

LEAGUE OF NATIONS

C.H./Malaria/278

Geneva, August 25th, 1939.

HEALTH ORGANISATION

MALARIA COMMISSION

Note by the Secretariat.

In the general remarks on clinical prophylaxis in the Fourth Report of the Malaria Commission it was stated that further investigations are desirable on the efficacy of the bi-weekly method - 2 x 0.20 gr. atebriane. Since this Report was issued wide investigations have been carried out in the field on weekly, ten and fifteen day prophylaxis methods with synthetic drugs (atebrine, quinacrine, premaline etc.).

This Note, which completes the data in documents C.H./Malaria/264 and 265, gives a record of experimental work which may serve as a basis of field work.

AN EXPERIMENT IN DRUG PROPHYLAXIS WITH ATEBRIN
(WEEKLY METHOD)

by

M. Ciuca, M. Ballif, M. Chelarescu and N. Lavrinenko.

Previous investigations¹⁾ have shown the relative efficacies of various methods of drug prophylaxis by atebriane and the limitations upon the effect of these methods in cases of repeated re-infection, as in areas of malarial endemicity.

The satisfactory results obtained by a number of malarialogists by means of field research in highly endemic countries have led us to complete the existing experimental data¹⁾ with a series of tests of the preventive value of weekly doses of atebriane.²⁾

Method applied:

(a) Weekly intravenous injection - for therapeutic purposes - of a suspension of sporozoites of P. falciparum (M.T.78) or P. vivax (B.T.HOHR) for 3 weeks. Numbering of sporozoites taken from one or two glands was carried out by Shute's method.

(1) Documents C.H./Malaria/264 and 265.

(2) Since November 1938 Prof. Ballif has assumed the survey and control of this research.

(b) Weekly administration of 0.30 gr. of atebirin for 6 weeks, the first dose being given two days after the first inoculation of sporozoites. There were no new re-infections during the last 3 weeks of prophylaxis.

A daily examination of the blood and the temperature was made throughout the period of observation of these methods, i.e. for 18-29 weeks. (Only one patient left, 2 weeks after the first inoculation).

Summarized observations of each patient are given below:

(A). P. falciparum (M.T.R. 78)

<u>Week.</u> <u>L.D.</u>	<u>Sporozoites</u> <u>inoculated</u>	<u>Atebrin</u>	<u>Fever</u>	<u>Parasites</u>	<u>Observations</u>
1st	17,700	0.30	0	0	
2nd	22,500	0.30	0	±	
3rd	27,000	0.30	+	200/1	One attack
4th	-	0.30	0	±	
5th	-	0.30	0	±	Gct.
6th	-	0.30	0	±	Gct.
7th	-	-	+	+	3 daily attacks
8th	-	-	+	+	8 " "
<u>Treatment with atebrin, 0.30 x 7</u>					
9th	-	-	0	+	25/2
10th	-	-	0	+	Gct.
11th	-	-	0	+	Gct.
<u>Treatment with Certuna, 0.02 x 5</u>					
12th	-	-	0	+	Gct.
13th	-	-	0	0	
14th	-	-	+	+	3 attacks
<u>Treatment with atebrin 0.30 x 7 and Certuna 0.02 x 5</u>					
15th	-	-	0	+	Gct.
16th	-	-	0	+	Gct.
17th	-	-	0	0	
18th	-	-	0	0	
<u>Gr. V.</u>					
1st	41,400	0.30	-	-	
2nd	24,400	0.30	+	±	39° on 1 day
3rd	18,400	0.30	+	+	2 attacks tertian
4th	-	0.30	-	±	
5th	-	0.30	-	0	
6th	-	0.30	-	±	Gct.
7th	-	-	-	+	
8th	-	-	±	+	Sub.febrile
9th	-	-	+	+	6 daily attacks
10th	-	-	+	+	5 " "
11th	-	-	+	+	3 " "
12th	-	-	-	+	Gct.
13th	-	-	-	+	Gct.

Gct. = Gametocytes

Certuna 0.02 x 5

14th	-	-	-	+	1 day. Gct.
15th	-	-	-	-	
16th	-	-	-	-	
17th	-	-	-	+	0
18th	-	-	+	+	1 attack. Gct.
19th	-	-	+	+	2 daily attacks
20th	-	-	-	+	Gct.

Certuna 0.02 x 5

21st	-	-	-	+	2 days. Gct.
22nd	-	-	-	-	
23rd-29th	-	-	-	-	

B.A.

