

2. A recovery rate of 70 to 90 per cent., with no after-sequel, and that in cases which had had three or four attacks.

3. The best and most effective treatment is a brisk purge at the commencement of the attack; it produces a complete evacuation of the bowels, and recovery is as complete and rapid as was the onset of the disease.

4. The administration of antimeningococcus serum did not improve results.

5. The child is either dead or has completely recovered within two to three days.

6. Even in the very severe cases which recover, recovery is as rapid as in the mild cases.

7. It has been suggested that the epidemic may be a mild one associated with a parameingococcus, but the symptoms are those of an overwhelming toxæmia; the complete flaccid relaxation of the muscles of the body is characteristic of such a condition rather than of cerebro-spinal fever.

8. The clinical diagnosis in most cases was either one of acute gastro-enteritis, or of possible infection with worms.

#### THE PLACE OF PLASMOCHIN IN THE TREATMENT OF MALARIA.

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and

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ON the 25th September, 1926, *Reuter* announced the discovery of Plasmochin, a new cure for malaria, and the results obtained by Professor Mühlens of the Tropical Institute, Hamburg. Through the courtesy of Professor Mühlens and the Farbenindustrie Aktiengesellschaft, we were able to obtain the first samples for trial early in December, 1926. By that time the malaria season of Bombay was over and hence the difficulty of getting a sufficient number of suitable cases for investigation. The observations were carried out in the wards of Major S. S. Vazifdar, I.M.S., Senior Physician, Sir J. J. Hospital and Professor of Medicine, Grant Medical College, Bombay, to whom we are highly indebted for his kindness and help.

Plasmochin is the outcome of team work by the chemical and chemo-therapeutic sections of the Elberfeld factory. Perkins, in 1856, as the outcome of a study of the possibility of quinine synthesis, isolated the first coal tar dye, mauvein. At that time it was supposed that the quinine molecule contained two chinolin rings, but in 1890 the workers at the Elberfeld factory proved that this view was wrong. Dr. Horlein describes Plasmochin as an alkyl-amino-6-methoxyquinoline salt, obtained by synthetic methods, and not a derivative of quinine. It is a tasteless, light-yellow, finely granular powder; fairly easily soluble in alcohol, soluble in water to 0.03 per cent. at 20°C., and rapidly converted into the hydrochloride by the hydrochloric acid of the stomach. The salt contains 10 per cent.

of plasmochin base. Dr. Rohl tried Plasmochin in the treatment of *Proteosoma* infection in canaries, and this led Professor Soili of Dusseldorf to use it in the treatment of induced malaria in cases of general paralysis. Finally, Professor Mühlens of Hamburg carried out an extensive series of trials with the drug in cases of naturally acquired malaria, and read a paper at the conference of Naturforscher und Artze at Dusseldorf in September, 1926.

Plasmochin is thus another triumph of German synthetic chemistry, and promises to be an outstanding landmark in the therapeutics of tropical medicine.

In the investigation of this drug we selected only those cases of malaria which showed malarial parasites in the blood. Before beginning the treatment, a complete blood examination was done as shown in Table I, and the patients were given Plasmochin according to the directions of the manufacturer.

The drug is put up for administration in tablet form in two varieties: Plasmochin, each tablet containing 0.02, gm. of the drug, is recommended for benign tertian and quartan infections, one tablet three times a day; and Plasmochin Co., each tablet containing 0.01 gm. of the new drug and 0.125 gm. of quinine sulphate is recommended for malignant tertian infections. All the cases under investigation were given only the tablets of the new drug and no other medicine whatsoever. A daily count of the malarial parasites in the blood was made and the counts to be of value for purposes of comparison were always done with a definite and known quantity of blood. Blood was taken by the hæmocytometer pipette up to the mark 0.5 c.mm. and the counts were made on this known quantity of 0.5 c.mm. of blood by film and drop methods. In a few cases cultures were made from the blood before and after treatment; and we found that no culture could be grown from blood after treatment with Plasmochin. However it was found that cultures could not be grown from blood which did not show parasites microscopically, either by the film or drop method; and therefore for the purposes of this paper, cultures were not made in every case. It is interesting to note here, however, that cultures made in Case 10 (cf. Tables I and II) of our series showed that all the amoeboid forms in the blood developed into crescents, and none went into schizogony. The infection in this case was most virulent and 2,365 malarial parasites were counted in 0.5 c.mm. of blood.

