suggested that this hæmolysin is the end result of a damaged liver and alterations in metabolism of both carbohydrates and fats, and that possibly it is of the nature of an unsaturated fatty acid or a lyso-lecithin.

REFERENCES

Bass, C. C., and Johns, F. M. (1912). The Cultivation of Malarial Plasmodia *in vitro*. *Journ. Exper. Med.*, Vol. XVI, p. 567.

Bass, C. C., and Johns, F. M. (1913). Cultivation of Malarial Plasmodia *in vitro* in the Blood of a Diabetic without the addition of Dextrose. *Amer. Journ. Trop. Dis. and Prev. Med.*, Vol. I, p. 246.

Blacklock, D. B., and Macdonald, G. (1928). The Mechanism of Blackwater Fever and Certain Allied Conditions. *Brit. Med. Journ.*, Vol. II, p. 145.

Blanchard, M., and Lefrou, G. (1922). Presénce de spirochètes dans le sang d'européens atteints de fièvre bilieuse hémoglobinurique. Le problème étiologique de cette spirochétose. *Bull. Soc. Path. Exot.*, Vol. XV, p. 699.

Giglioli, G. (1932). Epidemiological and Etiological Studies on Blackwater Fever in the Interior of British Guiana, 1923–32. *Trans. Roy. Soc. Trop. Med. and Hyg.*, Vol. XXVI, p. 204.

Hegner, R. W., and MacDougall, M. S. (1926). Modifying the Course of Infections with Bird Malaria by Changing the Sugar Content of the Blood. *Amer. Journ. Hyg.*, Vol. VI, p. 602.

Krishnan, K. V. (1933). Observations on the Mode of Action of Quinine in Malaria. *Indian Journ. Med. Res.*, Vol. XXI, p. 331.

Krishnan, K. V. (1935). The Reticulo-endothelial System in Malarial Hæmoglobinuria of Monkeys, Part I. *Indian Med. Gaz.*, Vol. LXX, p. 193.

Krishnan, K. V., and Ghosh, B. M. (1935). Reticulo-endothelial System in Malarial Hæmoglobinuria of Monkeys, Part II. *Ibid.*, Vol. LXX, p. 197.

Krishnan, K. V., Ghosh, B. M., and Bose, P. N. (1936). Cholesterol Changes in Monkey Malaria and Hæmoglobinuria. *Records of the Malaria Survey of India*, Vol. VI, p. 1.

Krishnan, K. V., Lal, C., and Napier, L. E. (1933). Large Mononuclear Cells in Monkey Malaria. *Indian Med. Gaz.*, Vol. LXVIII, p. 66.

Krishnan, K. V., and Pai, N. G. (1936). Biochemical Studies in Monkey Hæmoglobinuria. *Technical Report, Indian Research Fund Association.* Manager of Publications, Delhi.

Krishnan, K. V., Smith, R. O. A., and Lal, C. (1933). The Effect of Splenectomy on the Course of Malarial Infection in Monkeys. *Indian Journ. Med. Res.*, Vol. XXI, p. 343.

Leathes, J. B., and Raper, H. S. (1925). *Monographs on Biochemistry. The Fats.* Longmans, Green & Co., London.

Matko, J. (1918). Zur Therapie des Schwarzwasserfiebers. *Wiener. Klin. Woch.*, Vol. XXXI, p. 1038.

Napier, L. E., and Campbell, H. G. M. (1932). Observations on a Plasmodium Infection which Causes Hæmoglobinuria in Certain Species of Monkey. *Indian Med. Gaz.*, Vol. LXVII, p. 246.

Nocht, B. (1931). Report on the Activity of the Malaria Commission of the League of Nations and on some Experiments on the Pathogenesis of Blackwater Fever. *Trans. 8th Congress, Far Eastern Assoc. Trop. Med., Siam*, Vol. II, p. 239.

Nocht, B., and Kikuth, W. (1929). Uber hæmolytische Chininwirkungen. *Arch. Schiffs- u. Trop.-Hyg.*, Vol. XXXIII, p. 355.

