Only in one severe case he had recourse to an injection of 10 c.cm. of a 5 per cent solution in addition to the oral administration mentioned above. All his cases recovered.

Hill and Goodwin (1937) successfully treated 5 cases of *P. vivax* and 95 cases of *P. falciparum* with intramuscular injection of prontosil soluble (10 c.cm.) every twelve hours. Usually, not more than 4 injections were required in each case. Their results were very satisfactory.

Read and Pino (1938) dealt with 3 cases of *P. vivax*. The initial doses were 6 tablets (1.8 grammes) in 24 hours. Afterwards the dosage was reduced to 3 tablets a day. The patients who were suffering from distressing vomiting had intramuscular injections of prontosil soluble. They noted that sulphonamide has a poor specific antimalarial action because it has neither a sufficiently definite action on the schizogony cycle, nor is it a remarkable gametocide.

Very recently Pakenham-Walsh and Rennie (1938) treated a case of induced malaria (*P. vivax*) with prontosil. They gave 3 grammes of prontosil daily for 3 days. The temperature came down and the parasites cleared up, but a week later the fever relapsed and the parasite counts were nearly as high as in the original attack.

The failure of the latter workers may be due to the use of inadequate dosage, as is apparently confirmed by our experiments on monkey malaria. It will be seen from the experiments detailed above that a daily dose of 0.5 c.cm. was given to the first monkey as this was considered to be the proportionate dose, regard being had to the comparative weights of man and monkeys. This dose being of no avail, it was doubled. As this also failed we at last tried a still larger dose of 3 c.cm., which is overwhelmingly out of proportion to the human dose, and this succeeded in checking the course of the disease, leading to apparent recovery of the animal, although scanty parasites appeared in the blood later on, as also occurs following treatment with quinine.

To sum up, doses of 0.5 and 1 c.cm. altogether failed to check the multiplication of *P. knowlesi* in *rhesus* monkeys. But the disproportionately heavy dosage of 3 c.cm. proved effective. We may conclude, therefore, that prontosil in heavy doses has a definite action on plasmodial infections (at least on the monkey plasmodium), but does not possess any advantage over those drugs already in use.

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STUDIES ON THE ACTION OF SYNTHETIC ANTIMALARIAL DRUGS ON INDIAN STRAINS OF MALARIA

Cilional in the treatment of 'crescent carriers'

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Cilional was introduced by Schulemann of Messrs. Bayer-Meister-Lucius, Germany, a few years ago. It belongs to the plasmochin series of preparations and has the composition di-alkyl-amino-alkyl-amino-oxy-quinoline. Its action on the gametocyte of *Plasmodium falciparum* was claimed to be as potent as that of plasmochin, in doses far less than any that produced toxic symptoms.

A total dose of 0.18 to 0.3 gramme (in daily doses of 0.06 gramme) proved sufficient to make the crescents disappear from the peripheral blood. Atebrin was also given at the same time to control the asexual cycle. Regarding the toxicity of the drug, the makers have stated, after a series of experiments in mice, guinea-pigs, rabbits and cats, that it is about three times less toxic than plasmochin. Clinical trials on human beings have fully supported these findings. Daily doses of three times 0.01 gramme up to three times 0.06 gramme have been borne without toxic effects. Even the last-mentioned dose has been given for seven days without causing any subjective symptoms.

Missiroli and Mosna (1938) have recently treated a series of *P. falciparum* gametocyte carriers with varying doses of cilional. The gametocytes were enumerated, flagellation was looked for, and the infectivity of the blood for anophelines was determined each day for a week following the administration of the drug. A field experiment was also carried out with a population of about 1,000 individuals where malaria was hyperendemic. From 1st May to 15th October, 1937, cilional was given to the whole population including infants and children every three days in doses ranging from 1 to 6 cgm. These workers conclude that in respect of its toxicity the drug is far superior to plasmochin and that addition of such a drug to quinine or atebrin will give a complete antimalarial remedy.

As Chopra and Basu (unpublished) have noted that daily doses of 0.06 gramme for four days were not sufficient to check the development of the parasite in the mosquito, we tried a larger dose, *i.e.*, 0.09 gramme daily for five days in the following cases.

