ATEBRIN TREATMENT IN MALARIA

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As medical practitioners who have used the new synthetic drug, atebrin, in the treatment of malaria, both parenterally and orally, since January this year, we feel we would be doing a service to the public, and to the profession, by reporting our experiences with it.

We have a large outdoor practice, both amongst villagers and town residents: in the former case, we are not able to follow up all our treatments, but we receive confirmation of the good results of the atebrin treatment, from the attendances at the dispensary and requests for injections of the drug, from villagers coming from the same locality as those who have already been treated. In the case of town patients, and pupils of colleges and schools, we keep in touch with them all, and are able to confirm the good results that have followed.

In other cases, where we cannot maintain personal contact ourselves, we have the statements of friends of our patients, so that, on the whole, we exercise a certain amount of control over as large a number of cases as private practitioners can hope to do.

Since January this year we have treated over 3,500 cases *by injection* with atebrin di-hydrochloride, or atebrin musonate. In this series we have not had a single case of collapse after injection, and *no deaths* attributable to the drug. Cases of mental excitability after treatment with the drug have been extremely rare, about five per thousand. In such cases the condition is readily controlled by sedatives, such as the bromides and chloral, and eliminants such as citrate of potash, combined with glucose administration; but in view of the fact that we have seen mental excitability approaching insanity, as a result of malaria, in cases which have had neither atebrin nor quinine, we cannot solely attribute this symptom to the use of atebrin. Occasionally, patients complain of bad headaches after the drug, also restlessness and insomnia following the first injection, which symptoms disappear after the second injection. In a few instances, we have noticed plentiful crops of sudamina with itching of the skin, all of very temporary duration, till satisfactory excretion of the drug takes place, as evidenced by the discoloration of the urine. Instances of irritability of the stomach and vomiting of bile have occurred after oral treatment, but this we cannot put down to the use of atebrin, as these disabilities arise in cases of malaria treated with other drugs, or in untreated cases, in forms known as the 'bilious remittent', and algid types. We are of opinion from our prolonged use of atebrin, that any temporary disabilities, such as we have mentioned, are more than counter-balanced by the dramatic results obtained from its use. In our experience both salts have proved extremely efficacious, but we have used somewhat smaller doses than those advocated, and in all cases we have supplemented the parenteral treatment with subsequent oral administration.

As to dosage, we use for male adults injections of 0.15 gramme of the di-hydrochloride, and repeat this dose in 24 hours. This is followed by oral treatment of two tablets a day for six days, bringing the total of atebrin administered to 22½ grains (1.5 grammes) for the whole course, which is equivalent to a tablet taken three times a day for five days, as recommended by various writers.

In the case of females, or weak and debilitated males, we use two injections of 2½ tablets each of the di-hydrochloride and follow it up with ten tablets orally, two a day for five days. We have found this sufficient in the great majority of cases to prevent relapses. Previously-treated patients do come back at intervals of 5 or 6 weeks with a return of temperature but in view of the fact that they reside in heavily-infected localities, the probabilities are that they have been re-infected. It is not possible to make blood examinations of all cases in a dispensary practice, but we have often followed up our injection treatment by examining blood films after the second injection. We have rarely seen any ring forms after the third or fourth day and any such appeared in fragmentation, of quarter and half rings. After the fifth day, even after an excitant injection such as adrenalin, we have failed to discover parasites in the blood.

Blazé and Simeons, in their paper in the April number of the *Indian Medical Gazette,* assess the curative dose at 9 grains (0.6 gramme) and while this may be perfectly correct from the view-point of mass treatment, it would not appear to meet the needs of private practitioners in our position. In nearly all the instances in which we have given the drug in the doses prescribed by these writers, we have had our patients coming back after 10 to 14

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The main effects are :—

Pain and cough are immediately relieved,

The consolidation is arrested and regresses,

The patient's distress vanishes and he sleeps well, and

The 'defences' of the body are apparently not interfered with.

