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Control of Bancroftian Filariasis by Cooking Salt Medicated with Diethylcarbamazine

FRANK HAWKING [1] & RUY JOÃO MARQUES [2]

In small-scale pilot trials, filarial infection can usually be reduced to low levels by oral administration of diethylcarbamazine to all the persons concerned; but in mass campaigns it is often difficult to persuade large numbers of people to swallow the tablets. In order to overcome this difficulty the authors propose that the compound be incorporated into cooking salt, as has been done with chloroquine to control malaria. There are many reasons why this method of medication should be more effective against filariasis than it has often been against malaria.

Laboratory trials showed that cooking the compound in food did not make it toxic for rats or diminish its antifilarial activity. A pilot trial was carried out at Recife, Brazil, in which 1000 adults received salt containing 0.4 % diethylcarbamazine (corresponding to a daily intake of 100 mg/day) for 40 days, and then salt containing 0.1 % compound for a year. This medication was simple to administer; it was quite acceptable to the subjects; it caused no untoward effects; and it removed almost all the microfilariae from the blood. Administration of medicated salt (0.3 %) for 18 days to another group of 1300 adults was well tolerated and produced a considerable reduction of the microfilarial load; but this short period was insufficient to remove all the microfilariae.

The authors recommend that this method of administering diethylcarbamazine to large numbers of people should be investigated further to see if it could be used for mass campaigns to control filariasis.

INTRODUCTION

During the past 15 years many investigations have been carried out on the control of filariasis by mass therapy with diethylcarbamazine. Theoretically, if all the persons in a given region could be treated with an adequate amount of this compound there would be no microfilariae left to infect other persons and the disease would quickly die out. Experience has shown that in small pilot trials (or even in islands as large as Tahiti) this procedure is eminently successful in reducing filarial infection to negligible proportions. On a large scale, however, involving populations of 100 000 or more, as in India, the procedure has proved impracticable owing to the difficulty of persuading large numbers of people (who do not feel ill) to swallow tablets which may produce minor effects such as nausea, vomiting, etc. (The subject was reviewed by Hawking, 1962.) In these circumstances, it seemed to the authors that the difficulties of mass administration might be overcome by incorporating the compound in cooking salt, as has been done in the case of chloroquine for control of malaria.

The procedure for controlling malaria by incorporating antimalarial compounds in cooking salt was introduced by Pinotti in Brazil in 1952, and it has been applied on a large scale in Brazil, Guyana, West Irian and other parts of the world with varying degrees of success. Although the use of chloroquinized salt has been abandoned in many areas, its use produced satisfactory results in some places, particularly Guyana (Giglioli et al., 1967). More important, the control of filariasis by diethylcarbamazine differs in many ways from the control of malaria by chloroquine, and conditions seem

[1] Head of Division of Parasitology, National Institute for Medical Research, Mill Hill, London, England.

[2] Director, Instituto de Medicina Tropical, Faculdade de Medicina, Universidade Federal de Pernambuco, Recife, Brazil.

more favourable for its success, for a variety of reasons.

(*a*) In malaria, one sporozoite invading a patient may rapidly multiply into millions and initiate a severe infection; but in filariasis, one microfilaria stays one worm until it has developed for many months and then has managed to encounter another worm of the opposite sex to mate with. Even then, no further multiplication of adult worms occurs in the same host, and the microfilariae must pass out into a mosquito and back into a host before a new generation of adult worms can be produced. Thus even a partial reduction in the number of microfilariae available for transmission would be very valuable. Furthermore, the meeting of male and female worms (for fertilization) is probably difficult in a large host like man unless both sexes are present in fair numbers. If only a few worms were present in the host, it is possible that the two sexes might fail ever to meet and so the infection would die out, instead of multiplying (as with malaria).

(*b*) Owing to this slowness in the multiplication of filarial worms, filarial infection is slow to develop and spread. Each generation (from infective larva to infective larva) takes most of a year. Once a great reduction in the population of filariae has been produced in a given area, recovery is a slow process; and it might fail to occur, as has just been said.