Otero, F. Q. (1932). Malaria und Blutzuckerkonzentration. *Ibid.*, Vol. XXXVI, p. 461.

Ott (1932). Recherches sur la Pathogénie et le Traitement de la Fièvre bilieuse hémoglobinurique. *Bull. Soc. Path. Exot.*, Vol. XXV, p. 735.

(*Continued at foot of next column*)

ATEBRIN-PLASMOCHIN IN THE TREATMENT OF MALARIA

By D. MANSON, M.B., Ch.B. (Glas.), F.R.E.S.

Chief Medical Officer, Jorehaut Tea Co., Ltd., Cinnamara, Assam

Introduction

THE advent of atebrin and plasmochin into the realm of the chemotherapeusis of malaria was hailed with acclaim on all sides and the pendulum of public opinion swung rapidly upwards in favour of these new rivals to quinine. The new drugs were seized on with avidity, both by the medical profession and by the general public who were only too eager to escape from the thraldom of quinine, till then the sovereign remedy, albeit a remedy which offered no royal road to the goal of the 'magna therapia sterilisans'.

Both drugs were exhibited, sometimes in wrong doses, and the inevitable result was the appearance of a crop of reports, some laudatory, some damnatory, and some with the doubtful Scotch verdict of 'not proven'. The pendulum had commenced its downward swing. Since that time much has been written on the therapeutic action of atebrin and plasmochin and the dosages, particularly of plasmochin, have been altered and readjusted as the result of trial and error. One fact has emerged from the mêlée, namely, that these drugs have real merit and have come to stay. The present article was written as the result of trials with atebrin and plasmochin in revised dosages with a view to obtaining the most satisfactory therapeutic action and the lowest relapse rates.

Types of treatment

By the courtesy of the manufacturers, Messrs. Bayer-Meister Lucius, the writer was furnished with a series of tablets, etc., for use in this investigation.

The following types of treatment were chosen for trial :

(1) Combined tablet of atebrin 0.1 gramme with plasmochin 0.0033 gramme.

(*Continued from previous column*)

Ross, G. R. (1932). *Researches on Blackwater Fever in Southern Rhodesia.* London School of Hygiene and Tropical Medicine. Research Memoir Series, Vol. VI.

Rudolf, G. de M., and Marsh, R. G. B. (1927). Some Observations upon Carbohydrate Metabolism in Malaria. *Journ. Trop. Med. and Hyg.*, Vol. XXX, p. 57.

Tschilow, K., and Mladenow, Iw. (1934). Beitrag Zur Funktion der Leber bei Malaria. Belastung mit Galaktose und kombinierte Belastung mit Insulin-Glykose-Wasser. *Arch. Schiffs- u. Trop.-Hyg.*, Vol. XXXVIII, p. 282.

Thompson, J. G. (1924). *Researches on Blackwater Fever in Southern Rhodesia.* London School of Hygiene and Tropical Medicine. Research Memoir Series, Vol. VI.

Whitmore, E. R. (1928). The Blood in Blackwater Fever. *Seventeenth Annual Rep., United Fruit Co., Med. Dept.*, p. 123. Massachusetts, Boston.

(2) Combined tablet of atebrin 0.1 gramme with plasmochin 0.005 gramme.

(3) Atebrin tablet 0.1 gramme only.

(4) Atebrin-plasmochin dragées in same dosage as no. 1 but in keratinized capsules.

(5) Atebrin-plasmochin dragées in same dosage as no. 2 but in keratinized capsules.

(6) Atebrin musonate for injection, either intramuscularly or intravenously.

The object of the dragées was to determine whether the action of atebrin-plasmochin was interfered with in the stomach and whether possibly signs of intolerance or toxicity might be avoided when the drugs were liberated not in the stomach but in the bowel.

