Medical Memoranda

Treatment of Cerebral Malaria

During recent months certain contributions on malaria have appeared in the *Journal* which have apparently been written by authors with limited experience of this disease. Although these contributions have added little or nothing to existing knowledge, they have in the main been helpful to those who are encountering malaria for the first time. This cannot be said of the article by Surg. Lieut. Sneddon (*Journal*, 1943, 2, 814), reporting a fatal case of cerebral malaria, in which the commentary on treatment is seriously misleading.

DOSEAGE OF QUININE

The author records the administration of intravenous quinine in a dosage of 10 gr. daily, and comments that this dosage was higher than the 5 to 7 gr. daily advocated by Manson-Bahr (1942), leaving the impression with the reader that 10 gr. daily should be adequate for the treatment of cerebral malaria. It may be useful to present in tabular form the recommendations of various authorities on the optimum dosage of quinine in that disease.

Authority	Preparation	Initial Dose		Subsequent Dosage Indicated	
		gr.	Route	Amount (gr.)	Route
Field (1938)	Quinine dihydrochlor.	7½	I.V.	10½; up to total of 30 in 24 hours	I.M.
Manson-Bahr (1940a)	"	10	I.V.	" Free and frequent administration of quinine "	Not stated
Manson-Bahr (1940b)	"	15	I.V.	Not stated	—
Manson-Bahr (1942)	"	5-7	I.V.	5-7 daily	I.V.
Napier (1943)	Quinine dihydrobrom.	10	I.V.	Repeat 10 gr. a few hours later; intravenous therapy may be needed for 2 days	I.V.
Nocht and Mayer (1937)	Quinine dihydrochlor.	7½	I.V.	Not stated	—
Rogers and Megaw (1942)	Quinine dihydrochlor.*	7½-15	I.V.	" "	—
Stitt (1942)	Quinine bismutate	10	I.V.	Not more than 30 in 24 hours	I.V.

* Rogers advocates dihydrobromide.

It will be noted that the recommendations above are far from consistent. Though they may each have given satisfactory results in the particular conditions in which they were used, their diversity makes it difficult for the novice to decide on the correct line of treatment. In general it may be stated that the amount of treatment required will vary in inverse ratio to the amount of immunity possessed by the patient. Thus considerably larger doses of quinine may be required for the majority of Europeans and Americans, who usually possess little or no acquired immunity, than for patients living in endemic areas, who may possess partial immunity.

RECENT RECOMMENDATIONS

Since the outbreak of the present war large numbers of Allied troops with attendant medical services have been deployed in highly malarious areas, providing an unprecedented opportunity for the study of malaria in general and of its neurological complications in particular. The following simple directions have been compiled from the most recent recommendations of the Allied Forces on the treatment of cerebral malaria, and are founded on the experience gained before and during the present war. They are applicable to any case occurring in the adult male.

Drug of choice: Quinine dihydrochloride.

Route: Intravenous.

Rate of injection: Very slow. Maximum speed 1 minute per grain; optimum speed, 2 to 4 minutes per grain; 1½ to 2 minutes per grain.

Initial dose: 6 to 10 gr.

Dilution: Minimum, 6 gr. in 10 c.cm.

Diluent: Distilled water or normal saline if 10 c.cm. is used. Normal or glucose saline for larger quantities.

Subsequent dosage: 6 gr. 4-6 hourly, not exceeding a total of 30 gr. in 24 hours, or 10 gr. 8-hourly, until recovery from coma occurs and satisfactory oral administration is possible.

Intramuscular mepacrine as an adjuvant to intravenous quinine may give good results in the hands of those familiar with its use. I wish to emphasize the necessity for persevering with intravenous quinine in comatose cases even though the prognosis appears hopeless. This is well illustrated in a case reported by Whitehill (1943). Whitehill's patient was in coma for approximately 3½ days, excluding a lucid interval of 1½ days, and, although the coma was complicated by an acute malarial nephritis, recovery ensued after a total dosage of 75 gr. of intravenous quinine had been given.