Clinical notes were kept and the urine was examined every day and the drug in many cases has been prescribed even in the presence of complications. We have observed no untoward effect of the drug on any system or organ.

The drug begins to act within 24 hours and under its action the malarial parasites immediately disappear; within 5 or 6 days the blood is free from malarial parasites. (*Vide* Table II.)

TABLE I.

Examination of Blood of the Patients on admission.

J. J. Hospital, Ward XIV.

		Total number of red blood corpuscles per c. mm.	Total number of w.b.c.'s. per c. mm.	Haemoglobin percentage.	Colour index.	DIFFERENTIAL LEUKOCYTE COUNT.				Variety of Malarial Parasites.	Number of Parasites per 0.5 c.mm. of blood.	Van den Bergh reaction on blood serum direct and indirect.
						Polymorphs.	Lymphocytes.	Hyalines.	Eosinophiles.			
5043	Manigan Ganda Swami.	2,200,000	5,600	50	0.9	68	16	14	2 %	B. T.	95	- - +
5171	Gulam Rasul Syed Imam.	1,880,000	7,400	45	0.8	70	15	12	3 %	B. T. & M. T.	107	- - -
5248	Mohamad Shohela	3,780,000	4,800	80	0.8	58	24	14	4 %	Quartan.	178	- - -
5259	Daudmiya Fakir Ahmed.	3,200,000	5,200	70	0.8	60	22	15	3 %	B. T. & M. T.	301.76	- - +
5349	Durming Fernandez.	3,000,000	4,400	60	1	58	28	12	2 %	M. T.	347.203	- - -
5360	Riawat Sadal ..	4,200,000	6,400	80	1	64	23	11	2 %	B. T. & M. T.	287	- - -
5408	Haibulla Khairati	3,800,000	6,000	80	0.9	61	25	12	2 %	B. T.	237	- - -
5410	Mohamed Ismail	4,000,000	6,200	85	0.9	60	23	14	3 %	M. T.	98	- - -
300	Mustafa Baheb-khan.	3,200,000	5,800	70	0.9	58	23	16	3 %	M. T.	110	- - +
716	Fazirulla Sharfulla.	3,450,000	6,400	70	0.9	54	27	17	2 %	M. T.	2365	- - +
584	Mohamed Noor Gulam.	2,860,000	3,700	60	0.9	68	14	16	2 %	B. T. & M. T.	183.33	- - +
632	Abdul Rehman Karim.	4,000,000	4,800	80	1	61	25	11	3 %	Quartan.	440	- - -
464	Sambhunath Kaluram.	2,880,000	4,550	60	0.9	71	17	9	3 %	Quartan.	296	- - -
884	Alkhan Azee ..	3,900,000	6,340	80	0.9	60	23	15	2 %	M. T.	165.57	- - -
114	Najumiya Hasumiya.	4,200,000	4,750	85	1	59	26	14	1 %	B. T. & M. T.	210.67	- - -

TABLE II.

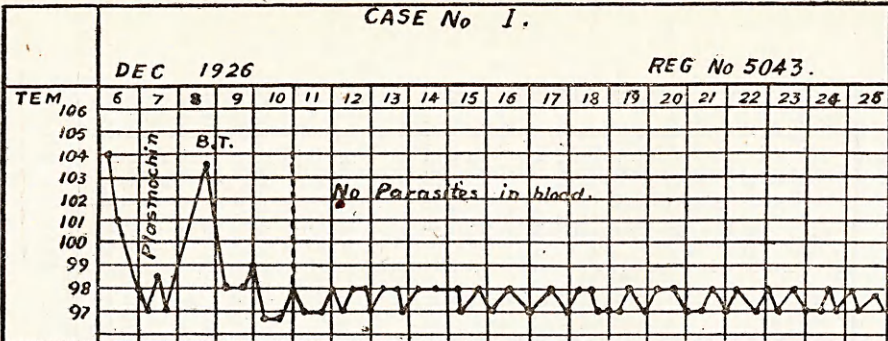
Daily count of the number of malarial parasites in 0.5, c.mm. of blood, from the day of the commencement of treatment.

