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Surfen C. Therapy in *Trypanosoma congolense* Infection in Bovines and Ovines.

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THE only drugs that have up to the present been shown to be effective in the treatment of *T. congolense* infections are the antimony compounds.

Prior to the advent of Antimosan reliance was placed on Potassium Antimony Tartrate. This drug however is not very satisfactory because it has to be administered by the intravenous route, which factor militates against its general application under ranching conditions, especially when repeated injections are necessary.

Antimosan which is described as a complex of a trivalent antimony preparation with a pyrocatechin derivative was subsequently placed on the market, and this drug can be administered either subcutaneously or intravenously. Parkin (1930) concluded that as far as ease of administration is concerned Antimosan is immeasurably superior to Potassium Antimony Tartrate and that sterilization of bovines infected with *T. congolense* is obtained by the subcutaneous injection of 3 gms. Antimosan when given at four weekly intervals.

While there can be no objection to Antimosan as regards efficacy and local tolerability the fact that it has to be repeated three or four times is certainly a disadvantage. When therefore Surfen C. was made available with a claim that about 10 mg. per Kg. bodyweight given in a single dose either intramuscularly or subcutaneously will be a certain sterilizing dose in animals infected with *T. congolense*, it was hoped that a drug had been produced, which would be as efficient as the antimony preparations while possessing none of the disadvantages of the latter.

Surfen C. (Hochst 6678) is a Bayer preparation and is stated to be an amino-quinoline derivative, easily soluble in water. It is claimed that intramuscular injections are well tolerated without producing any general or local reaction.

It is claimed that " in calves the early treatment of a fresh congolense infection with even a single intramuscular injection of 5 mg. per Kg. effects a cure. In an infection existing for three months, three treatments each with 10 mg. Surfen C. per Kg. effected a complete cure.

" In experiments on sheep infected with *T. congolense* it was found that 10 mg. per Kg. Surfen C. cures every stage of the infection both in early and late treatment. . . . Fresh artificial infections of *T. congolense* in which treatment is initiated immediately after the appearance of trypanosomes in the blood can be completely cured with two subcutaneous injections of 5 mg. per Kg. given at an interval of one week. Also infections which had existed for one and three and a half months respectively were similarly treated with a single administration of double the above dose."

Surfen C. has been subjected to tests in various parts of the African Continent, but the reports regarding its efficacy and local tolerability are conflicting.

In Tanganyika, Hornby (1933) concludes that " The result which may be expected to follow a single intramuscular injection of Surfen C. is at least as good as the result to be expected from a course of five weekly injections of Antimosan or Tartar Emetic. . . . A local effect of slight swelling and tenderness, with or without slight lameness, and persisting for a few days was produced. . . . Post-mortem examination three to five days after injection showed no definite necrosis; merely hyperaemia and discolouration of fascia. Subcutaneous injections produced severe swellings lasting for weeks and are contra-indicated."

Mettam (1934) used the drug in the treatment of 19 head of cattle infected with *T. congolense* in Uganda, with the result that one animal died, but the rest " cleared up ". He divided the dose (100 c.c.) into two parts and injected intramuscularly into either gluteal muscle and states that there is normally no local or systematic reaction. Mettam subsequently (1935) concluded that " this drug is the best trypanocidal agent available for the treatment of cattle trypanosomes. The antimonials are most efficacious against *T. congolense* and have but little action on *T. brucei*. Surfen C. on the other hand acts on all three cattle trypanosomes. Standardization of the preparation by the makers and the placing of it on the market as cheaply as possible is urgently needed ".

After testing the drug on 14 horses in the Sudan, Bennett (1936) states that it is certainly capable of curing nearly all, if not all, cases of *T. congolense* in horses, but he regards the extreme variability of individual response to the drug as a serious drawback. A single injection frequently fails to sterilize and in one case as many as eight injections totalling 28·75 gms. had to be given before subinoculation showed the animal to have been sterilized. Troublesome local swellings are stated to be an added disadvantage.

His co-worker Evans (1936) concludes that in the case of cattle a single dose of Surfen C. offers as high a hope of effecting a complete cure as does a full course of Antimosan treatment.

