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The Treatment of *T. brucei* Infection of Equines with Antimosan.

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THE writer (1930) reported on the use of Antimosan in the treatment of *Trypanosoma brucei* infection of equines. In that report the beneficial effect was clearly shown and in one case the horse was sterilised. It was decided to continue the experimentation to determine more exactly the probable requirements as far as the dose and the intervals between administration were concerned. The advantage of treatment with this drug would be the ease of administration, the subcutaneous route being the one employed.

ARRANGEMENT OF THE EXPERIMENT.

Five horses were utilised in the experiment. The intervals of administration were one week, two weeks, and three weeks. The doses were 3·75 gm. and 5·25 gm., repeated a number of times, and ascending doses of 3 gm., 5 gm., and 9 gm. Control of the results of the treatment was based on the result of the examination of stained blood smears, on the appearance of the temperature curve and on the complement fixation test. In a few cases it was possible to test the sterility further by subinoculation into horses and re-inoculation of the presumed sterile.

The table is arranged to give the various details in connection with the treatment of each horse.

TABLE I.

Antimosan Therapy.

Equines.	Weight in Kg.	Number of doses and dosage.	Intervals.	Total used.	Result.
18095	352	6 doses of 5·25 gm.....	3 weeks	31·5 gm.	Sterilisation.
17989	431	6 doses of 3·75 gm.....	3 ,,	22·5 gm.	Failure.
17990	423	8 doses of 3·75 gm.....	2 ,,	30·0 gm.	Failure.
19431	374	8 doses of 5·25 gm.....	2 ,,	42·0 gm.	Sterilisation.
19079	308	3 doses of 3, 6 and 9 gm...	1 ,,	18·0 gm.	Sterilisation.

The weights of the horses were obtained after the completion of the experiment, consequently the weights of the two failures were probably slightly higher, comparatively, than is indicated by the table, for, as a result of a successful treatment, there occurred an improvement in condition. However, even though the horses 17989 and 17990 were failures as far as sterilisation was concerned, yet they also showed a definite improvement in condition. Thus, notwithstanding the slight disparity of weights, the results are regarded as comparable.

It can thus be seen that the dose of 0·75 gm., even though given repeatedly and at intervals of two and three weeks, would appear to be too small to produce sterilisation in the two horses 17989 and 17990. In these two cases failure was determined by the detection of *T. brucei* in blood smears in the 9th week and 13th week respectively, by a positive complement fixation test in both, and by reappearance of the *T. brucei* temperature curves in the 11th week in both cases. Blood of horse 17989 was furthermore subinoculated into a number of other horses, it being used as a reservoir of *T. brucei* always with positive results. This horse died two years after receiving its last treatment. It harboured *T. brucei* during this period and remained in fair condition.

Of the three horses that were sterilised, one was treated at one-weekly intervals, one at two weeks and one at three weeks. Longer intervals were not feasible, because on account of the severity of *T. brucei* infection in horses the reappearance of trypanosomes in the blood is associated with a rapid loss of condition and the development of marked symptoms. Trypanosomes were not found in these three horses during the intervals between treatment, but were found during the intervals in the two failures in one case as early as the 11th day. This finding might be regarded as additional evidence that the dose used in the failures was on the small side.

A difficulty in the study of the chemotherapy of trypanosomiasis is that of determining when an animal is sterilised. For example, in the case of horse 19431 and also of horse 18095 it is quite likely that sterilisation had been obtained long before the cessation of treatment. Of great interest in the matter of the dosage is the sterilisation obtained in horse 19079. From the information obtained from the two failures, the first dose used, namely, 3 gm., may be regarded as too small to produce sterilisation. Consequently sterilisation must have been produced by either the 6 gm. or the 9 gm. dose. There would not, therefore, have been any interference with the efficacy of the subsequent doses by the administration of the first dose. The same probably holds good in the cases of the other two sterilised animals, for in the previous experiment the use of two doses each of 6 gm. at an interval of a week did not produce sterilisation.