Serial No.	Reg. No.	Name.	Kind of parasites.	1st day.	2nd day.	3rd day.	4th day.	5th day.	6th day.	7th day.	8th day.	9th day.	10th day.	Next week.
1	5043	Manigan Ganda Swami	B. T.	95	65	27	7	2	nil	nil	nil	nil	nil	nil
2	5171	Gulam Rasul S. Imam.	B. T. & M. T.	107	56	37	8	1	..	..	..	..	..	..
3	5248	Mohamad Shohela	Quartan	178	95	37	12	2	nil	nil	nil	nil	nil	nil
4	5259	Daudmiya Fakir Ahmed.	B. T. & M. T.	301	103	33	5	nil	nil	nil	nil	nil	nil	nil
5	5349	Durming Fernandez.	Crescents M. T.	76	47	29	17	11	7	3	nil	nil	nil	nil
			Crescents	347	127	43	15	5	2	nil	nil	nil	nil	nil
			Crescents	103	59	30?	17	10	7	5	2	nil	nil	nil
6	5360	Riawat Sadal ..	B. T. & M. T.	87	30	12	3	nil	nil	nil	nil	nil	nil	nil
7	5408	Habibulla Khairati	Crescents	22	11	7	5	2	2	nil	nil	nil	nil	nil
			B. T.	237	165	61	18	8	1	nil	nil	nil	nil	nil
8	5410	Mohamed Ismail	M. T. & B. T.	98	43	20	9	2	nil	nil	nil	nil	nil	nil
9	300	Mustafa Baheb-khan.	Crescents	110	71	60	43	27	14	9	4	2	2	nil
10	716	Fazirulla Sharfulla.	M. T.	2365	960	503	200	47	18	7	nil	nil	nil	nil
11	584	Mohamed Noor Gulam.	B. T. & M. T.	183	100	43	21	9	3	1	nil	nil	nil	nil
			Crescents	33	21	15	10	5	2	2	1	nil	nil	nil
12	632	Abdul Rehman Karim.	Quartan	440	189	90	33	7	1	nil	nil	nil	nil	nil
13	464	Sambhunath Kaluram.	Quartan	296	150	43	18	5	2	nil	nil	nil	nil	nil
14	712	S. A. Dandeker..	B. T.	95	45	22	11	3	1	nil	nil	nil	nil	nil
16	884	Alkhan Azee ..	M. T.	165	100	64	29	9	3	nil	nil	nil	nil	nil
			Crescents	57	29	18	11	5	2	2	1	nil	nil	nil

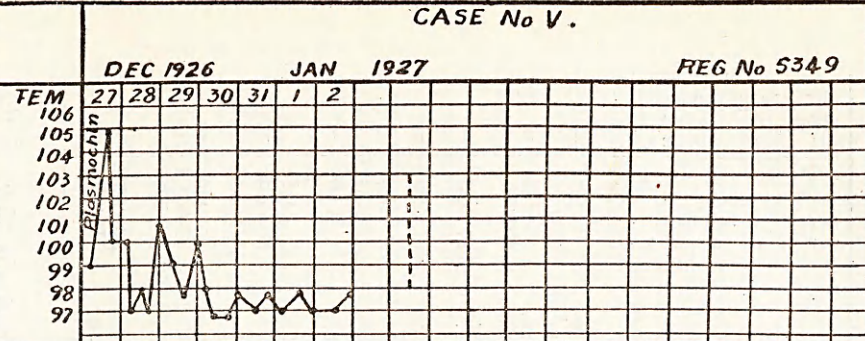
Temperature charts of cases under investigation.

. Dotted line in the chart indicates the day of disappearance of parasites.

