

(It was learnt after the exfoliative dermatitis had developed that he had been given 15 gm. M. & B. 693 in the 11 days before admission to the hospital.)

Treatment.—He was put on M. & B. 693, 4 tablets on admission, 4 tablets after 4 hours, and thereafter 2 tablets 4 hourly, for 36 hours and then 1 tablet 4 hourly.

The temperature was unaltered by this treatment and ranged between 100 and 104.5.

A skiagram taken three days after admission showed a large dense shadow in the left middle zone of the lung, which was thought to be a loculated empyema.

An exploratory paracentesis with a lumbar puncture needle in the seventh intercostal space produced 10 oz. of fairly thick creamy pus.

In this pus, pneumococci were seen on staining. These were typed by the agglutination method and found to be type I.

The white cell count on 16th May was 7,500, with polymorphonuclears 67 per cent, lymphocytes 31 per cent and monocytes 2 per cent.

The general condition had become worse. Because of the low white cell count, M. & B. 693 was stopped. The concentration of the drug in the blood on 13th May was 6 mgm. per cent. The white cell count continued to fall; it was 4,375, 3,125, 5,625 and 2,625 on 23rd May, 25th May, 28th May, and 3rd June, respectively.

A lumbar puncture produced normal CSF.

On 26th May the skin was covered with erythematous blotches which progressed to typical exfoliative dermatitis in which the whole of the skin was shed. Aspiration was done twice more and a few ounces of thick pus removed. As the condition was becoming still worse rib-resection was done on 4th June under local anæsthesia; but the patient died on 5th June.

Pentnucleotide injections were begun on 4th June. It was not available earlier. Unfortunately blood transfusion was not done. A total dose of 38.5 gm. M. & B. 693 was given in 26 days. It was stopped when the diagnosis of the skin condition was made.

Case 2.—Treated in Lahore City by a private practitioner. A Muslim male child, aged 5, suffering from fever, duration 6 months. He had catarrhal signs present in the chest. X-ray showed tuberculous infiltration of the lungs. Sputum was negative for tubercle bacilli. Mantoux reaction was positive. An exact diagnosis was not made. Because of the few pneumococci present in the sputum, he was put on M. & B. 693, 1½ tablets daily for 7 days. After 10 tablets had been given, he developed a morbilliform rash all over the body and high temperature. The drug was continued in spite of the rash which was thought to be measles. The rash progressed to exfoliative dermatitis. The condition became worse and the child died four days after the skin condition developed. The total dose given was 15 tablets, i.e., 7.5 gm., in 10 days. Further details are not available, as neither of us saw the case ourselves.

This case seems to us to show that M. & B. 693 should only be given under strict medical supervision.

Summary

1. In 159 cases of pneumococcal pneumonia treated at the Mayo Hospital, Lahore, 11 deaths occurred, a mortality rate of 6.9 per cent.

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M. & B. 693 IN INDIAN STRAINS OF MALARIA

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For the last few years sulphonamide derivatives have been the subject of intensive study on the part of chemists, experimental pathologists, and clinicians. Prontosil, whose active principle has been shown to be p-amino-benzene-sulphonamide, has proved to be an excellent drug for the treatment of various infective conditions. A number of new compounds have also been produced, whose activity depends on the presence of this molecule, and which have

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2. The causes of the temperature not coming down to normal after 48 hours of giving M. & B. 693 in pneumococcal pneumonia are discussed.

3. It is concluded from the study of the use of the drug in 8 cases of pneumococcal empyema that it is useless and dangerous to continue its use for longer than 4 or 5 days.

4. Seventeen cases of pneumococcal meningitis are reported of which 3 recovered with M. & B. 693 and daily lumbar puncture treatment, a recovery rate of 17.4 per cent.

5. Two cases of exfoliative dermatitis due to M. & B. 693, in one of which there was agranulocytosis, are reported.

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been found to possess similar therapeutic properties. With regard to their effect in the treatment of malaria, the views are divergent; for instance de Leon (1937), who was the first to report the effect of prontosil in malaria, treated a number of cases with apparently good results. Other reports have not been favourable (Read and Pino, 1938). Recently, Chopra *et al.* (1939) tested the efficacy of prontosil in human malaria. They found 3 to 4 gms. daily for 5 days possessed an undoubted action in causing disappearance of malaria parasites from the peripheral blood and controlling the symptoms of the disease.

