small size of the lesions or to a slow rate of development and, like myocardial infarction, may be a "pluricausal cardiopathy."

I am grateful to Professor J. R. Anderson and Dr. A. T. Sandison for their help and encouragement in preparing this paper.

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Preliminary Communications

Use of Dexamethasone in Cerebral Malaria

Brit. med. J., 1968, 3, 31–32

Summary: In a man who had been in a coma for 24 hours with cerebral malaria dexamethasone had a dramatic, and probably life-saving, effect. We believe dexamethasone should be given routinely, together with antimalarial therapy, to patients with cerebral malaria.

INTRODUCTION

The mortality rate in cerebral malaria has continued to be considerable even though the introduction of haemodialysis in the treatment of patients with severe malaria who develop uraemia and renal failure has enabled such patients to be kept alive, in most instances until kidney function recovers (Jackson and Woodruff, 1962). The principal obstacle to recovery is usually continued coma and the respiratory infection which frequently complicates it. We recently treated a patient in deep coma with Cheyne–Stokes breathing whose prognosis appeared to be very grave. At this stage dexamethasone was administered intravenously with the object of reducing the cerebral oedema which so often is a major pathological feature in cerebral malaria. The response was so dramatic that we suggest that use of this drug might become standard practice in cases of this kind. We are not aware of other reports on use of dexamethasone in this regimen for cerebral malaria having so far appeared in the literature, and for this reason we consider it important to draw attention to this case.

CASE HISTORY

The patient, a 40-year-old man, had spent a month on a shooting expedition approximately 150 miles (240 km.) to the east of Nagpur, India; he had never visited any part of Africa. He arrived in Britain by air, having for the previous 7 to 10 days felt unwell with headache, aches and pains of the limbs, and attacks of shivering; there is documentary evidence that three days before his arrival he had had a temperature of 102° F. (38.9° C.); on this day a blood film had been examined, but no malarial parasites had been noted in it and he had been given treatment with Achromycin V in doses of 250 mg. six-hourly; of this it seems he took a total of 1.5 g. On arrival in Britain he had, with help, managed to reach

his destination, the residence of a friend, who immediately called a medical practitioner who had the patient admitted to a nursing-home. There a blood film was examined and malaria parasites were found in it. The patient was given 600 mg. of chloroquine by mouth and managed to swallow the dose; in spite of this, five hours later he was in coma and arrangements were made for his transfer to the Hospital for Tropical Diseases.

On admission he was comatose, unable to speak, and restless; and at times he was struggling, but he momentarily ceased to do so when his name was loudly called; he resisted medical examination. An hour later his coma became deeper and there was no response when his eyelashes were touched. A blood film at this time showed that 5% of erythrocytes were parasitized with *Plasmodium falciparum*. His blood urea on admission was 84 mg./100 ml., plasma sodium 128 mEq/l., and potassium 3.4 mEq/l. An intravenous drip infusion was set up and through this 200 mg. of chloroquine was administered in 45 minutes; a further 100 mg. was given six hours later, and three hours later still a blood film showed only 0.1% erythrocytes parasitized. The temperature on admission was 104° F. (40° C.), and 18 hours later it was still 102° F. (38.9° C.). During these 18 hours he continued to be critically ill, was completely unconscious, and responded only to painful stimuli. There were extensor plantar reflexes, and 12 hours after admission—that is, after he had been unconscious for approximately 16 hours—there followed a period in which respiration from time to time took on Cheyne–Stokes characteristics with considerable periods of apnoea.

During the 12 hours following admission he was given 1,500 ml. of fluid intravenously and the urinary output was 1,300 ml., but at the end of this 12-hour period the blood urea remained 84 mg./100 ml. In view of his critical condition, continuing deep coma, and the possibility that dialysis might become necessary he was transferred to the intensive care unit. Here the question of administering dexamethasone intravenously was considered, and in view of the fact that the malarial infection was already satisfactorily controlled and no evidence of respiratory infection was present—this possibility having already been covered by the previous administration of tetracycline—it was decided that dexamethasone administration could not aggravate any infection and that its effect in diminishing cerebral oedema could be valuable. Twenty hours after admission—that is, after he had been in coma for approximately 24 hours—10 mg. of dexamethasone was injected intravenously. Four hours later coma had sufficiently lightened for the patient to ask for a drink, and 12 hours later he was fully conscious and ate breakfast. Dexamethasone in doses of 4 mg. was administered intravenously on two occasions during the 24 hours following the initial dose.

Progress thereafter continued uninterruptedly. During the succeeding four days the plasma urea dropped from 84 to 26 mg./

100 ml., the plasma sodium rose from 128 to 137 mEq/l., and the plasma potassium from 3.4 to 4.0 mEq/l. Total serum bilirubin rose to 2.1 mg./100 ml. but fell after four days to 0.9 mg./100 ml. (see Table). An electroencephalogram taken four days after admission showed marked generalized slow-wave activity, and a complete series of tracings taken five days later showed that this had returned to normal.