Patient I., aged 28 years, admitted to the hospital on 12th August, 1938, with a history of fever for three

days only. On the day of admission quite a good number of rings (*P. falciparum*) were found. On 13th August the patient was given prontosil, 2 tablets four times daily for 5 days. Rings were completely eradicated and gametocytes appeared for the first time on 16th August.

Date	Total dosage of cilional	Crescents per 500 leucocytes	Remarks
16-8-38	..	3	
17-8-38	..	42	
18-8-38	..	43	
19-8-38	0.09 gramme	85	
20-8-38	0.18 „	64	
21-8-38	0.27 „	20	
22-8-38	0.36 „	3	Very scanty parasites present, showed marked degenerative changes.
23-8-38	0.45 „	0	One parasite seen in the thick film.
24-8-38	..	0	
25-8-38	..	0	
26-8-38	..	0	
30-8-38	..	0	

Comments.—This is apparently a case with fresh infection as the patient is said to have had no febrile attacks during the past few years. Prontosil controlled the schizogony cycle, but it had no action on the gametocytes. Crescents made their first appearance in the blood about the eighth day of the initial fever. We may attribute the gradual reduction in number and finally the complete eradication of the gametocytes to the effect of cilional, as it seems unlikely that in a primary infection the crescents would disappear with such unusual rapidity. It should be noted that after the treatment with cilional there is a definite increase in the number of crescents followed by a marked decrease culminating in total extinction.

Patient P., aged 38 years, admitted on 9th August, 1938, for pain in the abdomen. History of fever (? malaria) two months back. Spleen not palpable. While in hospital, he had an attack of fever with rigor on 16th August. Next day a fair number of rings and crescents were found in the blood. Put on to atebrin on 18th August for 5 days. On 21st August blood showed crescents only.

Date	Total dosage of cilional	Crescents per 500 leucocytes	Remarks
23-8-38	..	62	
24-8-38	..	76	
25-8-38	0.12 gramme	362	
26-8-38	0.18 „	8	
28-8-38	0.36 „	0	Very scanty crescents found in thick films.
29-8-38	0.45 „	0	
30-8-38	..	0	
31-8-38	..	0	

Comments.—This is a case of relapse. Both sexual and asexual forms were present in the blood. Atebrin eradicated the asexual cycle. A total dosage of 0.36 gramme of cilional practically exterminated the crescents, although there was a surprisingly remarkable rise in the crescent count after the administration of the first few doses.

Patient C., aged 16 years, admitted on 23rd August, 1938, with a history of intermittent fever with rigor for a month. Spleen just palpable. On the day of admission, the blood (thick and thin films) showed crescents only.

Date	Total dosage of cilional	Crescents per 500 leucocytes	Remarks
23-8-38	..	95	
24-8-38	..	100	
25-8-38	0.12 gramme	82	
26-8-38	0.21 „	118	
27-8-38	0.3 „	6	
28-8-38	0.39 „	0	None in thick films.
29-8-38	0.45 „	0	
30-8-38	..	0	

On 31st August, 1938, the patient had a slight rise of temperature. Scanty rings and no crescents were found in the thick films. Put on to prontosil 2 tablets four times a day for 5 days.

1st September .. Rings: no crescents.
2nd „ .. Scanty rings: no crescents.
3rd „ .. Very scanty rings: no crescents.
4th „ .. Very scanty rings in thick films: no crescents.
5th „ .. No parasites seen in thick films.

Comments.—This is a chronic case showing only crescents in the blood. No asexual forms could be detected even in thick films on careful search. Crescents completely disappeared after a total dosage of 0.39 gramme. Almost immediately after receiving a full course of cilional the patient had fever, blood smears showing only rings. He was put on prontosil which apparently checked the fever and the infection gradually cleared up. Evidently cilional did not show the slightest action on the schizogony cycle in this case.

Patient R., aged 22 years, admitted on 25th August, 1938, with a history of fever (? malaria) for one year. Spleen 2 inches below costal margin. Blood on admission showed both rings and crescents. On 26th August, put on to prontosil for 5 days. On 30th August, crescents only were seen in the thick and thin blood films. On 2nd September, 1938, put on to cilional 0.03 gramme three times a day for 5 days.