POINTS FOR COMMENT

There are two other points in Surg. Lieut. Sneddon's article which are worthy of comment:

1. *Use of Intravenous Salines.*—A not infrequent terminal event in cerebral malaria is pulmonary oedema, and caution should always be exercised not to give more intravenous saline than is necessary, and to give it slowly. The administration of fluids through a Ryle's tube passed into the stomach and connected to a drip apparatus has

been recommended by Lieut.-Col. G. A. Ransome, I.A.M.C. (personal communication). It is advisable to nurse patients in a semi-recumbent position rather than dead flat, in order to prevent hypostatic congestion.

2. *Lumbar Puncture.*—This should be carried out as a routine in coma. A certain proportion of cases of cerebral malaria suffer from cerebral oedema with a raised C.S.F. pressure, and, in these, improvement may follow the judicious removal of C.S.F. Further, in malarious areas cases of cerebrospinal meningitis may suffer simultaneously from malaria. The dual pathology may here easily be missed unless a lumbar puncture is carried out.

In conclusion I would like to express my emphatic concurrence in Surg. Lieut. Sneddon's statement that if treatment is to be successful it must be prompt. More than any other factor in the management of the case, the prognosis in cerebral malaria depends upon the speed with which the diagnosis is made and treatment instituted.

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Two Cases of Snake-bite

The following cases are recorded for the reason that snake-bite is an uncommon accident in this country and that it must be still more unusual for two patients to be bitten by the same snake. The great difficulty experienced in obtaining antivenene is also a matter for consideration.

CASE HISTORIES

On May 18, 1944, two healthy boys—A. T., aged 12, and J. O., aged 14—were playing on an open heath when A. T. saw and caught hold of what proved to be an English viper (*V. berus*), commonly known as an adder, 24 in. long. The snake bit him and he dropped it, whereupon his companion gave chase and, having grabbed the snake, was also bitten a few minutes later. A. T., who received the first bite at 3.30 p.m., vomited immediately and felt so ill that he lay down on the grass, where he was found 20 minutes later by his schoolmaster, who stated that the boy was very pale and drowsy, was unable to walk, and complained of sore throat, pain in his abdomen and feet, and great thirst. He was vomiting. The bite was on the dorsum of his right hand, which was much swollen, with a dark-blue area surrounding the bite. The master incised the bite with a penknife sterilized in dettol, but very little blood flowed and it clotted immediately.

The boy was admitted to the West Suffolk Hospital, Bury St. Edmunds, at 5.30 p.m., in a condition of extreme shock. His colour was grey-blue, and he was cold, limp, and semi-conscious. Respiration was very shallow and the radial pulse was not palpable. Temperature was subnormal. He complained of thirst and sore throat. His right hand was swollen, shiny, and grey-blue in colour; there was no lymphangitis, but the axillary lymph glands were enlarged and very tender.

Nikethamide (coramine) and adrenaline were administered, and the usual measures for treatment of shock were taken. By 7.45 p.m. his general condition had considerably improved and he was complaining of pain in his hand and abdomen and of sore throat. Examination showed no haemorrhages in his skin or mucous membranes. Pulse 120 and of good volume; heart and lungs normal; abdomen somewhat distended, and tympanitic and tender; deep reflexes present. A puzzling sign was wide dilatation of both pupils with loss of light and accommodation reflexes. It was discovered subsequently that during the morning atropine had been instilled by an ophthalmic surgeon by whom he had been examined.

He was given 12 minims of nepenthe, and had a fairly comfortable night. On the 19th his general condition was much improved. The right arm, however, was swollen up to and beyond the elbow and was extremely tender. In the afternoon of that day a supply of antivenene was obtained through the Ministry of Health, but the boy was so much better that administration was withheld. On the 20th he complained more of sore throat and dysphagia, and a hot, red, and very tender oedema involved the whole of his right arm and shoulder and upper part of chest, back and front. 10 c.cm. antivenene was given intramuscularly at midday. On the 21st his general condition was much improved and there was no increase of the oedema. On this and the next day he developed extensive ecchymoses in the skin of his right arm and chest. There were no haemorrhages elsewhere, and his urine showed no red blood corpuscles. Recovery was subsequently uneventful, and he was discharged on May 30. His temperature had never risen above 100°.