(*c*) For malaria eradication, it is probably necessary to maintain the chloroquinized salt regime for several years. With filariasis, the period of medication could probably be much shorter. There is now ample evidence that diethylcarbamazine kills the adult worms of *Wuchereria bancrofti* as well as the microfilariae (Ch'en, 1964; Hawking, 1966). A regime of carbamazine salt for months might well be sufficient to remove most of the worms and microfilariae in a given area (after which the infection might die out, as mentioned above). If this did not happen, then the procedure could be repeated after 2 or 4 years, or after any other suitable period (see the experience of McGregor & Gilles (1960) 4 years after carbamazine in Gambia).

(*d*) In malaria the main reservoir of infection is maintained in young children, who often consume little salt. In filariasis the infection rate among those under 5 years old is usually negligible, and it does not become high until about 15 years old.

(*e*) Diethylcarbamazine has little taste (slightly sweetish) so that it would not cause complaints, as does chloroquine, which is bitter.

(*f*) Diethylcarbamazine is eminently a *safe* compound. It has now been administered to millions of persons, and although it may have provoked nausea, pyrexia, etc., it has never been shown to have been responsible for a fatality.

(*g*) Drug-resistance is not likely to be encountered in filariasis, because drug-resistance is practically unknown among helminths, and because the generation time (one year) is extremely slow compared with that of bacteria or protozoa.

In view of all these considerations, the use of cooking salt medicated with diethylcarbamazine seemed a promising method for the control of filariasis, and the investigation reported here was undertaken to study it in practice. The investigation is divided into two parts:

(1) A laboratory investigation to show that diethylcarbamazine is stable to cooking (undertaken by F. Hawking at the National Institute for Medical Research, London).

(2) A field investigation on two closed communities (undertaken by R. J. Marques and F. Hawking at the Instituto de Medicina Tropical, Recife, Brazil).

LABORATORY INVESTIGATIONS OF THE STABILITY OF DIETHYLCARBAMAZINE DURING COOKING

This part of the paper reports laboratory investigations on the stability of diethylcarbamazine during procedures similar to those used in cooking food. It was necessary to ensure that the heat of cooking would not convert diethylcarbamazine into toxic products on the one hand or destroy the antifilarial activity on the other.

MATERIAL AND METHODS

Diethylcarbamazine was used as the dicitrate salt and all weights refer to this preparation. The diet used was the standard one of the National Institute for Medical Research, London (No. 41). Diets containing compound were prepared by grinding the

food pellets to powder, mixing with appropriate quantities of carbamazine, making into a stiff paste with a little water, and baking at 150°C for half an hour to form biscuits. The rats were the Institute hooded strain, and the mice were Parkes' mice. For testing antifilarial activity our laboratory strain of *Litomosoides carinii* in cotton rats was used.

EXPERIMENTAL RESULTS

Toxicity after cooking

Acute toxicity for mice. A solution of diethylcarbamazine 50 mg/ml was prepared in 0.95% sodium chloride and half of it was autoclaved at 121°C for 2 hours. The two halves were then administered to mice by intraperitoneal injection as shown in Table 1. The mice were followed for 7 days, but actually all deaths occurred within 1 hour. It was concluded that autoclaving for 2 hours did *not* increase the toxicity of solutions of diethylcarbamazine.

TABLE 1
ACUTE TOXICITY FOR MICE OF DIETHYLCARBAMAZINE BEFORE AND AFTER AUTOCLAVING FOR 2 HOURS

Intraperitoneal dose (mg/20 g)	Mortality	
	Controls (solution not autoclaved)	Autoclaved solution
5.0	0/10	0/10
7.1	0/10	0/10
10	1/10	1/10
14.2	6/10	7/10

Effect on the growth of young rats. The drug was mixed with powdered animal diet and baked as described above. It was then used to feed young rats. In order to allow for the possible harmful effect of baking on the diet itself (e.g., destruction of vitamins), control groups of rats, fed on diet baked without the drug, were included in the series. Furthermore, some groups of rats were fed on a mixture consisting of normal diet, plus diet mixed with drug and then baked. There were 5 male and 5 female rats in each group and the results with the two sexes are considered separately.