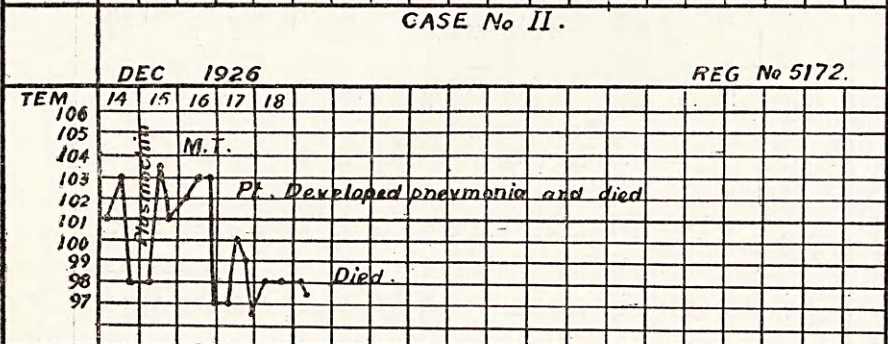
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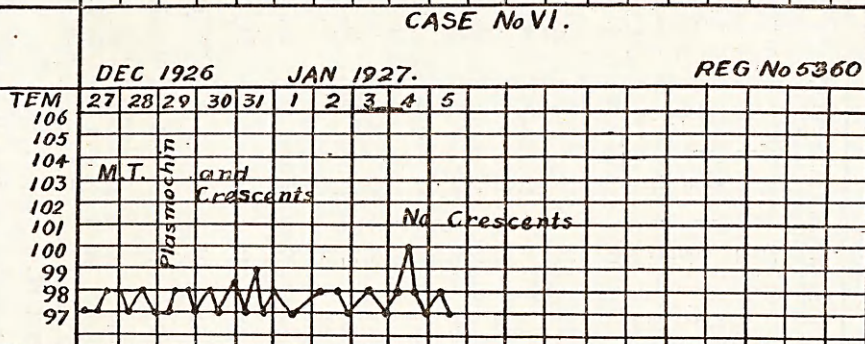
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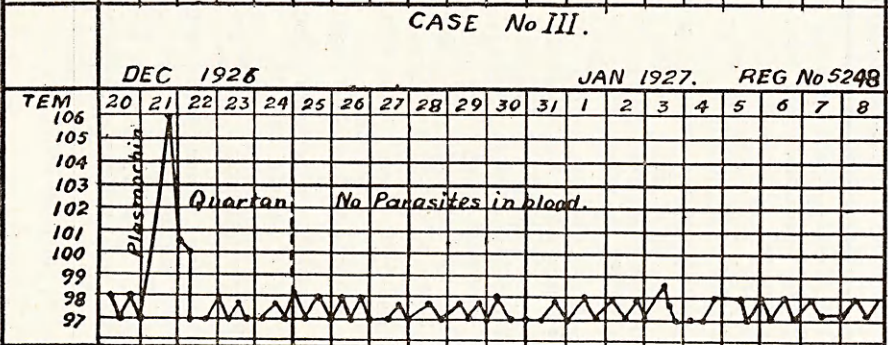
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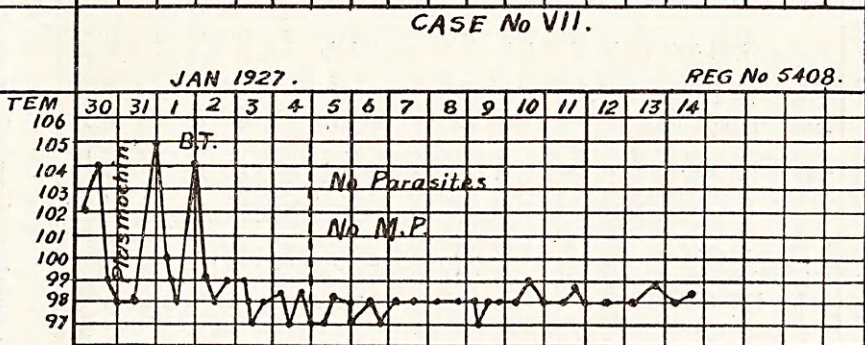
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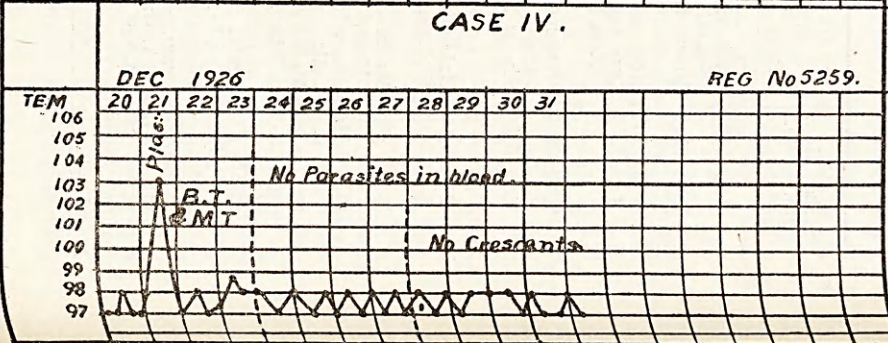
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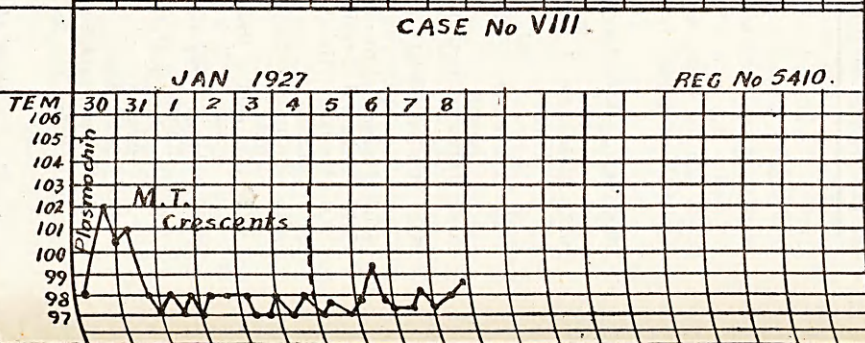
CASE No VII.