The other patient (J. O.) was bitten on the outer side of the little finger of his right hand. Another boy promptly sucked the wound and tied a ligature round his arm. He developed no symptoms until 1½ hours later, when he vomited and complained of sore throat and difficulty in speaking. His right hand became swollen and painful.

He was admitted to hospital at 8 p.m. There were no signs of shock, but tender swelling and redness of his right hand, with marked lymphangitis and axillary lymphadenitis. The site was incised under gas anaesthesia and bled freely: a potassium permanganate dressing was applied. No other symptoms developed, and except for slight swelling of his finger he was well on May 22.

COMMENT

It is interesting to note that in this instance the viper did not discharge all its venom at the first bite.

The condition of the boy A. T. on admission was most alarming, and it is clear that antivenene as a life-saving measure would need to be administered within a few hours of the bite. Whether the dose given in this case prevented further oedema and lymphangitis is a matter for speculation. It proved impossible to procure antivenene through the usual channels, and the supply obtained through the good offices of the Ministry of Health was received only after nearly 24 hours' delay. It was prepared by the Pasteur Institute, Algiers, against the venom of the horned viper of Africa (*Cerastes cornutus*). Barrett (*Lancet*, 1934, 2, 60) says: "As the minimum lethal dose of the adder venom for an adult is probably 50 mg. and the amount injected by a British adder is between 5 and 10 mg., the results are seldom grave, but in small children and invalids energetic measures are called for." Apart from first aid, these measures should be directed to the treatment of vasomotor shock and relief of pain.

Nevertheless, in the first of the two cases here described it would have been a great comfort to be in a position to give intravenous antivenene on admission, for the boy seemed likely to die.

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Spontaneous Expulsion through the Rectum of a Kocher Forceps left in the Abdomen 14 Months

I could not find, in the literature in my hands, a case similar to the one recorded below, so I thought it might be interesting enough to merit publication.

CASE HISTORY

A woman aged 40 was admitted to the county hospital on Dec. 30, 1943, complaining of the existence of a piece of scissors in her anus. 14 months previously she had been operated upon for a tumour of the uterus in a maternity hospital elsewhere. She was told that she had a large tumour of the uterus, which was removed. Except for a mild swelling on the left lower extremity no complication had occurred and the wound healed completely. The patient was discharged from the hospital 45 days after operation. At home she was quite well for about 8 months, then she began from time to time to feel pains in the left lower quadrant of the abdomen. Shortly after the onset of these pains she developed intermittent diarrhoea and vomiting. Some 20 days before attending hospital she felt a hard substance in her anus and was unable to crouch and sit. Finally, 17 days later, she touched a part of a pair of scissors which came to the mouth of the anus, and after working hard for two days succeeded in expelling it. She failed to extract the other part. The extracted piece proved to be a branch of a Kocher forceps.

Examination revealed a poorly nourished woman, semi-ambulant and appearing ill, with a temperature of 99.8° F. The pulse was 104. There was an operation scar in the midline between the umbilicus and the symphysis pubis. Vaginal examination revealed a freely movable cervix but no corpus luteum. The fornices were free of masses or infiltration; the patient's menses had ceased since the operation. There was some slight tenderness and redness on the left side of the anus. On deep palpation rectally the other branch of the Kocher forceps could be felt; this was in an inclined position, so that the pointed end had plunged into the left ischio-rectal fossa. Under general anaesthesia the anus was dilated and the remaining branch of the forceps was extracted. After intervention the patient improved steadily and made a complete recovery.

The extracted piece was 14 cm. long, and formed a complete Kocher forceps with the part removed by the patient. Both pieces of this forceps were discoloured. After remaining 13 days under observation she was discharged home in excellent health.