The growth of the different groups is shown in the accompanying figure and the final gains in weight after 9 weeks are shown in Table 2. This table shows that baking the diet (even in the absence of drug) causes a slight diminution of weight gain (by 10% for females and 13% for males). Presumably this is due to destruction of vitamins, etc. Men living on a mixed diet would not be affected by such loss of vitamins in their cooked food. As regards the animals on baked diets containing carbamazine, the results are slightly different in the two sexes. With the female rats, there is no loss of weight gain in the third group receiving carbamazine (group 3) compared with the corresponding control (group 4) and slight loss of weight gain in groups 1 and 2 (difference −10% and −13% respectively; these differences are not statistically significant). With the male rats, there was no diminution of weight gain during the first 6 weeks of the diet. Between the sixth and ninth weeks, there was a slightly smaller gain of weight in the groups receiving carbamazine than in the controls. (Statistically, the probability of the difference between male groups 3 and 4 occurring by chance is about 1/20; the probabilities of the differences between groups 1 and 5, and groups 2 and 5, are between 1/5 and 1/10. All these probabilities would be considered statistically as borderline, and not conclusive of any definite effect having been produced.) Similar investigations with young rats have been kindly carried out by Dr S. R. Bushby of the Wellcome Research Laboratories with similar results.

This slight harmful effect on weight gain of male rats is probably no greater than would occur in animals or men receiving tablets of diethylcarbamazine in the orthodox manner during a conventional mass-therapy campaign. For a human population, this slight detriment would be outweighed by the great benefit of reduction of filariasis. Furthermore, it must be remembered that these figures relate only to rats which received these particular concentrations of carbamazine. Assuming that a 100-g rat eats 15 g of diet per day, each rat in groups 1 and 3 would receive 0.9 mg drug/day, i.e., 9 mg per kg body-weight, equivalent to 540 mg/day for a 60-kg man. In human populations the relative amounts would be much less (e.g., 25 mg to 100 mg per man per day), and probably these smaller amounts would be sufficient to control *W. bancrofti*. (See also the second part of this report, on the pilot trial in Recife.)

Effect of baked diet containing diethylcarbamazine on reproduction in mice. Ten breeding pairs of mice were put on a diet containing 80 mg diethylcarbamazine per kg (diet) and baked as above. (The mice

TABLE 2

GAIN IN WEIGHT OF GROUPS OF 5 YOUNG RATS FED ON DIETS MIXED WITH DIETHYLCARBAMAZINE AND BAKED, OR ON CONTROL DIETS

Group	Diet	Females			Males		
		Initial weight (g)	Gain in weight after 9 weeks		Initial weight (g)	Gain in weight after 9 weeks	
			Absolute (g)	% of control		Absolute (g)	% of control
1	Carbamazine 60 mg/kg; 1/2 diet baked	247	496	90 % of group 5	263	822	76 % of group 5
2	Carbamazine 30 mg/kg; 1/4 diet baked	248	480	87 % of group 5	258	793	73 % of group 5
3	Carbamazine 60 mg/kg; all diet baked	244	522	99 % of group 4	265	738	80 % of group 4
	Controls without diethylcarbamazine						
4	All diet baked (control for group 3)	227	527		234	922	
5	Half diet baked (control for groups 1 and 2)	220	555		233	1 087	
6	Diet not baked (general control)	255	586		244	1 056	

GROWTH OF GROUPS OF 5 RATS EACH FED ON DIETS MIXED WITH DIETHYLCARBAMAZINE AND BAKED (GROUPS 1-3) OR ON CONTROL DIETS (GROUPS 4-6)