In a memorandum submitted to the Conference for Co-ordination of Tsetse and Trypanosome Research in East Africa (1936), Danks and Daubney, of Kenya, give the results obtained by treating bovines with different issues of Surfen C.:—

(1) Two treated, both relapsed.

(2) Two treated, both sterilized.

(3) Five treated, four relapsed.

(4) Four treated, all regarded as cured.

Daubney is doubtful about the effect of the drug and believes that it has not yet been adequately standardized.

Stewart (1935) after treating animals with antimosan, tartar emetic and Surfen C. in the Gold Coast, expresses the opinion that treatment by Surfen C. does not appear to be nearly as effective as tartar emetic and other antimony preparations, though Surfen C. appears to be useful after antimony treatment to prevent relapses.

In Nigeria, Lester (1934) found that with sheep infected with *T. vivax* and *T. congolense* a dose of 10 mg. per Kg. proved to be more effective than a standard dose of tartar emetic, but three doses of Surfen C. given at weekly intervals did not prevent relapse. Six bovines were given three weekly doses of Surfen C. (10 mg. per Kg.) and twelve were given single doses of the drug. The experiments were complicated by an outbreak of rinderpest but from the point of view of a definite cure the results were not good as the majority of animals relapsed within a few weeks.

According to the 1935 report of the Veterinary Pathologist for Nigeria, six animals artificially infected with *T. vivax* which is the common trypanosome of cattle in Nigeria were treated with Surfen C. Two of these succumbed to trypanosomiasis, one continued to show *T. vivax* in smears, and though smears from the other three were negative, they continued to remain in a very emaciated condition. Large swellings, especially after injection of the salt solution, are mentioned as an objection to the use of Surfen C.

In a progress report on research on trypanosomiasis in Southern Rhodesia, Bevan (1937) states: "A number of drugs . . . have been tested as to their curative and preventive effects against various species of trypanosomes. The results in small animals have been disappointing. The so-called Surfen C., much vaunted as a remedy for *T. congolense* infection elsewhere, has not proved as successful against the local strains of trypanosome."

Method.

The animals used in the experiments under review were all artificially infected with various strains of *T. congolense* and were at no time exposed to natural infection.

Three different issues of the drug were used, and for the purpose of differentiating between these they are referred to as A, B and C.

Batch A consisted of the powder made up in ampoules each containing 2·5 gms., which was dissolved in 100 c.c. sterile distilled water.

Batch B was in liquid form as a 2·5 per cent. solution for intramuscular injection.

Batch C was a powder similar in appearance to A but stated to be less irritant. This was also injected in a 2·5 per cent. solution in sterile distilled water.

In view of the severe local and general reactions obtained by some of the other workers by the subcutaneous and intravenous injections of the drug, it was administered only by the intramuscular route in the present series of experiments. In bovines the injections were made into the gluteal and semi-tendinosus muscles and in sheep exclusively into the latter. No two injections were made at the same place.

Temperatures of the animals were taken twice daily, and blood smears daily excepting Sundays. In those cases in which smear examination was negative for some period following treatment subinoculations into cattle or sheep were carried out, and only when the latter yielded negative results were the animals in question pronounced sterilized.

The site of injection was examined at frequent intervals to observe the local reaction, and two bovines were subsequently killed for post-mortem examination of the injected areas. The injection of the first full dose given to bovine 9158 was made in one place, but subsequently all doses of 10 mg. per Kg. were divided into two equal parts and were injected at two different sites.

Local Tolerability.

In sheep the injections caused some degree of swelling accompanied by pain and lameness, which persisted for three or four days. In only one case (Sheep 45345 treated with batch C) did the swelling persist for about two months subsequent to the injection.

The local reaction was much more severe in bovines. Intramuscular injection of doses of 5 mg. per Kg. Surfen C. in a 2·5 per cent. solution produced in all cases painful swellings accompanied by lameness. The swellings persisted for some weeks or even months after injection and eventually subsided gradually and became hard persistent areas in the skin at the site of injection.

Bovines 5189 and 5198 were slaughtered on 18th November, 1936—over seven months after the last injection was made. Post-mortem examination showed localised schlerodermia with chronic myositis, subcutaneous melanotic areas at the sites of injection, and infiltration of the perivascular tissue and interfibrillar connective tissue with macrophages containing dark brown granules.

