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6 April 1948.EXPERT COMMITTEE ON MALARIA✓ CONTRIBUTION TO CHEMOTHERAPY WITH PALUDRINE OF
EXPERIMENTAL MALARIA INFECTION
EFFECTIVE MINIMUM DOSES

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The general conclusions stated in H. FAIRLEY's writings (1) confirm the schizonticide action of paludrine achieving, in some infections, even radical cure, this drug is now one of the most efficacious for the treatment of malarial infection, since it has no toxic properties and a high therapeutic value.

Its efficacy, however, is related to the duration of the treatment; and we must not forget that patients are not very much inclined to submit to a long course of treatment once the temperature has reverted to normal. On the other hand, the cost of the medicament, to which must be added the general costs involved in its application, should also be taken into account in connection with mass treatment. We publish the results of our work on cases of experimental infection with P. vivax and P. falciparum in the hope of contributing some new elements to the technique of this treatment.

I. P. vivax Infection - Patients whose mental condition required malariotherapy were infected by inoculation with blood infected with our old 'BT^{HOHR}' strain which originated in Madagascar.

Paludrine treatment was administered at various stages of the infection in accordance with the duration required for the attack in terms of malariotherapy and the patient's general condition. Doses varying from 100 to 300 mgms. daily were administered, the treatment lasting from 7 to 15 days.

(1) Trans. R. Soc. Trop. Med. Hyg. 40, 105-153, 1946.

In Table I the reader will find results of the treatment in terms of forms of infection, duration of fever (in days) at the beginning of the treatment and the dose employed.

TABLE I
(P. vivax)

Patients	Method of infection (by inoculation of infected blood)	Incubation in days		Form of infection	Treatment-Paludrine		Time-lag before disappearance in days	
		Para-site	Fever		Dose mgms x days	Begun day of fever	Fever	Para-sites
1 C.C.	i.v.	3	4	A+P+	100 x 7	7th	1	5
2 C.R.	i.m.	7	10	A+P+	200 x 7	7th	2	6 *)
3 M.D.	"	10	13	A+P+	200 x 7	6th	1	9
4 D.V.	"	17	19	A+P+	200 x 7	9th	1	6
5 F.G.	"	4	5	A+P+	200 x 7	11th	1	7
6 T.G.	i.v.	1	1	A+P+	200 x 7	8th	2	7
7 S.E.	i.m.	10	10	A+P+	200 x 7	10th	1	4
8 D.M.	i.v.	9	12	A+P+	200 x 7	10th	1	5
9 C.P.	"	2	2	A+P+	200 x 7	10th	1	6
10 L.I.	i.m.	10	10	A+P+	200 x 7	10th	1	5
11 F.C.	i.v.	2	2	A+P+	300 x 15	7th	1	9
12 I.M.	"	9	9	A+P+	300 x 15	19th	1	8

*) Parasitic relapse following inoculation with P. falciparum.

Abbreviations : i.v. : intravenous,
i.m. : intramuscular.

Summary : Twelve subjects were treated by malariotherapy, the infection being induced by inoculation of infected blood (P. vivax^{HOHR}) intramuscularly or intravenously. They all developed the disease (A+P+) after an incubation period of varying length, according to the method of inoculation.

Paludrine treatment was administered from the 6th to 11th day of fever onwards. The daily doses of paludrine given varied as follows: 100 mgms (one patient); 200 mgms (9 patients); 300 mgms (2 patients). The duration of the treatment varied from 7 days (10 patients) to 15 days.

In ten patients the fever disappeared generally 24 hours after the administration of the first dose of the drug; two of the twelve patients treated had no fever after the first two doses of paludrine. The disappearance of parasites from the blood was observed in a thick drop after intervals varying from 4 to 9 days. The average was

6.4 days from the administration of the first dose of the drug. A parasite count also showed the presence of degenerate parasites and shadows.

In infections with virulent blood quantities of paludrine varying from 100 to 300 mgms daily and administered for a period of 7 to 15 days have shown similar therapeutic efficacy.

II. P. falciparum - Twelve patients, infected with our strain MT⁷⁸ in order to induce therapeutic malaria, were treated with daily doses of 200-300 mgms of paludrine for a period of 5-10 days. Five of these were infected with blood and seven with sporozoites.

In Table II the reader will find details on the development of the infection and the results of the treatment.

TABLE II
(P. falciparum)

Patients	Manner of infection	Duration of incubation in days		Form of infection	Treatment-Paludrine		Time-lag before disappearance in days		
		para-sites	fever		Dose mgms x days	Begun day of fever	fever	trophozoites	gametocytes
1. A.D.	b, i.v.	2	5	A+P+	100 x 7	15th	1	7	53
2. V.M.	b, i.m.	16	19	A+P+	200 x 7	5th	2	4	28
3. A.V.	"	13	15	A+P+	100 x 7	9th	1	3	36
4. C.I.	"	9	8	A+P+	200 x 7	8th	2	5	30
5. R.M.	"	16	18	A+P+	200 x 7	6th	2	5	47
6. O.S.	200,000 sp, i.v.	25	29	A+P+	100 x 7	11th	1	4	31
7. L.N.	300,000 sp, i.v.	16	16	A+P+	200 x 7	7th	1	4	44
8. C.M.	rep.sp. i.v.	15	15	A+P+	300 x 5	7th	3	5	*)
9. P.D.	"	30	35	A+P+	300 x 10	4th	2	8	*)
10. P.G.	"	17	20	A+P+	300 x 7	5th	1	7	*)
11. N.M.	"	13	13	A+P+	300 x 10	15th	1	9	*)
12. P.V.	"	13	14	A+P+	300 x 10	7th	2	8	48

*) Gametocytes present when patient was discharged after treatment.

Abbreviations : b. : infected blood,
 sp. : sporozoites,
 i.v. : intravenous,
 i.m. : intramuscular,
 rep. : repeated inoculations.

Briefly, the average time required for the disappearance of fever and trophozoites in the 5 patients inoculated with virulent blood and treated for 7 days with 100-200 mgms of paludrine daily was 1.6 day for the disappearance of fever and 4.8 days for that of the trophozoite. All the 5 patients carried gametocytes for a long period.

In the 7 patients inoculated with sporozoites the average times required were 1.5 day for the fever to abate and 6.4 days for the disappearance of the trophozoites.

All were gametocyte carriers. These patients had been previously given a prophylactic treatment with paludrine which was not effective; but it did not introduce an element of variance.

A dose varying between 100 and 300 mgms of paludrine daily and a treatment lasting between 5 and 10 days did not constitute any variation factors.

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The conclusions of this Note confirm the effective schizonticide action of paludrine. The number of cases treated is too small to permit of a comparison with other schizonticide substances. This treatment does not prevent the development of gametocytes.