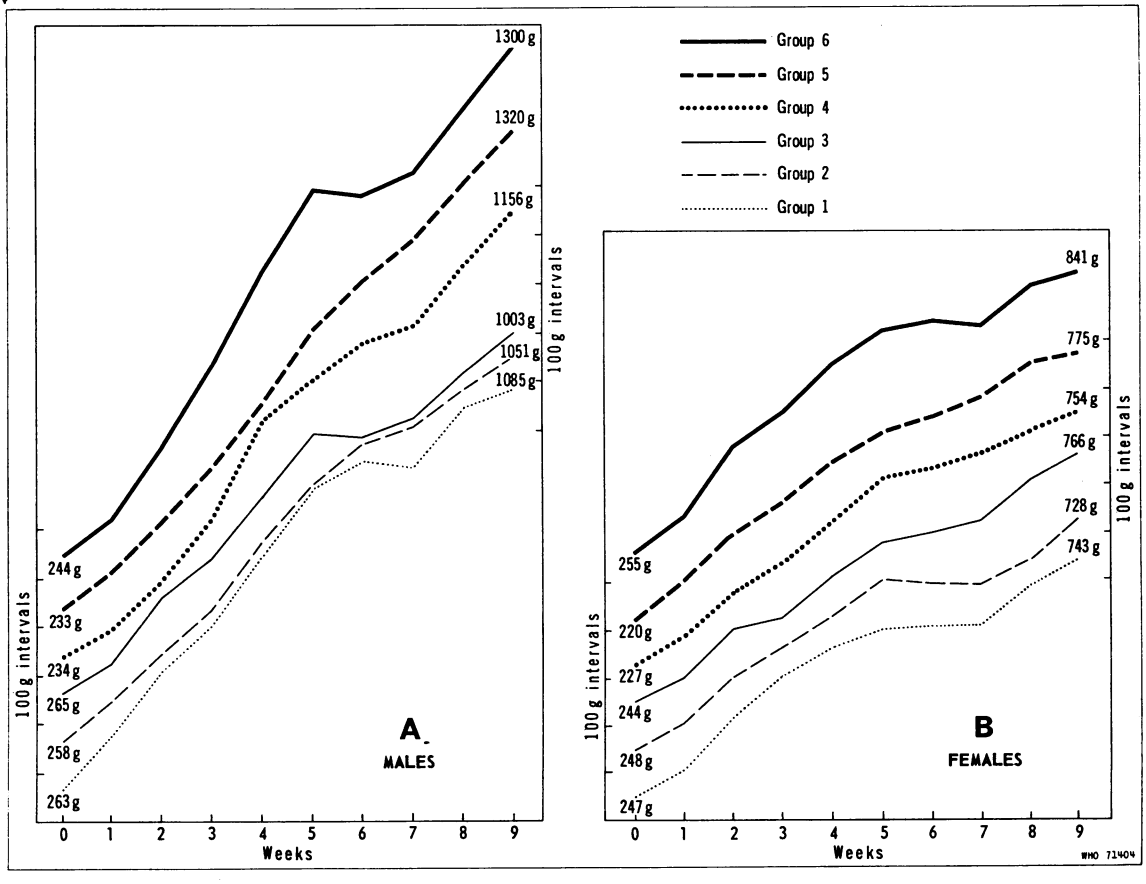

TABLE 3
ANTIFILARIAL ACTIVITY OF DIETHYLCARBAMAZINE AFTER BOILING FOR 3 HOURS

Rat No.	Drug	Intraperitoneal dose (mg/100 g)	Microfilaria count in blood			
			Initial count per 5 mm³	Subsequent counts as % of initial count		
				1 hour	2 hours	24 hours
783	Boiled	40	700	5.4	11.8	5.3
784	Boiled	40	232	1.4	—	5.1
781	Unboiled control	40	305	20.5	6	5

consumed about 4 g of diet per day per 20-g mouse; therefore each mouse received about 15 mg drug/kg body-weight daily.) The number and type of young mice born were watched carefully. The results were compared with those of 10 control breeding pairs kept on the diet baked without the drug.

After 4 months, the control mice had borne 15 litters, containing 97 baby mice, all normal in shape. The mice on the drug diet had borne 20 litters containing 114 baby mice, all normal in shape. Therefore, diethylcarbamazine baked in the diet appears to have no teratogenic effect in mice.