It was also proposed to note the action of the gastric juice in relation to the production of adverse symptoms and particularly the rôle of the gastric hydrochloric acid as a possible factor in cases which showed signs of intolerance or distress. Unfortunately the number of cases of abnormality in the gastric secretion met with in this experiment was limited to 5 cases in all and the results cannot be taken as definitely conclusive. Nevertheless these cases present some points of considerable interest.

In assessing the results of the various treatments, no cases are reported which have not been under observation for a minimum period of 6 months, and, in many instances, the period of observation is considerably longer.

No note was taken in these cases of the parasite densities in the peripheral blood as, in the experience of the writer, the intensity of infection has no relation either to the severity of the symptoms or to the relapse rate. As a matter of fact the smaller infections are often the most liable to relapse, either from lack of sufficient treatment or from the smaller degree of immunity resulting from the attack. In other words, the defensive mechanism is not roused to activity. It has also been the experience of the writer that cases of malaria with very few parasites in the peripheral blood often present more urgent symptoms of gastric distress, cerebral complications, or the asthenic type of malaria with grave algid symptoms.

James classifies the return of malaria after a primary attack in three categories :—

(A) *Recrudescence.*—A return of fever and parasites within 8 weeks of recovery.

(B) *Relapse.*—A return of fever and parasites between 8 and 24 weeks after recovery.

(C) *Recurrence.*—A return of fever and parasites at some time later than 24 weeks.

For clinical purposes there is no advantage in separating up recrudescence and relapse as specified above, and, in the tables printed below, this distinction is not made and all cases which showed fever and parasites within six months are classified as relapses.

It should be noted here that the area from which these cases were taken has been under anti-larval control for three years and that the small number recorded represents the bulk of the malaria cases admitted to hospital for a period of 9 months. Thus, whilst reinfection cannot be entirely eliminated in assessing the relapse rates, this factor is not likely to be potent enough to vitiate the results. The population of the area from which these patients were received is roughly 25,000 and the area about 50 square miles.

All cases were treated in hospital and were kept under observation for not less than 7 days, during which time the blood was examined daily. On leaving hospital, a record was kept of all these admissions for 6 months, and every case was seen at least once weekly.

The results of treatment and the relapse rates are shown in table I.

Blood films (thick and thin) were taken daily in each case and the types of infection noted. The times of disappearance of parasites from the peripheral blood are noted in table II. Slides in every case were taken on completion of the day's treatment, so that, on the first day for example, each patient had 3 tablets before his blood was examined, and so on for each day. The table therefore shows the results obtained after 24 hours, 48 hours, etc., of the particular treatment specified.

A comparison of combined treatment with atebrin-plasmochin and atebrin alone shows that the combined treatment seems definitely to shorten the period of pyrexia by roughly one day on the average.

From the table it will be seen that there is little to choose between the four methods of treatment with combined atebrin and plasmochin, but that when atebrin alone is administered there is a definite prolongation of the life of parasites in the peripheral blood; this is if anything more marked in the case of atebrin musonate. Atebrin musonate was given in two doses of 0.250 gramme each, injected intramuscularly on successive days. The addition of plasmochin appears to shorten the time of persistence of the parasite in the peripheral blood.

In administering atebrin musonate, care must be taken to prepare the solution in the dark and also to keep the patient away from light as far as possible, following the injections. Unless precautions are taken, the drug exhibits some undesirable effects due to photo-synthetic action. If proper precautions are taken, no untoward symptoms arise.

Toxicity

A considerable literature has accrued on the subject of toxic symptoms following the administration of atebrin-plasmochin. A careful analysis of cases reported will show that these effects have often followed treatment carried out without proper control and often in patients not under hospital supervision.