CASE No IV.

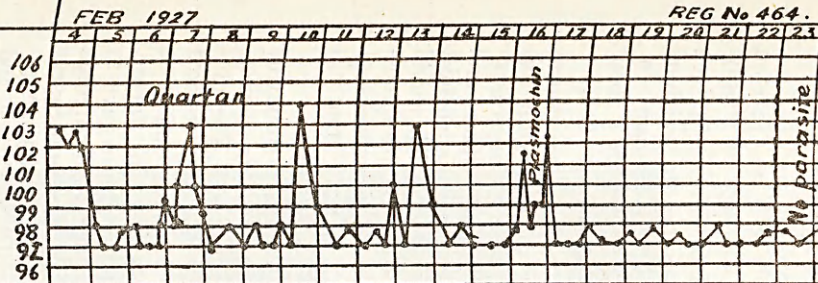
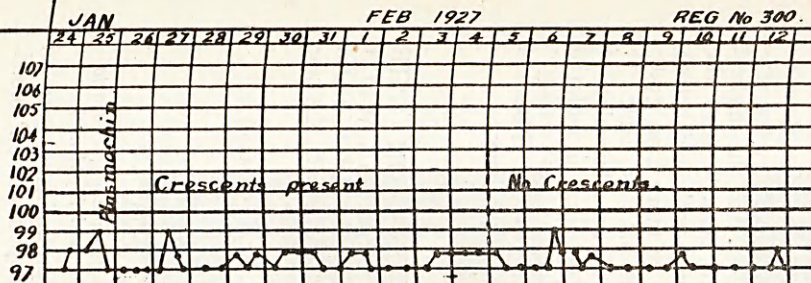


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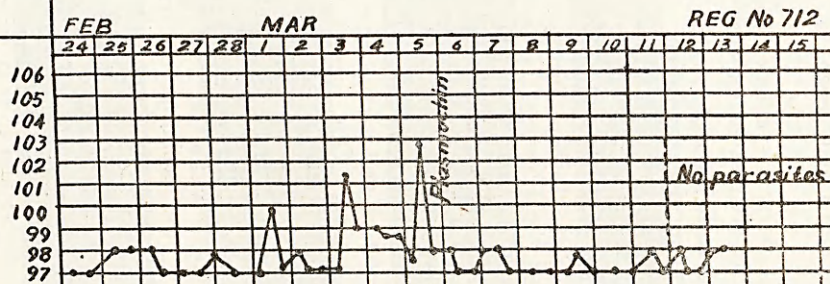
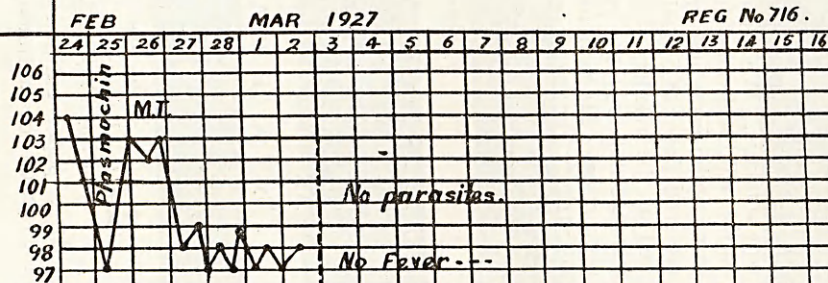
CASE No IX.