Antifilarial activity after cooking

Effect of boiling. Diethylcarbamazine 20 mg/ml in water was boiled for 3 hours and it was then injected intraperitoneally as a single dose (approximately the minimum effective dose) into cotton rats infected with *L. carinii*. The effect on the microfilaria count of the blood during the next 24 hours was observed as shown in Table 3.

These responses to boiled diethylcarbamazine were similar to those which we usually get with this dose of unboiled compound, and it was concluded that boiling for 3 hours did not greatly diminish the antifilarial activity.

Therapeutic effect of diet mixed with diethylcarbamazine and baked. Cotton rats infected with *L. carinii* were taken and the microfilariae in blood from the tail were counted; the rats were then placed on a diet of laboratory food which had been mixed with diethylcarbamazine and baked. The results of one such experiment are shown in Table 4.

Another series of rats fed similar diets gave the same results. This disappearance of most (but not all) microfilariae following administration of diethylcarbamazine is typical of the results which are obtained for *L. carinii* with moderate doses of the drug.

It was concluded from these experiments that the antifilarial action of diethylcarbamazine was not destroyed by baking.

TABLE 4
MICROFILARICIDAL ACTION OF DIETHYLCARBAMAZINE ON *L. CARINII*, AFTER BAKING WITH ANIMAL DIET

Carbamazine in diet (mg/kg)	Baked	Microfilaria count per 5 mm³									
		Day −3	Day −1	Day +1	Day +2	Day +3	Day +6	Day +9	Day +12	Day +21	Day +28
160	Yes	—	660	—	9	—	1	0	0	1	3
160	Yes	—	410	—	281	—	5	12	0	7	5
160	Yes	—	4 194	—	3 256	—	3 029	64	11	21	13
80	Yes	78	84	38	—	76	—	—	—	—	1
80	No (control)	1 399	1 509	1 009	—	701	—	—	—	—	65

PILOT TRIAL ON CONTROL OF BANCROFTIAN FILARIASIS BY SALT MEDICATED WITH DIETHYLCARBAMAZINE

METHODS

This trial was initiated at Recife with the kind support of the appropriate authorities. Two institutions were selected for the purpose: (*a*) the Casa de Detenção (prison) with approximately 1000 inmates, all healthy male adults; and (*b*) the Hospital dos Alienados (mental hospital) with approximately 1300 inmates, all adults.

In each case all the food consumed in the institution is prepared in one common kitchen (one for each). The daily consumption of salt at the prison was estimated at 25 kg, i.e., approximately 25 g/head. The consumption at the hospital was estimated at 20 kg/day, i.e., approximately 15 g/head. The salt was stored in 60-kg sacks, and was slightly deliquescent. For this investigation the compound was mixed with the salt manually by transferring the salt in scoopfuls from the bag to a large wooden box, and sprinkling the appropriate amount of drug into it through a sieve, with frequent mixing; at the end, further mixing occurred as the salt was transferred back into the sack. This simple method seemed satisfactory in ensuring an approximately uniform mixture of the compound through the sack. The chosen concentration of compound in the salt was greatly affected by the difficulties of obtaining the necessary additional supplies of the compound. Unfortunately there were long delays, so that the concentrations in the later periods were lower than had been planned.

As regards the microfilarial rate, surveys of these institutions had kindly been carried out by the Departamento Nacional de Endemias Rurais. Owing to various causes, however, the number of identified microfilaria carriers was lower than had been anticipated. Nevertheless as the time available for one of the authors (F. H.) was limited, it was decided not to delay longer for the purpose of carrying out new surveys on these 2300 persons but to proceed with the small number of known carriers, whose reactions would indicate the therapeutic (microfilaricidal) action of the medicated salt for the whole group. These known carriers were men whose infection was certain because it had been confirmed by the authors themselves before the trial began; otherwise they were not subject to selection and they were considered to be a representative sample of the larger group. The true microfilaria rate for the two institutions was probably about 3%–5%. This is lower than the rate in many parts of Recife, because some of the inmates come from non-filarious areas. The blood was examined at approximately 21.00 hours, 40 mm^3 being taken as a thick drop and stained with haematoxylin. All the blood samples up to 2 weeks from the beginning of the diet were examined by one of the authors (F. H.). After that they were examined by an experienced technician of the Departamento Nacional de Endemias Rurais, under the general supervision of Dr F. Barbosa.