There has also been a tendency to attribute symptoms which are due to malaria itself to

TABLE I

Treatment	Malignant tertian			Benign tertian			Total		
	Cases	Relapse	Per cent	Cases	Relapse	Per cent	Number of cases treated	Number of relapses	Rate of relapse, per cent
Atebrin only, 0.1 gramme, t.d.s., for 5 days.	21	3	14.29	5	1	20.0	26	4	15.38
Atebrin 0.1 gramme and plasmochin 0.0033 gramme, t.d.s., for 5 days.	23	2	8.7	8	1	12.5	32 *	3	9.38
Atebrin 0.1 gramme + plasmochin 0.005 gramme, t.d.s., for 5 days.	27	3	11.1	4	1	25.0	32 †	4	12.5
Atebrin musonate injection 0.250 gramme on two consecutive days.	4	..	..	..	..	..	5 ‡	1	20.0
Atebrin dragées. Atebrin 0.1 gramme + plasmochin 0.0033 gramme, t.d.s., for 5 days.	4	..	..	..	..	..	4	..	..
Atebrin, 0.1 gramme + plasmochin, 0.005 gramme t.d.s., for 5 days.	6	..	..	1	..	..	7	..	..
TOTAL ..	85	8	9.4	18	3	16.6	106	12	11.32

* Including one quartan case in which there was no relapse.
† Including one mixed infection case in which there was no relapse.
‡ Including one quartan case in which a relapse occurred.

the drugs administered. Symptoms arising from intercurrent disease have also to be excluded in estimating the effects of atebrin-plasmochin treatment. Green (1934) reports a case which developed epileptiform fits twenty days after treatment with atebrin. The patient, on questioning, admitted that he had had similar fits since childhood.

Again, abdominal pain and gastric tenderness are both common concomitants of a malaria attack and are independent of the drugs exhibited. Headache also is common in malaria and degrees of cerebral disturbance are met with in every severe attack.

In the present series of cases, adverse symptoms were surprisingly few. Three cases showed transient yellowish discoloration of the skin, associated with constipation.

Tropp and Weise (1933) have shown by colorimetric observations that atebrin is excreted in equal quantities in the stools and urine, and that the excreted pigment physically and biologically is identical with atebrin. If care is taken to prevent constipation and to promote diuresis by the plentiful use of fluids during the febrile period, yellow discoloration of the skin seldom occurs.

Hecht (1933) has shown that atebrin does not bring about the formation of methæmoglobin either *in vitro* or *in vivo*, and that the drug does not cause hæmolysis.

In the 106 cases reported in this paper, five only exhibited signs of intolerance. In these five cases, gastric analysis showed abnormality in the secretion of HCl. Two cases showed hyperchlorhydria and three showed complete achlorhydria.

Case I.—Persistent hyperchlorhydria with subsequent development of gastric ulcer. This case developed benign tertian malaria and on completion of a five days' course of atebrin 0.1 gramme and plasmochin 0.005 gramme developed tachycardia, substernal tenderness and transient blueness of the lips and finger nails. The symptoms subsided quickly after cessation of treatment and the use of glucose by mouth.

Case II.—Benign tertian malaria and hyperchlorhydria. Completed the course of atebrin 0.1 gramme + plasmochin 0.005 g., t.d.s., but developed marked yellowness of the skin, tachycardia and slight abdominal pain. The symptoms, excepting the yellowness of the skin, subsided rapidly.

The subsequent history of this case is interesting. She relapsed and developed benign tertian malaria five months later. On my advice, she took atebrin 0.1 gramme with plasmochin 0.005 gramme in dragées. There were no symptoms of intolerance and there has been no further relapse within one year of treatment.

These two cases would seem to indicate that the presence of excessive hydrochloric acid was a possible factor in determining the symptomatology.

The experiments of N. D. Kehar (1935) seem to indicate that atebrin excretion, when the drug is administered on an empty stomach or 2½ hours after a meal, is greater than at, or within 2 hours of, a meal. This might also indicate a possible connection between the pH of the gastric juice and the absorption or retention of atebrin in the system.

Case III.—Achlorhydria. No free hydrochloric acid in gastric juice. Developed malignant tertian malaria. Treatment—atebrin 0.1 gramme + plasmochin 0.0033 gramme, t.d.s., in combined tablet. Blood negative on second day. On third day of treatment, patient complained of dyspnœa, pain in precordial region and

epigastric tenderness. Epigastric pain and tenderness persisted for days. The course of treatment was omitted on the fourth day and resumed on the fifth day with two tablets only daily.