1st	24,000	0.30	-	-	
2nd	12,300	0.30	-	-	
3rd	24,000	0.30	±	±	39.4° on 1 day
4th	-	0.30	-	-	
5th	-	0.30	-	-	
6th	-	0.30	-	-	
7th	-	-	±	-	39.6° on 1 day
8th	-	-	-	-	
9th	-	-	-	-	
10th-29th	-	-	-	-	

C.Fr.

1st	20,700	0.30	-	-	
2nd	14,400	0.30	-	-	
3rd	22,800	0.30	-	-	
4th	-	0.30	+	-	38° on 1 day
5th	-	0.30	+	-	40° on 1 day
6th	-	0.30	-	-	
7th	-	-	-	-	
8th	-	-	-	-	
9th-20th	-	-	-	-	

Control subjects inoculated once with sporozoites and not undergoing prophylactic treatment:

Brc.A.	A+ P+	9 days'	incubation	-	daily form
T.E.	A+ P+	11 "	"	"	"
Ax. M.	A+ P+	10 "	"	"	"

(B). P. vivax. B.T. HOHR (Madagascar strain.)

Gr. Lcr.

1st	114,400	0.30	-	-	
2nd	18,600	0.30	-	-	
3rd	17,600	0.30	-	-	
4th	--	0.30	-	-	
5th	-	0.30	-	-	
6th	-	0.30	-	-	
7th	-	-	+	+	2 attacks tertian
8th	-	-	+	+	4 " "
9th	-	-	±	+	Subfebrile
10th-17th	-	-	-	+	
18th	-	-	±	+	1 attack
19th	-	-	-	±	{ 1 day
20th-28th	-	-	-	±	{ momentary appearance { for 1 day

Cr. Sim.

1st	29,000	0.30	+	-	{ 3 days' opening (?) { fever
2nd	35,000	0.30	±	±	Subfebrile 2 days
3rd	17,000	0.30	-	±	
4th	-	0.30	-	-	
5th	-	0.30	-	-	
6th	-	0.30	-	-	
7th	-	-	-	-	
8th-11th	-	-	-	-	
12th	-	-	+	+	2 daily paroxysms
13th	-	-	+	+	2 " "
14th	-	-	-	±	2 days
15th	-	-	+	+	2 daily paroxysms
16th-27th	-	-	-	±	{ passing appearance { of parasites for 1 or { 2 days.

P.C.

1st	16,400	0.30	-	-	
2nd	33,000	0.30	+	+	2 days' fever 39°
3rd	20,000	0.30	-	-	
4th	-	0.30	-	-	
5th	-	0.30	-	-	
6th	-	0.30	-	-	
7th-11th	-	-	-	-	
12th	-	-	+	+	2 attacks tertian
13th	-	-	+	+	3 " "
14th	-	-	+	+	2 " "

Treatment with atebrin 0.30 x 7.

15th-20th	-	-	-	-	
21st	-	-	+	+	Irregular fever
22nd	-	-	-	±	Parasite traces

P.N.

1st	17,600	0.30	-	-	
2nd	40,200	0.30	+	+	2 daily attacks
3rd	20,000	0.30	-	±	
4th	-	0.30	-	±	1 day
5th	-	0.30	-	-	
6th	-	0.30	-	-	
7th	-	-	-	-	
8th-14th	-	-	-	-	
15th	-	-	-	±	1 day
16th	-	-	+	±	irregular fever 1 attack
17th	-	-	-	±	
18th	-	-	+	+	1 attack
19th	-	-	-	-	

It.M.

1st	26,000	0.30	-	-	
2nd	37,000	0.30	-	-	
3rd	22,000	0.30	+	+	(2 days' remittent fever 39-40
4th	-	0.30	-	+	3 days
5th	-	0.30	+	-	1 day at 39.2°
6th	-	0.30	-	-	
7th-11th	-	-	-	-	

subject then left the hospital.

Resp.C.

1st	23,000	0.30	-	-	
2nd	66,000	0.30	+	+	(3 days' fever (37.5 - 38.8°
3rd	25,000	0.30	-	+	
4th	-	0.30	-	±	1 day
5th	-	0.30	-	-	
6th	-	0.30	-	±	1 day
7th	-	-	-	-	
8th	-	-	-	-	
9th-27th	-	-	-	-	

Control subjects:

- (1) C.A. single inoculation of sporozoites A± P+ incubation 13 days
- (2) In.Fr. " " " " Ao Po immune?
- (3) R. Iac. " " " " A+ P+ (incubation 9 days, (daily form, (Cortepan treatment (at 7 x 1 gr.