CASA DE DETENÇÃO

Salt medicated with diethylcarbamazine (0.2% w/w) was supplied for use in the kitchen of the prison starting on 9 February 1966, and continued at this level until 18 February (with a salt consumption of 25 g/day/head, this would provide 50 mg compound/day/head; 9 days, total 450 mg). Then the concentration was raised to 0.4% until 30 March (i.e., 100 mg/day/head for 40 days; total 4000 mg). After that there was a gap, due to lack of supplies, until 4 June when the compound was supplied again at 0.1% and continued until 31 December (i.e., 25 mg/day/head for 208 days; total 5200 mg). In January 1967 there was an interruption owing to changes in the supplies of salt to the prison, but on 1 February the compound was supplied again at 0.1% and continued until 1 April 1967 (i.e., 25 mg/day/head for 60 days; total 1500 mg). Altogether each man presumably received about 11.2 g during 415 days; assuming an average body-weight of 60 kg, that would be a total of 186 mg/kg.

Urine samples

On 18 February 1966, 5 samples of urine were collected from 5 random inmates of the prison at about 16.00 hours. (Meal times were 06.00 hours, 11.30–12.00 hours and 17.00 hours.) These samples were sent by air to the National Institute for Medical Research, London, where they were found to contain 6 μg/ml–17 μg/ml diethylcarbamazine (average 11 μg/ml). On 23 February, urine was collected at 21.00 hours from microfilaria carriers, at the time of taking blood samples. These were analysed in London and found to contain between 1 μg/ml and 45 μg/ml diethylcarbamazine (average

20 μg/ml). This is a concentration which might be expected in persons taking 100 mg of the compound daily.

Tolerance

No complaints were received and no signs of intolerance were observed during the whole period of this investigation. On 23 March 1966, the men providing blood samples were asked about their health during the previous 2 weeks and none reported any disturbance although they knew that medicine had been added to the cooking salt.

Effect on microfilaria count

The microfilaria counts of 16 subjects are shown in Table 5A. By the end of 2 weeks, there had been a rapid fall in the average microfilaria count to 12% of its initial value; by the end of 6 weeks it had fallen to 2.5%, and 70% of the subjects had become negative (i.e., no microfilariae were seen in 40 mm^3 of blood). After that the figures fluctuated somewhat but they did not significantly further improve during 45 weeks from the start, although the medicated salt continued to be administered at a low level (0.1%). In 4 of the 7 subjects who were followed for a long period, the blood became free of microfilariae, but in the other 3 subjects a few microfilariae were found irregularly. The average number of microfilariae present was, however, only about 1/50 of that initially present in the group as a whole.

HOSPITAL DOS ALIENADOS

Salt medicated with 0.3% (w/w) diethylcarbamazine was started for use in the hospital kitchen on 9 February 1960. Assuming a daily salt consumption of 15 g/head, this would provide 45 mg compound/head/day. This was continued until 27 February, i.e., for 18 days, after which supplies were exhausted. Accordingly the total dose per head was approximately 810 mg, corresponding to 13.5 mg/kg.

Urine samples

On 17 February urine samples were collected from 5 inmates at random at 21.00 hours for estimation of carbamazine. They contained 17 μg/ml–78 μg/ml (average 33 μg/ml). On 24 February at 21.00 hours, 5 samples of urine were collected from the microfilaria carriers. These contained 18 μg/ml–88 μg/ml of compound (average 46 μg/ml). These figures show that the inmates were in fact receiving diethylcarbamazine from their food.

Tolerance

No complaints of the diet were received from patients and no untoward effects were reported by the medical staff. Most of the nursing staff consumed at least one meal a day cooked in the hospital kitchen (and thus containing medicated salt), and no adverse comment was received from them.