M. & B. 693 is another drug, allied to prontosil, which has also been extensively used by the medical profession in various infective conditions with remarkable success. Recently, Chopra and Das Gupta (1939) tested the efficacy

symptoms, anti-malarial treatment was withheld for a few days in order to select only those cases which did not show any tendency to spontaneous recovery. Approximate estimations of the number of parasites were made daily and the treatment was started when the parasite counts were fairly uniform for two or three days. Daily examinations of blood for malarial parasites were carried out during the course of treatment and also for a few days after the completion of the treatment. The effects of the drug on (1) temperature, (2) the sexual and the asexual forms of the parasites, and (3) the time taken for the disappearance of the parasites from the peripheral blood were studied. Any untoward effects produced were recorded. Whenever possible the patients were kept under observation for a fortnight or so after the treatment was completed and the cultural examina-

TABLE

Race, Sex and Age	FINDINGS OF PARASITES BEFORE TREATMENT PER 500 LEUCOCYTES			Total dose of M. & B. 693 in grammes	FINDINGS OF PARASITES DURING AND AFTER TREATMENT. PARASITES PER 500 LEUCOCYTES										Days of fever after beginning treatment
	Species	As.	Sex.		2nd day		3rd day		4th day		5th day				
					As.	Sex.	As.	Sex.	As.	Sex.	As.	Sex.			
H., M., 38	B. T.	850	V. Sc.	7.5	150	V. Sc.	Sc.	0	V. Sc.	0	0	0	3*		
M., M., 21	M. T.	Sc.	V. Sc.	7.5	Sc.	Sc.	Sc.	Sc.	0	Sc.	0	Sc.	3*		
H., M., 25	M. T.	1,000	0	7.5	650	0	250	0	90	0	Sc.	0	4*		
M., I.Ch., 20	B. T.	Sc.	0	10	Sc.	0	Sc.	0	0	0	0	0	2*		
H., M., 23	B. T., M. T.	++	Sc. (Crescents).	15	Few (Cr.)	Sc. (Cr.)	Sc. (Cr.)	Sc. (Cr.)	V. Sc. (Cr.)	Sc. (Cr.)	0	0	3†		
H., M., 52	B. T.	1,500	Sc.	15	700	Sc.	550	Sc.	180	0	0	0	4†		
H., M., 39	B. T.	Sc.	Sc.	15	Sc.	Sc.	Sc.	0	0	0	0	0	2†		
M., M., 25	B. T.	V. Sc.	0	15	V. Sc.	0	Sc.	0	0	Sc.	0	0	1†		
M., M., 31	M. T.	++	0	15	+	0	Few	Sc.	Sc.	Sc.	Sc.	Sc.	3†		
H., M., 36	B. T.	1,200	Sc.	15	200	Sc.	350	Sc.	Sc.	Sc.	0	0	3†		
A.-I., F., 5	Qt.	Sc.	Sc.	7.5	Sc.	Sc.	Sc.	Sc.	Sc.	Sc.	Sc.	Sc.	4†		

* indicates' recrudescence.

† " no " parasite-free two days after treatment was finished.

of this drug in monkey malaria. They found that unlike prontosil this compound is capable of destroying the monkey plasmodium (*Plasmodium knowlesi*) in dosage which is even less than what is regarded as the proportionate dose for a monkey as compared with that of man. Moreover, the parasites once disappearing after a five days' course of treatment do not appear again in the peripheral blood, at least in sufficient numbers to be detected in thick films.

In view of the encouraging results obtained with this drug in monkey malaria, we carried out a preliminary investigation in the Carmichael Hospital for Tropical Diseases on a series of cases of human malaria in order to find out how effective the drug is in Indian strains of malaria. The results of this trial have been recorded in the present paper.

The patients were all admitted into hospital and, with the exception of those showing urgent

tions of blood were also carried out in a number of cases to determine if the infection had been eradicated.

The drug was administered by the mouth in all cases. We first started with one tablet (0.5 gm.) three times a day for 5 days, and later increased the dose to 2 tablets four times a day.