Case IV.—Malignant tertian malaria—hæmoglobin 35 per cent (Hellige). Gastric juice showed no free hydrochloric acid. Treatment—atebrin 0.1 g. + plasmochin 0.0033 gramme, t.d.s. The patient complained of severe epigastric pain, nausea and vertigo on first day which persisted on second day. Treatment was stopped on second day but resumed on third day with atebrin 0.1 gramme + plasmochin 0.0033 g. in dragée, t.d.s. There was no further complaint of epigastric pain. Temperature was normal on fourth day. Blood positive until fourth day.

Case V.—Quartan malaria with nephritis, admitted on 23rd December, 1934. Gastric juice showed no free hydrochloric acid. The patient was pregnant. Treated with atebrin musonate 0.250 gramme intramuscularly on two successive days. Blood negative on second day. Patient complained of precordial distress and vertigo with epigastric tenderness. She aborted on the third day. Blood negative for next two weeks. Patient remained in hospital under treatment but relapsed on 14th February, 1935. Blood showed quartan malaria. She was treated with atebrin 0.1 g. + plasmochin 0.0033 gramme in dragée and had no complaint. Blood negative on seventh day.

In addition to these cases, two other cases, which are not included in this series, are of correlated interest :

Case A.—Female with complete achlorhydria and cholecystitis, treated for malignant tertian malaria, with atebrin 0.1 g. and plasmochin 1/6th grain daily. Developed signs of intolerance with gastric and abdominal pain and cardiac distress, and vomiting on second day. Subsequently given quinine.

Case B.—Female. Gastric secretion normal. *X*-rayed for bilious attacks. Well marked cholecystitis. She developed malignant tertian malaria and was treated with atebrin-plasmochin. The dose given was atebrin 0.1 gramme in tablet form. To this was added plasmochin 1/6th grain daily on the second day of treatment. She developed signs of intolerance after 24 hours with severe gastric pain, tenderness on the liver and headache. Blood negative on second day. This patient has since been operated on for cholecystitis.

These two latter cases are not included in the 106 cases recorded in the above series, but are noted as they seem to bear on the five cases reported above.

From the evidence of these cases, there seems to be a definite connection between achlorhydria, the biliary system, and the production of toxic symptoms after the exhibition of atebrin and plasmochin.

It seems logical to conclude that the symptoms of intolerance in these cases after the administration of these drugs were due to abnormality of the gastric juice alone or accompanied by pathological changes in the gall-bladder.

In none of the remaining 101 cases were any untoward symptoms evolved.

Hecht has shown by making use of the fluorescent effect of atebrin under the influence of ultra-violet rays, in experiments on mice, that atebrin is retained markedly in the gall-bladder and less markedly in the bowel and liver.

It seems reasonable to infer that such retention may cause the production of toxic symptoms when the gall-bladder is already the seat of pathological changes with deficiency or slow excretion of bile. It seems also a reasonable inference that, in normal individuals, the exhibition of atebrin and plasmochin in the doses devised for these experiments is perfectly safe and not likely to produce any toxic symptoms.

The scope of this paper does not permit any evaluation of the parts played by atebrin and by plasmochin or which of the two assumes the leading rôle. In the doses used, it is clear that plasmochin is well tolerated.

The effects of treatment

The results show a relapse rate of 11.32 per cent within 6 months. This rate compares very favourably with the relapse rate of quinine-treated cases. The relapse rate with quinine in a series of 200 cases treated on three gardens during 1930-31 was 40 per cent. Not only is the relapse rate reduced from 40 per cent with quinine to 11 per cent with atebrin-plasmochin, but the bulk of the patients infinitely prefer the atebrin-plasmochin treatment to quinine, in whatever form. The period of treatment is also much shorter and this is a factor of considerable commercial value.

A comparison of treatment in table II shows that the combined treatment is better than atebrin alone.