Effect on microfilaria count

These are shown in Table 5B. During the first 2 weeks there was a considerable fall in the average microfilaria count to 11% of its initial value, but after that stage it fell no further. During the following 43 weeks, the average count fluctuated irregularly but it did not show a consistent increase or decrease.

DISCUSSION

From this investigation the following conclusions can be drawn.

(1) Salt containing diethylcarbamazine in concentrations of 0.4% is quite acceptable to consumers—there were no objections or complaints on account of alteration of taste of food, or diminution of palatability. Higher concentrations were not investigated because of the expense which would be incurred with large numbers of persons.

(2) The treatment in this series caused no ill-effects, even when it was continued over 10 months (mostly at the 0.1% level). Such ill-effects might conceivably be of two kinds. The first are immediate reactions due either to direct pharmacological effects of the compound or to " allergic " or hypersensitivity reactions provoked in microfilaria carriers. No direct pharmacological effects were seen in the 2300 subjects and none was to be expected in view of the low amounts of compound received. As to " allergic " or hypersensitivity reactions, the 22 known carriers were seen 1 or 2 weeks after the beginning of the medication, and none complained of any such reactions. There were probably other unidentified carriers of microfilariae, but no complaints of reactions were received. Although it is possible that in more heavily infected communities such reactions might be encountered, there is no evidence for them as yet; further pilot trials are certainly desirable to obtain more information on this point. In any case, such reactions are never dangerous, although they may sometimes cause annoyance or discomfort. The second type of ill-effects is chronic reactions, due to consumption of the compound for

TABLE 5

EFFECT OF DIET CONTAINING MEDICATED SALT ON MICROFILARAEMIA IN MAN

Subject	Age (years)	Number of microfilariae per 40 mm³ of blood at time shown												
		Start	1 week	2 weeks	6 weeks	11 weeks	15 weeks	19 weeks	23 weeks	27 weeks	32 weeks	36 weeks	40 weeks	45 weeks
A. Subjects at Casa de Detenção														
A	24	10		1	0									
B	30	8		2										
C	19	35		6	5	0		0	0		0	0	0	0
D	45	16		7.5	0	1	0	0	0	0				
E	31	12		1	1	0	0			0	1	1	6	0
F	28	32		6										
G	37	12		1	0	0	0			0	0	0	0	0
H	30	2		0	0							1	0	1
I	21	30		2	1	7								
J	24	146		11	0	1	2			5	2	9	0	1
K	36	4		1	0	0	0	4	1	0	0	0	0	0
L	23	9		0	0	0	0	0	0	0	0	0	0	0
M	35	2		3.3	0	0								
N	41	8		2	0	0								
O	30	40		2	1									
Average No. of microfilariae in all subjects		24		3.05	0.6	0.9	0.3	1	0.3	0.8	0.5	1.6	0.9	0.3
Percentage of subjects negative		0		13	69	70	83	75	75	83	67	56	89	71
B. Subjects at Hospital dos Alienados														
P	40	98	2	0.5	4	3	8	11	5	5	12	3	2	0
Q	69	9	1	1	0	4	5	1	1		4	3	0	3
R	60	121	22		31	14	12			51	51	5	22	52
S	50	15	6	1	3	1	0	7	6	6	13	12	2	11
T	42	12	2	2	7									
U	45		14	11	16	7	1							
V	39	43		19	13	7	17	20	13	0	15	3	2	2
Average No. of microfilariae		50	7.8	5.8	10.6	6	7.2	9.8	6.3	15.5	19	5.2	5.6	13.6

many months. No such reactions were seen in the 1000 men who received the medicated salt for 10 months. If this procedure was employed for mass control of filariasis it is probable that shorter periods of 3 to 6 months would be sufficient. Furthermore, in other trials by other workers, diethylcarbamazine has been administered as tablets in various regimes for long periods to many thousands of people and no such chronic reactions have yet been reported.

(3) The procedure is simple and convenient to apply in closed communities such as those described above. It is efficient in providing all the inmates with a standard daily dose of the medicament (which would have been quite impossible by the handing out of tablets).

