recovery rate	—	65.1%
<b>B. Untreated group (46 persons):</b>		
No. infected	46	44
.. cleared	—	2
Recovery rate	—	4.3%

TABLE V.—Apparent Reinfection Rates

	December, 1951	November, 1954
<b>A. Treated group (79 persons):</b>		
No. infected	0	17
Infection rate	—	21.5%
<b>B. Untreated group (222 persons):</b>		
No. infected	0	11
Infection rate	—	4.9%

Table IV compares the recovery rates in both treated and untreated groups of individuals over the period December, 1951, to November, 1954. As the difference in these rates (65.1% as opposed to 4.3%) is statistically significant, the higher recovery rate in the treated group is assessed to be, in the main, a result of treatment.

Table V shows the apparent reinfection rates in both treated and untreated individuals over the same period. Again the difference in the rates (21.5% as opposed to 4.9%) is statistically significant, and the assumption is made that the high infection rate in the treated group is likely to be due principally to the production of microfilariae by filaria worms that have survived treatment.

### Discussion

Perusal of the above results reveals three important points. Firstly, the recovery rate in a group of persons infected with Bancroftian filariasis and treated with diethylcarbamazine

was higher after three years and nine months than it was ten months after drug administration. Secondly, a group of treated individuals observed in the tenth and forty-fifth months following treatment showed a significantly higher recovery rate over the same period than did a comparable group of infected but untreated persons. Thirdly, of those members of the treated group who still showed evidence of infection three years and nine months after treatment, 46.8% appeared to have maintained their original infection throughout the period of observation, while 53.2% seemed to have "relapsed" after a period of apparent cure.

These points are seemingly in conflict. The first and second indicate that in one section of the treated group diethylcarbamazine is still exerting a curative effect, while the third suggests that in the remainder of the same group the effect of the drug has been lost without achieving complete cure.

The explanation of this apparent paradox is hampered by the lack of precise knowledge of the action of diethylcarbamazine in *W. bancrofti* infections. It is known that in sufficiently high dosage the drug had a pronounced destructive effect on microfilariae (East African Filariasis Research Unit, 1950). Its action, however, on the parent filaria worm is not known. The results expressed in this paper cannot be explained merely by the action of the drug on circulating microfilariae at the time of administration. The recovery rate, rising for many months after treatment, strongly suggests that the drug at the time of its administration terminated the production of microfilariae, yet left a number of these circulating in the blood, and that in each treated individual the evidence of clinical cure was delayed until these parasites had reached the end of their life-span and had been destroyed. Such an effect could be achieved by diethylcarbamazine destroying or sterilizing the parent worms at the time of administration; but the fact that, in the investigation being described, exacerbation of the original infection developed in a number of treated subjects some months after apparent cure suggests a more selective action.

We believe that the facts here reported can best be explained by the hypothesis that the very active reproductive organs of mature filariae possess a marked avidity for diethylcarbamazine and that at the time of administration these mature parent worms are either killed or sterilized. Those filariae which have not reached maturity and do not possess large and active reproductive organs may not be greatly affected by treatment and may survive to mature, mate, and produce offspring.

### Summary

In 1951 a field trial of diethylcarbamazine ("hetrazan") in the control of Bancroftian filariasis was conducted in a Gambian village. The present paper describes the results obtained three years and nine months later and contrasts them with the findings ten months after treatment.

One hundred and twenty-two persons infected with *W. bancrofti* and treated with diethylcarbamazine (25 mg. per kg. of body weight) in February, 1951, were subsequently examined in December, 1951, and November, 1954. The percentage cured was found to have risen from 64.7% in December, 1951, to 73.8% in November, 1954. Of the 32 cases found still infected in November, 1954, 46.8% appeared to have maintained their original infection, while 53.2% seemed to have "relapsed" after a period of apparent cure.

A hypothesis that diethylcarbamazine exerts a sterilizing effect on the reproductive organs of the mature filaria worm is submitted.

### REFERENCES

- East African Filariasis Research Unit (1950). Annual Report.  
McGregor, I. A., Hawking, F., and Smith, D. A. (1952). *British Medical Journal*, 2, 908.

## Medical Memoranda

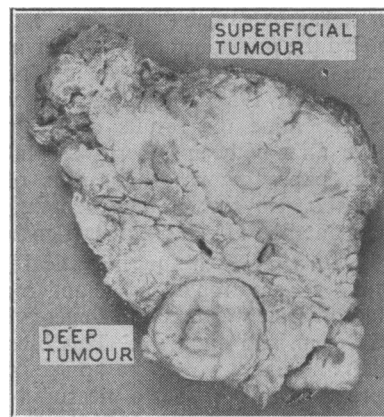
### Multiple Parotid Tumours

In the two cases reported below, a total parotidectomy was performed for an apparently isolated tumour of the parotid gland, but section of the gland after the operation revealed a second, discrete, encapsulated tumour.

### CASE REPORTS

*Case 1.*—A man aged 62 had been aware of a lump on the right side of his face for three months. This painless lump had slowly increased in size. Examination revealed that the lump, 2 cm. in diameter, was situated in the lower part of the parotid gland; it was quite mobile and the skin moved freely over the smooth surface. No other abnormality could be felt. On May 11, 1951, the parotid gland

was removed on the right side; both superficial and deep lobes were removed. Section at the conclusion of the operation revealed two separate tumours, one 2 cm. and the other 1.5 cm. in diameter. Microscopical examination revealed that one tumour was a mixed parotid tumour and the other an adenolymphoma. Four and a half years later he was free of recurrence; he stated that the only after-effect of the operation had been the appearance of excessive sweating over the parotid region when eating.



Case 2. The parotid gland after removal to show the superficial tumour surrounded by fibrous tissue discrete from the deep tumour.

operation had been the appearance of excessive sweating over the parotid region when eating.

*Case 2.*—A man aged 47 had had a lump on the right side of his face for at least four years. A portion had been removed by his doctor and the pathologist had reported "a mixed parotid tumour." Examination revealed a scar behind the angle of the jaw, under which an ill-defined lump could be felt. It was about 2 cm. in diameter and adherent to the skin, but mobile over the mandible. No other abnormalities were found. On April 5, 1955, the parotid gland was removed. Section of the gland after operation showed that, in addition to the tumour embedded in the scar tissue under the old incision, a second tumour, 2 cm. in diameter, was situated deep in the superficial lobe in the region of the isthmus. His convalescence was uneventful, and six months later there was no evidence of recurrence (see Fig.).

### COMMENT

Redon (1953) reported that, whilst examining a specimen obtained by parotidectomy from a patient with a third recurrence, Professor Jacques Delarue was surprised to find, in addition to the clinically recognized tumour, eight isolated independent nodules of mixed tumour. At first he thought that they represented inoculations, but he later found "aberrant foci," not only in cases of recurrence but also with primary tumours. Redon believes that the incidence of tumours with multiple foci varies from 20 to 33%. Fitzgibbon (1953) states that on two occasions he has seen small satellite tumours, closely associated with the main one. Willis (1948) suggested that there was a zone of salivary tissue which was potentially neoplastic and that these tumours might well be multicentric in origin.