The ascending doses which totalled 18 gm. were the most economical in this experiment, but it is quite likely that a reduction in the total amount used in the other two cases of sterilisation might be brought about by decreasing the number of doses. From the point of handling which is always of importance in dealing with horses which are not as a routine handled daily, the use of large doses is indicated, whether of the same size or ascending cannot now be stated.

The most important and, as has already been pointed out, difficult point in the efficient control of the results obtained in the treatment of trypanosomiases is the determination of sterility. After treatment with antimosan *T. brucei* becomes extremely rare in the blood. Consequently negative blood smear examinations is not of great significance unless it be carried on over a long period and receives the support of other evidence, e.g. the temperature curve. But better still is the subinoculation of blood into horses which are then examined. The complement fixation test and re-infection have also been utilised for the purpose. The former gives good results but, unfortunately a horse does not become negative for some little time after sterilisation. The latter was used in all three cases. It naturally results in the re-infection of the animal if it is sterilised, a condition which might not always be desirable even under laboratory conditions and never can be under field conditions. It is proposed to deal with each of these methods of determination of sterility in the three sterilised horses in turn.

Blood smear examination showed that each of the three horses was positive before treatment was commenced. Smear examinations were carried out three times weekly. To illustrate the difficulty of detecting *T. brucei* which one meets with at times, one might mention horse 19079 which only showed *T. brucei* once in blood smears over a period of 13 weeks. During the treatment of horse 19079 no trypanosomes were found. Complete smear examination subsequent to treatment was not carried out, for there were horses available for subinoculation. In horse 19431 smear examination was carried out during and for 12 weeks after cessation of treatment with negative results. In horse 18095 similarly for a period of 11 weeks negative results were obtained.

The temperature curve was available for horse 19079 for six weeks when re-infection was carried out, and for horses 19431 and 18095 for 17 weeks. The indications were that none of the three were infected. The temperatures were somewhat irregular in horses 19431 and 18095 during the last interval, i.e. before the administration of the last dose.

The complement fixation test was carried out on the horses in the experiment. They all gave positive results either before or during treatment. The ultimate test, of course, in horses 18989 and 17990 was positive. In horse 19079 the test was positive two days before the last dose of antimosan, but was negative on the 28th day after cessation of treatment. This negative result was obtained on the 42nd day after commencement of the treatment. In horse 19431 the test was positive after four doses had been given and became negative 11 weeks after the last dose, being doubtful during the 7th week. In horse 18095 the test was negative after the third dose and also during the 6th week after the last dose. The former of the two results in horse 18095 is rather surprising, for it seems to indicate that sterilisation must have been produced by either the first or the second dose, a possibility which is not supported by the temperature curve. At any rate, it can be said that the complement fixation test becomes negative within a short period after sterilisation.

As further cases of *T. brucei* infection were required for another experiment the opportunity was taken to test the sterility of horse 19079 by the injection of 50 c.c. of blood of this horse into horses 18095 and 19431. These two were then kept under observation for 15 days with negative results as far as the blood smears and temperatures were concerned. Their susceptibility was proved by the injection of 50 c.c. of blood of horse 17989, one of the failures. In both cases trypanosomes were found in the blood smears on the 4th day, temperatures of 106 and 106·2° respectively being recorded on that day.

The observations in connection with the susceptibility of horses 18095 and 19431 and subsequently of horse 19079 which when injected with blood of horse 17989 also became infected, are regarded as a good method of determining sterility, because the same strain of *T. brucei* was utilised.

These results obtained in the treatment of *T. brucei* infection of horses are definitely promising. It would seem that no difficulty would be experienced in obtaining sterilisation if the dose be sufficiently larger. The ease of administration and furthermore the cost of the course of treatment are both in favour of the use of Antimosan for this trypanosomiasis of horses.

LITERATURE.

PARKIN, B. S. (1930). Antimony therapy in equine trypanosomiasis (*Trypanosoma brucei*). *16th Rept. Dir. Vet. Serv. & Anim. Indust.*, Union of S.A., pp. 55-60.