(4) The compound resists cooking and produces its expected therapeutic (microfilaricidal) effects in the subjects in spite of the usual culinary procedures. The microfilariae were all removed from the blood in about half the subjects in this small group of microfilaria carriers, but in the other half they persisted in small numbers. Presumably a corresponding reduction is produced in the number of filariae transmitted by mosquitos.

No control group given unmedicated salt was included in this study because the relative stability of microfilarial parasitaemias is well known. Although the microfilaria count in one carrier might fall spontaneously in the course of a few weeks, a simultaneous fall in all members of a group would be highly improbable. Further evidence that the fall in the microfilaria counts was definitely due to the consumption of diethylcarbamazine is provided by a comparison between the two groups of subjects. At the Casa de Detenção, where the calculated intake of compound was 4450 mg per head during the initial period of 49 days, the average microfilaria count per 40 mm^3 of blood fell from 24 to 0.3 or 0.9 in 15 weeks. At the Hospital dos Alienados, where the calculated intake was only 810 mg per head during 18 days, the average microfilaria count fell from 50 only down to 6–10. Thus the fall in the microfilaria count was roughly proportional to the calculated intake of compound.

This investigation demonstrates particularly the good acceptance and harmlessness of the procedure and its ease of administration in suitable circumstances compared with other methods of distributing the compound. More investigations by further pilot trials are required to explore the minimum concentration which is required to be effective, and the minimum period which is necessary to produce a permanent reduction (or, better, eradication) of the microfilariae.

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RÉSUMÉ

Un essai pilote de lutte contre la filariose à *Wuchereria bancrofti* par incorporation de diéthylcarbamazine au sel de cuisine a été effectué à Recife, Brésil.

On a vérifié en premier lieu la stabilité de la diéthylcarbamazine pendant les manipulations culinaires. L'expérimentation sur l'animal a montré que le produit, après cuisson ou ébullition, conservait ses propriétés antifilariennes et n'acquérait aucune toxicité anormale. On a procédé ensuite à la fourniture de sel médicamenté à la diéthylcarbamazine aux membres de deux collectivités (environ 1000 détenus et environ 1300 malades d'un hôpital psychiatrique). On a pu, par la recherche du médicament dans l'urine des participants à l'essai, démontrer qu'il était réellement ingéré.

Le groupe de détenus a reçu du sel de cuisine contenant 0,2 % de diéthylcarbamazine pendant 9 jours, du sel médicamenté à raison de 0,4 % pendant 40 jours, puis, pendant 268 jours, du sel médicamenté à 0,1 %. Chez les porteurs de microfilaires (*W. bancrofti*) soumis à ce régime, la densité microfilarienne moyenne est descendue à 12 % de sa valeur

initiale après 2 semaines et à 2,5% après 6 semaines. A ce moment, les examens de sang usuels ne décelaient plus aucune microfilaire chez 70% des porteurs. Sept détenus ont été suivis pendant 11 mois après le début du traitement. Chez 4 d'entre eux, les examens de sang sont restés négatifs; chez les 3 autres, malgré la prise quotidienne de l'équivalent de 25 mg de diéthylcarbamazine, quelques microfilaires ont été observées occasionnellement.

Le sel médicamenté (0,3% de diéthylcarbamazine) a été fourni aux malades de l'hôpital psychiatrique pendant 18 jours. Après ce traitement, la densité microfilarienne moyenne n'atteignait plus que 11% de sa valeur initiale. Au cours des 9 mois suivants, elle a présenté des variations irrégulières, sans tendance notable à l'augmentation ou à la baisse.

Dans les deux groupes, l'efficacité thérapeutique de la méthode a été du même ordre que celle constatée à la suite de l'administration de doses équivalentes de diéthylcarbamazine sous forme de comprimés. On n'a observé aucune réaction fâcheuse immédiate, par hypersensibilité, ou chronique. L'incorporation de diéthylcarbamazine au sel de cuisine apparaît comme un procédé sûr et commode, lorsqu'il s'agit de traiter des collectivités importantes. Des recherches ultérieures devront préciser la concentration minimale efficace et la durée optimale d'administration du sel médicamenté.

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