CASE No XIII.



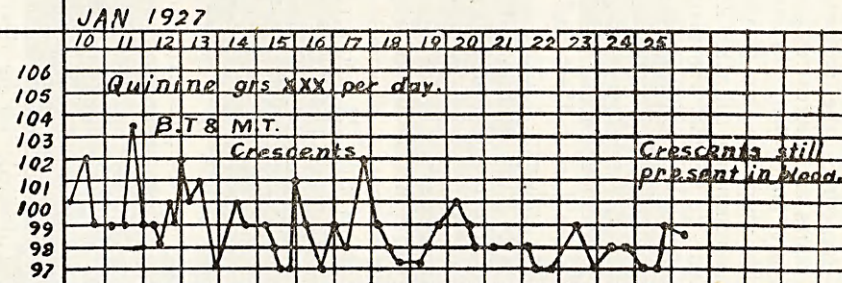
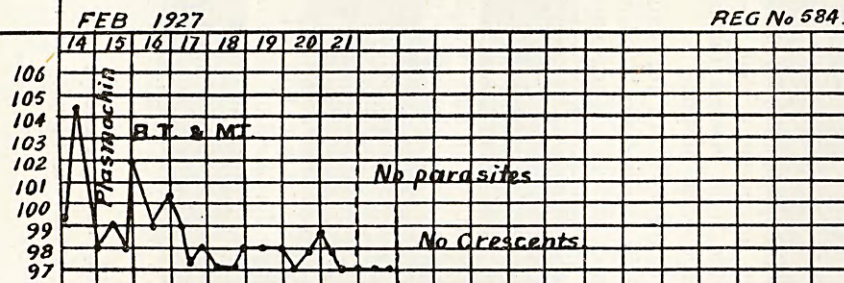
CASE No X.

CASE No XIV.



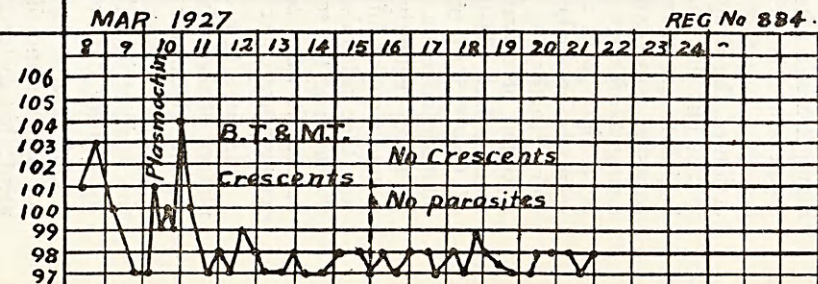
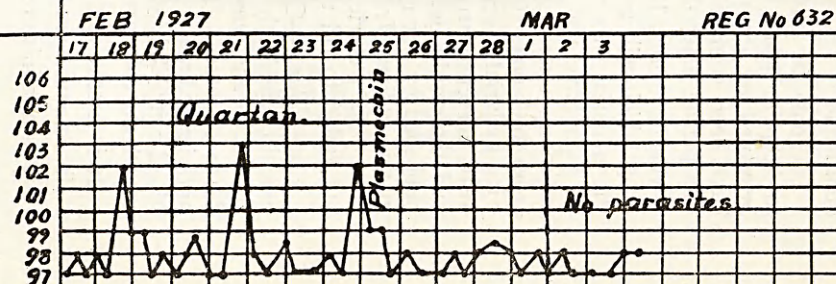
CASE No XI.

CASE No XV.



CASE No XII.

CASE No XVI.