The table shows that M. & B. 693 has a mild but definite action on the malaria parasites. In cases of infection with *P. falciparum* the asexual forms disappear from the peripheral blood within three to six days, but the sexual forms remain unaffected (cases no. 2, 3, 5 and 9). In infections with *P. vivax*, both the asexual and the sexual forms disappear from the peripheral blood within three to five days (cases no. 4, 5, 6, 7, 8 and 10). In the case with quartan infection, the parasites persisted for two days after the course of treatment. It

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COOLEY'S ERYTHROBLASTIC ANÆMIA

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ERYTHROBLASTIC anæmia, or Cooley's anæmia, is a distinct clinical syndrome that was first described by Cooley (1927) about 12 years ago. Koch and Shapiro (1932) collected 18 cases from the literature and added 5 cases from their own experience. Most of the cases have been reported from the United States and nearly all the patients have been of Mediterranean stock, usually Italian or Greek, but one patient was an English child. We have seen no reference to the incidence of the disease in an Asiatic. The condition appears to have a familial tendency as in 10 of the 23 recorded cases, referred to above, a brother or a sister was also affected.

All the reported cases have been in young children. The first symptom appears in early infancy, in one case there were typical mani-

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is clear from the table that the patients who were given smaller doses of the drug (0.5 gm. three times a day for five days) were relieved of their symptoms and the blood also was negative for malaria parasites, but the patients relapsed during their stay in the hospital. No relapse, however, occurred in those patients who received the higher dose.

A few untoward effects were, however, noticed, but they were of a very mild character. Beyond a slight epigastric distress and flatulence, no toxic effects were recorded.

Summary and conclusions

M. & B. 693 in doses of 4 gm. daily for five days cause disappearance of malaria parasite from the peripheral blood and controls the symptoms of the disease. (2) It destroys both the asexual and sexual forms of *P. vivax*, but only the asexual forms of *P. falciparum*. (3) In smaller doses the symptoms of the disease abated and the parasites too disappeared from the peripheral blood, but recrudescence of the disease occurred within a fortnight. (4) M. and B. 693 undoubtedly possesses mild anti-malarial properties in infection with Indian strains of malaria and is worthy of trial when other anti-malarial drugs are not available, or are contra-indicated. The present series is very small and further investigations are therefore desirable.

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festations at 6 months, but the patients are usually about 3 years old before the disease is diagnosed, and they usually die before the age of 10, but Ordway, Gorham and Isaacs (1937) reported a child aged 11 years who was still alive.

Clinical picture.—The patient has a very characteristic appearance: the features are described as Mongolian, on account of the thickening of the cranial bones and of the prominence of the malar eminence. Added to this is a peculiar yellowish muddy tint of the skin. The pigmentary changes which occur are similar to those in hæmochromatosis.

The spleen is always enlarged, usually markedly. The liver is usually palpable and the lymphatic glands are often slightly enlarged.

There are other signs and symptoms of anæmia. There is sometimes high irregular fever, suggesting an acute infectious process, but this is apparently due to the anæmia, as it disappears after blood transfusion.

The disease tends to run a chronic but steadily progressive course. Hæmolytic crises do not occur. Spontaneous fracture of the rarefied long bones has been reported.

Radiological features.—The long bones and small bones of the hand and foot are porous-looking, with sharp trabeculations and thinning of the cortex. The flat bones of the skull show medullary thickening, while the tables are usually thin. The profile of the skull gives the appearance of a surface studded with small radiating spicules (Vaughan, 1934).

The bony changes in the skull are most noticeable in the parietal and frontal bones, to a less extent in the occipital, and are usually absent from the temporal.

These bony changes are said not to be specific and to occur in achloruric jaundice (Friedman, 1928), and in sickle-celled anæmia (Vogt and Diamond, 1930) but we have only seen these extreme degrees of diploic thickening reported in Cooley's anæmia.

Blood picture.—It is a leuco-erythroblastic anæmia. The anæmia is often extreme, and the hæmoglobin may be as low as 1.4 grammes per cent (about 10 per cent Haldane) with the red cells at about 1,700,000 per c.mm.; that is to say, it is a hypochromic anæmia. The most striking feature in the blood picture is the large number of nucleated red cells, mostly normoblasts; there are frequently more nucleated red cells than leucocytes. There is usually a persistent leucocytosis of about 13,000 to 20,000 per c.mm. with only a few immature cells. Despite the hypochromia the mean red cell diameter is said to be about normal, but there is a high coefficient of variability. This is well shown in the Price-Jones curve of the case of Moncrieff and Whitby (1934), but the curve given by Vaughan (*loc. cit.*) shows a low variability.

The van den Bergh reaction is positive and the icterus index high. There is a considerable increase of urobilin in the urine.