Date	Total dosage of cilional	Crescents per 500 leucocytes	Remarks
30-8-38	..	120	
31-8-38	..	92	
1-9-38	..	385	
2-9-38	..	380	
3-9-38	0.12 gramme	408	
4-9-38	0.21 „	80	
5-9-38	0.3 „	32	Mostly degenerating.
6-9-38	0.39 „	15	
7-9-38	0.45 „	0	
8-9-38	..	0	

Comments.—Before the administration of cilional the crescent count did not show any downward tendency but the infection practically cleared up after a total dosage of 0.39 gramme.

Discussion.—Those concerned with the treatment of malaria are agreed that plasmochin has a very markedly destructive action on the gametocytes of *P. falciparum*. On the other hand, most of them complain of its toxicity. Further, the toxicity appears to be a phenomenon of individual susceptibility rather than one of dosage. One cannot ascertain beforehand whether a particular patient will or will not develop toxic symptoms.

Knowles and Das Gupta (1931) have, however, found that the dosage advocated by the manufacturers was unnecessarily large and a much smaller dose could eradicate the crescents from the blood in the case of the Indian species of *P. falciparum*. These workers showed that a total dose of 0.06 gramme (0.02 gramme daily for 3 days) was sufficient to destroy all crescents, even when the infestations were heavy and the cases treated with such a small dosage, under their observation, never developed any untoward symptoms.

The destructive action of plasmochin on crescents may be studied under the microscope. Within 24 hours of commencing administration of plasmochin the crescents are seen to become swollen and their outline irregular, and the chromatin breaks up.

Whitmore (1929) stated that a single dose of .019 gramme is sufficient to render non-infectious, for *A. albimanus*, all crescents in the blood at the time the single dose is taken. Lately, Chopra and Basu (1937) also made similar observations and found that a dose of .02 gramme prevented further development of the crescents in *A. stephensi*. Since 1931 the senior author has treated no fewer than 500 crescent carriers in the Carmichael Hospital for Tropical Diseases with plasmochin, using the small dosage advocated by Knowles and Das Gupta (1931). In no case were there any toxic symptoms exhibited by the patient, nor was there any evidence to show that this small dose had ever failed to exterminate the crescents. Under these circumstances the question of toxicity of plasmochin does not arise when it is administered in proper doses, at least in this country. On the other hand, cilional, as will be seen from the foregoing tables, requires a much larger dose and longer time to achieve the same result. It therefore follows that there is no justification for using cilional in place of plasmochin which has acquired an unchallenged reputation for its action on crescents.

Summary and Conclusion

A total dosage of 0.35 to 0.4 gramme of cilional, administered as a dose of 0.03 gramme

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THE ISOLATION OF *VIBRIO CHOLERÆ* FROM NON-CHOLERA INDIVIDUALS

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ALTHOUGH there are many records of the finding of vibrios in the stools of healthy individuals, there is no means of establishing whether the strains isolated were those conforming to the vibrio now generally accepted as *Vibrio cholerœ*. Recent work on the antigenic structure of vibrios has shown that *V. cholerœ* possesses a specific 'O' antigen and that the thermo-labile 'H' antigen is shared by a large group of vibrios. The important practical application of these findings is that, because of this inter-relationship that exists between *V. cholerœ* and certain other vibrios through common antigenic factors, it is no longer possible to rely, as was formerly done, on an agglutination test performed with an H and O serum for the identification of *V. cholerœ*. Serologically, *V. cholerœ* can be distinguished from certain other vibrios by agglutination test performed with a pure O serum.

During the past five years the stools of more than 2,000 in-patients in the Carmichael Hospital for Tropical Diseases have been examined for vibrios. The individuals examined were suffering from a variety of diseases, other than cholera, and there was no history of either a

(*Continued from previous column*)

three times a day, is usually sufficient to eradicate practically all gametocytes of *P. falciparum* from the blood and even this high dose has been borne by the patients experimented upon, without any ill effects.

On considering the points discussed above we cannot, however, help arriving at the conclusion that plasmochin is preferable to cilional, inasmuch as a much smaller dose of the former effects the eradication of crescents in a comparatively short time, and as the dosage of plasmochin (as advocated by Knowles and Das Gupta) is not at all toxic and perhaps cheaper than its rival.

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