The temperature is generally controlled also within 24 hours. But sometimes the patients may get a rise after 24 hours and thereafter the temperature is permanently controlled. In the beginning we thought this might be due to the action of the drug not commencing till after 24 hours, but the truth seems to be that the drug begins to act at once and the destruction of the parasites is so extensive that the dead parasites, acting as foreign proteins in the blood, being on a rigor with a rise of temperature. This seems to be analogous to the Jarisch-Herschheimer reaction in syphilis, following after the injection of salvarsan. The truth of this statement is best illustrated in the temperature chart of Case 13 of our series. It was a case of quartan infection and there was a rise of temperature regularly every 72 hours before the commencement of the treatment. Plasmochin was then administered and within 24 hours of the last rise the temperature went up once again before it was permanently checked. Every temperature chart tells a similar story.

The first few of our cases invariably complained of some dull aching pain in the epigastric region. However when we administered the drug after meals, none of them complained of this epigastric pain. In none of our series, fortunately, did we observe any cyanosis or pallor.

One case, a patient who came to the hospital for malaria and diarrhoea was put on this treatment; his malaria was controlled, but he developed pneumonia and died. An autopsy was not obtainable.

In some of our cases where it was possible to keep in touch with the patients, they have informed us, even after two months, that they have been completely free from malaria during this period after discharge from hospital.

We have long been on the look out for some drug which will completely sterilize the blood of the malarial infection and get rid of crescents. In vain have we tried quinine, mercurochrome, antimony tartrate, etc., to get rid of crescents from the blood. Other workers in the field have tried malarial vaccines but without success. Last year, mercurochrome was tried in our wards, and the results which were disappointing, were published by our colleagues, Dundas and Telang, in the *Indian Medical Gazette* for March, 1926. Last year we tried antimony tartrate injections but failed to rid the blood of crescents.

**Conclusions.**—Our conclusions are that Plasmochin completely sterilizes the blood of malarial infection and controls the temperature within 24 to 48 hours. The results obtained are lasting and immediate. Crescents are removed from blood completely within a week. The advantages of Plasmochin are:—

It is a sure and quickly acting remedy.

It removes crescents from the blood.

It is administered orally.

It has no unpleasant taste or odour, and hence children and even fastidious adults will take it.

Being a synthetic drug, there is no fear on the grounds of expense and shortage of supply.

It has no untoward or after effects. (Even when given to patients in poor health, weighing only 5 or 6 stone, in doses really meant for Europeans weighing on an average about 10 stone, no untoward effect was observed.)

Dr. Horlein, Director of the drug department of the Elberfeld factory where Plasmochin was evolved, points out that quinine is so unpleasant to take, has such troublesome after effects and is so expensive that the ever optimistic chemist felt that a drug should be evolved which would destroy the malarial crescents which infect mosquitoes and yet be free from the drawbacks of quinine. Our observations indicate that in Plasmochin this ideal is well realised.

The days of quinine are numbered. By virtue of its surpassing merits Plasmochin has successfully challenged the place of quinine. The prophetic vision of Paul Ehrlich is being realized by the evolution of synthetic drugs and it is certain that they will hold sway in future. Ehrlich, after 605 unsuccessful attempts gave to the medical world his 606th successful attempt, called salvarsan, for syphilis. In subsequent years, his school gave us Bayer 205 for trypanosomiasis; and it is a tribute both to Ehrlich and synthetic chemistry that the new drug should be evolved in his fatherland. Our experience with Plasmochin makes us realize that Plasmochin is for malaria what Bayer 205 is for trypanosomiasis. We are confident that the medical world will welcome the new remedy with the same enthusiasm and frankness with which they received Bayer 205, and will be more than gratified at the results. Plasmochin is sure to advance not only the cause of cure but also of prevention. Medical men practising in malarial countries, who have seen the ravages wrought by malaria, will feel grateful to the Elberfeld factory for this epoch-making discovery.

#### FURTHER OBSERVATIONS ON THE SERUM TEST FOR KALA-AZAR WITH ORGANIC ANTIMONY COMPOUNDS. A SIMPLE BLOOD TEST FOR KALA-AZAR.

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and

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In a paper entitled "A preliminary note on the action of antimony compounds on blood.