Following the administration of a total of 300 mg. of chloroquine intravenously, further doses of 300 mg. were given on each of two successive days. After the fall in the proportion of parasitized

such antimalarials slowly, as by drip infusion whereby the dose can be given over an optimal period of approximately three-quarters of an hour, is likely, as in this case, to bring about minimal reduction of blood pressure with an acceptable speed of antimalarial activity.

We believe this to be the first recorded case, certainly in the British literature, in which dexamethasone has been used in this way for the treatment of cerebral malaria. Since using it in this patient we have found in an editorial (*Annals of Internal*

Laboratory Findings During the Period of Treatment

Day of Observation	Time of Collection	Plasma Urea	Plasma Electrolytes				Serum Bilirubin		Haemo- globin (g./100 ml.)	P.C.V. (%)	R.B.C. (mil./ cu.mm.)	Other Investigations
			CO ₂	Cl	Na	K	Direct	Total				
1	01.00	84	26.0	92	128	3.4						P.As.T. = 51 Karmen units/min./ml. Urine: Bilirubin = + +. Urobilino- gen—no excess C.S.F.: Protein, 26 mg/100 ml., Globs, no excess, Sugar, 66 mg./ 100 ml., Cl, 118 mEq/l. P.As.T. = 37 Karmen units/min./ml. Urine: Bilirubin = 0. Urobilinogen = strong excess
2	16.00	84	25.5	90	128	4.1	+	2.1	10.7	33	3.49	
3		77	26.5	89	128	3.8	+	1.1	10.4			
4		54	29.5	96	134	3.6	+	1.9	10.4			
5		44	29.0	99	137	3.8			9.9			
6		33	29.0	101	137	4.0	—	0.9	10.0	31	3.11	
7		26	29.5	104	141	4.2						

P.As.T. = Plasma aspartate aminotransferase.

erythrocytes from 5% to 0.1% nine hours later the therapeutic response to chloroquine was considered to be satisfactory and no parasites were detectable 60 hours after admission. The temperature became normal 36 hours after admission and remained so throughout the period of observation.

The blood pressure on admission was 120/75, this dropped to 100/50 12 hours later, and before the administration of dexamethasone was 100/60. Two weeks later it had risen to 120/80.

DISCUSSION

The prime point of importance which emerges from this case is that dexamethasone appeared to have a dramatic and life-saving effect. The rationale for its use was that in severe cerebral malaria there is usually cerebral oedema associated with the many petechial haemorrhages in the brain caused by damage to vessels brought about by anoxaemia resulting from shock and occlusion of vessels with parasitized erythrocytes. This oedema presumably causes further pressure on blood vessels and diminution in the blood flow through them. Relief from oedema might be expected to improve this blood flow, help to remove sludges composed of parasitized erythrocytes, and thus increase oxygenation of cerebral tissue and benefit the patient's clinical condition.

A second point of interest is that the patient had taken no prophylactic antimalarial, believing that India is malaria-free at the present time. This impression has gained widespread prevalence, and, though malaria control in India and in parts of India malaria eradication have been highly successful, clearly there are areas, particularly perhaps rural areas such as those likely to be visited by persons on sporting expeditions, in which dangerous infections with malaria can be contracted. Wider use of prophylactic antimalarials for persons visiting such areas appears to be essential.

A third point is that experience shows that after the intravenous injection of almost all antimalarials to patients with cerebral malaria the patient's cerebral condition may for a period deteriorate, possibly as a result of the fall in blood pressure which follows the injection. The administration of

Medicine, 1967, vol. 66, p. 807) a recommendation that it should be used for such cases and a report in which a dosage half that given here was used along with much other therapy, so that no clear-cut result could be observed, but it and dextran were "felt to be important to the patient's recovery." (Daroff *et al.*, 1967.) We believe it important that its use should be widely explored in cases of this kind, for in the case here it was spectacularly effective and may have saved the patient's life. Certainly the prognosis is usually extremely grave in patients who have been unconscious for 24 hours or more as a result of cerebral malaria. That was the situation in this case, yet within four hours of administration of the drug some degree of consciousness had returned and 12 hours after administration consciousness was complete.

CONCLUSION

It is concluded that standard practice in the treatment of cerebral malaria should at the present time probably be to administer dexamethasone intravenously along with appropriate antimalarial therapy, attention to fluid and electrolyte balance, and where necessary dialysis. Prompt treatment in cerebral malaria is always important, and it is to be expected that dexamethasone, if its use is to prevent irreversible cerebral damage, should be given at the inception of such treatment.

We are grateful to Dr. G. Stern for the reports of the electroencephalographic tracings, to Dr. D. S. Ridley and Dr. S. Flynn for pathological reports, and to Professor P. C. C. Garnham, F.R.S., who kindly examined and confirmed the identity of the parasites.

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