Regarding the combined treatment, the results obtained by atebrin-plasmochin in dragées are better than with the combined tablet, and toxic symptoms are avoided. There is nothing to

TABLE II

Atebrin and plasmochin (all types of treatment)

Showing first day in which blood film was negative

	1st day	2nd day	3rd day	4th day	5th day	6th day	7th day	Total cases	Average duration, days
In M. T. cases	20	28	8	3	1	..	..	60	2.0
In B. T. cases	8	3	1	1	..	..	..	13	1.7
In quartan cases	..	..	..	1	..	..	..	1	4.0
In M. T. and B. T. cases ..	..	..	1	..	..	..	..	1	3.0
TOTAL ..	28	31	10	5	1	..	..	75	2.0

TABLE II*a*

Atebrin alone

		1st day	2nd day	3rd day	4th day	5th day	6th day	7th day	Total cases	Average duration, days
Atebrin by mouth.	In M. T. cases ..	2	9	5	..	5	..	..	21	2.85
	In B. T. cases ..	..	..	2	..	1	1	1	5	4.8
	TOTAL ..	2	9	7	..	6	1	1	26	2.32
Musonate by injections.	In M. T. cases ..	1	1	..	1	..	..	1	4	3.5
	In quartan cases	..	..	1	..	..	..	..	1	3.0
	TOTAL ..	1	1	1	1	..	..	1	5	3.40
Either form		3	10	8	1	6	1	2	31	3.26

TABLE II*b*

Atebrin and plasmochin

		1st day	2nd day	3rd day	4th day	5th day	6th day	7th day	Total cases	Average duration, days
Atebrin 0.1 g. + plasmochin 0.0033 g.	In M. T. cases ..	9	10	3	..	1	..	..	23	1.9
	In B. T. cases ..	4	2	1	1	..	..	..	8	1.9
	In quartan cases	..	..	..	1	..	..	..	1	4.0
	TOTAL ..	13	12	4	2	1	..	..	32	1.9
Atebrin 0.1 g. + plasmochin 0.005 g.	In M. T. cases ..	8	13	5	1	..	..	..	27	2.0
	In B. T. cases ..	3	1	..	..	..	..	..	4	1.2
	In M. T. and B. T.	..	..	1	..	..	..	..	1	3.0
	TOTAL ..	11	14	6	1	..	..	..	32	1.9
Atebrin 0.1 g. + plasmochin 0.0033 g. (dragées).	In M. T. cases ..	..	3	..	1	..	..	..	4	2.5
	TOTAL ..	..	3	..	1	..	..	..	4	2.5
Atebrin 0.1 g. + plasmochin 0.005 g. (dragées).	In M. T. cases ..	3	2	..	1	..	..	..	6	1.8
	In B. T. cases ..	1	..	..	..	..	..	..	1	1.0
	TOTAL ..	4	2	..	1	..	..	..	7	1.7

choose between the two doses of plasmochin so far as results go.

Duration of fever

The average duration of fever in these cases was closely correlated to the presence of malarial parasites in the peripheral blood, and fever usually abated when the blood was negative. In a few cases fever persisted for about twelve hours after the peripheral blood was negative.

The average duration of fever was therefore about 48 to 60 hours.

Treatment of relapses

Relapses were treated with atebrin 0.1 gramme + plasmochin 0.005 gramme, t.d.s., for

5 days. Treatment was omitted for the next 3 days, and a subsequent treatment of atebrin alone for 3 days given, the dose being 0.1 gramme, t.d.s. The blood is examined daily during this course. Blood is examined on completion of the second short treatment. The patient is then put on quinine gr. x daily at night for 10 days. At the end of the period, the blood is re-examined and, if negative, atebrin alone, 0.1 g., t.d.s., is given for 3 days. This completes the treatment. So far none of the cases so treated has relapsed. The treatment is designed to anticipate the possibility of relapse about the beginning of the third week after the initial attack.