COMMENT

A Kocher forceps left in the abdomen during a gynaecological laparotomy began to give rise to symptoms after nearly 8 months and travelled from the peritoneal cavity into the large intestine. The mechanism of this remarkable (and fortunate) migration is hard to explain. However, one may say with Jalaguier and Mauclair (1893) that first the foreign body encysted and some adhesion occurred with the intestine: this was accomplished in 8 months. Then under the protection of these adhesions the perforation of the intestine took place and the migration started: this phase lasted 6 months.

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Reviews

CLINICAL SYPHILIS

A Synopsis of Clinical Syphilis. By James Kirby Howles, M.D., M.M.S. (Pp. 671; illustrated. 30s.) London: Henry Kimpton.

The appearance of this book is most opportune, partly because it is good on the whole, and partly because up-to-date monographs on syphilis are few. It is divided into three main sections: general considerations, systemic and regional syphilis, and familial and public health aspects. The first includes primary, secondary, latent, and tertiary syphilis, clinical and pathological diagnosis, treatment, and prognosis; the second, syphilis of the various organs and systems of the body, the treatment of each stage; organ, or system being given in the appropriate chapter. Section 3 is devoted mainly to congenital syphilis and syphilis in pregnancy; it includes the epidemiology of the disease and the organization of the syphilis clinic. In an appendix is a brief account of the history of the disease, and there is a long list of references.

The book is somewhat artificially arranged, but, as the author points out in his preface, the gain in clarity and the saving of space more than outweigh the obvious disadvantages. It can be said at once that, speaking broadly, this is a book which will be of great value to the syphilologist; it sets out the subject-matter with commendable clarity, experts are frequently quoted on debatable subjects, and there are numerous illustrations. Most of these are first-class, but some are hardly up to standard—e.g., Figs. 5, 6, and 9. Fig. 18, labelled "Pipestem lymphadenopathy [*sic*] of Dorsum of penis," shows what looks like a rather prominent dorsal vein, and Fig. 58 hardly represents what spirochaetes really look like under the dark-ground microscope; incidentally, it might have been useful if a more detailed account of how to set up and examine a dark-ground specimen had been included.

Here and there we find what seem to be rather important errors, such as (p. 152): "serologic test is of the greatest value from two weeks after the infection has occurred." Surely this should read, "after the appearance of the primary lesion." And on page 154, "report results as . . . doubtful (complete haemolysis)," should read, "incomplete haemolysis." In general the average reader would have been glad of a rather fuller section on false positive serum reactions. On page 256 occurs the word "seroprimary," which conveys to us no meaning at all; while on page 473 is the statement, "Organism (*Spirochaeta pallida*) . . . does not remain active, even under the most propitious conditions, for more than 48 hours"; this has been disproved by specimens which have crossed the Atlantic by ship several times and still retained their motility. These are a few shortcomings in an otherwise excellent account; it is the treatment described which lends itself most to criticism. Few modern syphilologists would agree with Plan A for early syphilis: why wait to start treatment till the first visit after the diagnosis; why not start at once, and why not start with an arsenical? On page 243 bismuth subsalicylate is described as oil-soluble, whereas on page 222 it is called a suspension, and the average weekly dose is 1 c.cm.—surely a very small one. The introduction of mercury rubs for early syphilis seems unconventional, and would hardly be necessary if the dosage of bismuth had been larger. No particular preference is shown for mapharsen over neoarsphenamine, but it is at least questionable if 0.01 g. of the former is equal to 0.1 g. of the latter in therapeutic effect; in the massive 5-day therapy it took 1.2 g. of mapharsen to produce as good results as 4.5 g. neoarsphenamine. It is of interest to note that for certain types of neurosyphilis Howles favours the Swift-Ellis treatment, one which many regard as *démodé*; and for non-specific protein therapy he gives his typhoid vaccine subcutaneously (p. 453); most people find the intravenous route more effective.

Taken as a whole this book gives an excellent account of the clinical picture, but the treatment recommended will not appeal to everyone; errors and omissions will, it is hoped, be corrected in a future edition. Nowadays, with syphilis so rife, what is wanted is an authoritative guide for the practitioner, and one which can be relied upon as correct in every detail.