REFERENCES

Landau, A., Feigin, M., and Bauer, J. (1931). *Presse Méd.,* Vol. XXXIX, p. 523.

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days with relapses or re-infections. This has led us to supplement the parenteral treatment with the oral, up to 22½ grains, which seems to confer an immunity for at least a month and in many cases for a much longer period; this is all that can be expected with patients living in heavily-infected areas.

A total dosage of 22½ grains seems to be a safe limit for adults, although in resistant cases we have increased the dosage by 9 grains, prolonging the treatment accordingly. Whether occasional resistance is due to the inability of the patient to produce antibodies, or to the recalcitrant nature of a certain type of parasite, we cannot say. In a few cases which did not respond to atebrin we have not hesitated to give quinine.

In very few cases where the temperature had not come down after the second injection, we have given a third injection of 4 c.cm. (2 tablets of 0.75 grain each); but we wish to emphasize the fact that these were rare exceptions, while in a considerably greater number of cases the opposite had occurred, namely, one injection sufficed to reduce the temperature; in these latter cases (where one injection reduced the temperature), there was a good deal of sweating.

In a number of cases where a tonic and stimulant appeared indicated, we have followed up our treatment with 'plasmochin silver tonic' with excellent results. We do not otherwise use plasmochin.

Pregnant uterus.—We have used atebrin in pregnant cases with the happiest results. Uterine contractions and premature labour, as observed after the administration of quinine, were entirely absent.

Spleen.—The effect of atebrin in large spleens is truly remarkable.

Kidney.—In a case of pyelitis, with blood and pus in the urine, atebrin was injected, owing to a concomitant malaria, with very satisfactory results.

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MENTAL DERANGEMENT IN MALARIA CASES TREATED BY ATEBRIN-MUSONATE INJECTIONS

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MENTAL excitation, psychoses and other forms of temporary insanity following the oral administration of atebrin have been described by various writers, including Kingsbury (1934). Disordered mental conditions are now well recognized sequelæ of the treatment of malaria

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Pain and abscess.—Pain at the site of injection is negligible, and most patients never complain at all. We have, in our series of cases, *never had an abscess*, nor has a single case of tetanus occurred. We may mention that we have used atebrin injections on a child 21 days old, with a very large spleen; complete recovery followed.

Cerebral cases.—Cases of cerebral malaria, brought in in an unconscious condition, have responded marvellously to intravenous injection, two tablets of the di-hydrochloride being found sufficient to effect a return to consciousness.

Toxicity.—As regards the toxic effects of the drug, we would like to cite one case we had, in which after an injection of 0.15 gramme of the di-hydrochloride, the patient confessed to the doctor that he had already swallowed 10 oral tablets on that day, in his desire to shake off the fever quickly. He suffered no ill-effects from the big dose and was at his work the next day.

As regards atebrin musonate, we use a smaller parenteral dose than that used by Blazé and Simeons. We give adults parenterally half the quantity recommended by them, and follow it up with oral treatment to bring the total dose up to 22½ grains (1.5 grammes). The following is the table of dosage adopted by us :

	Hydrochloride			or	Musonate		*plus* Oral treatment following either		
	Number of injections	Number of tablets in each injection	Total in grains		Number of injections	Number of ampoules in each injection	Total in grains	Tablets daily	Days	Total grains by mouth
Adults ..	2	3	4½		2	1½	4½	1 × 2	6	18
Children—										
up to 1 year ..	2	½	¾		2	¼	¾	½	6	4½
1 to 2 years ..	2	1	1½		2	½	1½	½	5	3¾
2 „ 3 „ ..	2	1	1½		2	½	1½	½	8	6
3 „ 5 „ ..	2	1½	2¼		2	¾	2¼	½ × 2	6	9
5 „ 8 „ ..	2	2	3		2	1	3	½ × 3	5	11¼
8 „ 10 „ ..	2	2	3		2	1	3	1 × 2	5	15