Atebrin musonate

Only 5 cases were treated in this series with a relapse rate of 20 per cent. Two injections only were used on consecutive days. Some modification of this treatment would seem to be essential and more extensive trial is necessary before any conclusions can be drawn.

Summary

Atebrin-plasmochin in combined tablet and in dragées and atebrin musonate in the various doses were tried in a series of 106 cases. The relapse rate was 11.32 per cent. Excluding the atebrin musonate series in which one out of five cases relapsed and the atebrin only series in which the relapse rate was 15.38 per cent, the relapse rate with atebrin-plasmochin combinations was 9.33 per cent.

The small difference in the dose of plasmochin in the combined tablets or dragées had no appreciable influence on the results.

Toxic symptoms in this series were limited to cases which showed excess or deficiency of gastric hydrochloric acid or pathological changes in the gall-bladder. No toxic symptoms were noted in normally healthy patients. The percentage of cases showing toxic symptoms was 4.7. Atebrin-plasmochin in dragées form was successfully exhibited where the ordinary tablets caused epigastric distress. This bears out the relation of the gastric pH to the production of toxic symptoms.

A scheme for the treatment of relapse is outlined.

Conclusions

Atebrin 0.1 gramme with plasmochin 0.0033 or 0.005 gramme given in dragées is the best treatment for malaria at present available, with the lowest relapse rate.

Atebrin musonate requires further trial before a definite conclusion can be arrived at. The dosage is probably insufficient.

Atebrin-plasmochin dragées are least likely to cause symptoms of intolerance, even in the presence of gastric or biliary disease. No relapses occurred in the series, in which dragées were used.

(Continued at foot of next column)

MASS TREATMENT WITH INJECTABLE ATEBRIN

By A. T. W. SIMEONS, M.D. (Heidelberg)
Bombay

IN the course of experiments conducted at the Colombo General Hospital during the malaria epidemic in Ceylon with atebrin-dimethylsulphonate (musonate) a method was elaborated by which it became possible to effectively treat severe cases of malaria with two injections given at an interval of 24 hours without any other additional treatment (Blaze and Simeons, 1935).

The results obtained in these experiments showed that it is possible to exercise a very rapid and lasting effect on a malaria infection by this particularly simple method. Although it is usually possible to cure a case of malaria with oral atebrin only, it is obviously a great advantage to have a simple, effective and quick treatment in certain cases. Apart from those very severe cases where quick results are urgently required this method would seem to have particular and hitherto unrealized advantages for conducting a 'blanket treatment'. It was therefore desirable to continue my experiments on a larger scale under well-controlled conditions permitting exact observation.

'Blanket treatment' of hospital staff

For this purpose the staff of the Kurunegalle Hospital was selected. Kurunegalle is a provincial town in Ceylon situated in one of the worst epidemic centres. The hospital staff consists of 65 persons, practically all of whom had had malaria within the last two months. Thirty-eight were actually suffering from clinical symptoms at the time and on an average there was a daily absence of about 20 per cent, in spite of the fact that nearly all were taking quinine or quinoplasmochin in varying doses. Twenty-eight persons had enlarged spleens and 36 blood slides were found to contain parasites

(Continued from previous column)

Acknowledgments

The writer thanks Dr. A. Brocke, PH.D., of Bayer-Meister Lucius for supplying the drugs for these experiments.

He also acknowledges the assistance of Dr. L. R. Dey and the staff of the Cinnamara Central Laboratory for their help in the compilation of the tables.

REFERENCES

Green, R. (1934). *Malayan Med. Journ.*, Vol. IX, p. 22.

Hecht, G. (1933). *Arch. Exper. Path. u. Pharm.*, Vol. CLXX, p. 328.

Kehar, N. D. (1935). *Rec. Mal. Surv. India*, Vol. V, p. 405.

Manson, D. (1936). *Ibid.*, Vol. VI, p. 19.

Tropp, C., and Weise, W. (1933). *Arch. Exper. Path. u. Pharm.*, Vol. CLXX, p. 339.