There appeared to be no variation in the intensity of the local reaction set up by the three batches of the drug.

The intramuscular injection of Surfen C. in the recommended doses was not followed by any general symptoms.

Discussion.

Full details concerning the experiments carried out to test the therapeutic value of Surfen C. in the treatment of *T. congolense* infection in bovines and ovines are given in Tables I and II. In the former it will be seen that the full recommended dose of 10 mg. per Kg. was given in the first instance to bovine 5198. This failed to sterilize, and in view of the very severe local reaction which it produced, an attempt was subsequently made to ascertain whether it was possible to obtain better results by administering smaller doses at varying intervals.

This animal was, therefore, given two doses of 2·5 mg. per Kg. each at an interval of twenty-four hours followed later by three similar doses. Thereafter two doses of 5 mg. per Kg. were given on two consecutive days and ultimately two injections, each consisting of 2·5 mg. per Kg. Surfen C. and 15 c.c. Antimosan, all of which failed.

The initial treatment for bovine 5189 consisted of two doses of 2·5 mg. per Kg. within twenty-four hours. After this, treatment at longer intervals was tried, five doses each of 5 mg. per Kg. being given at intervals of seven days.

Over a period of seven months bovine 5198 thus received 10 injections totalling 37·5 mg. per Kg. Surfen C. and 30 c.c. Antimosan without sterilizing, while 30 mg. per Kg. Surfen C. administered to 5189 in seven doses failed similarly.

Treatment at longer intervals, consisting of five doses Surfen C. each of 5 mg. per Kg. applied at weekly intervals to bovine 5526 failed to produce even a temporary disappearance of the parasites.

The full dose of 10 mg. per Kg. was reverted to in the treatment of No. 6026. The first two injections failed and sterilization was only effected by the third which, incidentally, was responsible for very marked swellings at the sites of injection.

In sheep initial treatment, consisting of two doses of 2 and 2·5 mg. per Kg. each given at twenty-four hours interval failed, while two injections of 5 mg. per Kg. given at a similar interval sterilized in one case (40933) and failed in another (41104).

As in the case of bovines, treatment at longer intervals with 5 mg. per Kg. given weekly failed (41104).

The full dose of 10 mg. per Kg. given all at once sterilized in one case (42768) but failed in two others (41029 and 45354).

It is apparent that the workers who have recorded good results from the use of Surfen C. are not all entirely convinced as to its efficacy. Mettam and Daubney both draw attention to the fact that the drug is not adequately standardized, and Danks and Daubney

are of opinion that later issues appear to be more effective. This view is not confirmed by the results of the present series of experiments, all three issues of the drug having failed equally badly.

The animals in these tests were stabled, and whether this lack of exercise could in any way have aggravated the local reactions cannot be definitely stated at present. These reactions, however, were of such a serious nature that even if the drug was 100 per cent. efficient therapeutically one would still be hesitant in recommending its general use by the intramuscular route.

The damage done by the drug to the subcutis and the musculature would seriously reduce the value of treated animals for slaughter purposes.

Conclusions.

(1) The intramuscular injection of Surfen C. in the treatment of *T. congolense* infection in bovines and ovines was found to be ineffective.

(2) The intramuscular injection of Surfen C. into bovines caused serious local reaction.

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TABLE I.

Surfen C. Therapy in T. congolense *Infection in Bovines.*

Bovine No.	Date Infected.	Date Trypanosomes Appeared.	Date Treated.	Dose in mg. per Kg.	Batch of Drug Used.	Smear Examination Negative.		Remarks.
						From.	To.	
5198	23.8.35	2. 9.35	12.9.35	10	A.	16. 9.35	11.10.35	Unsuccessful.
			31.10.35	2·5	A.	6.11.35	12.11.35	Unsuccessful.
			1.11.35	2·5	A.			
			20.11.35	2·5	A.			
			21.11.35	2·5	A.	23.11.35	5.12.35	Unsuccessful.
			22.11.35	2·5	A.			
			11.12.35	5	A.	17.12.35	31.12.35	Unsuccessful.
			12.12.35	5	A.			
			9. 3.36	2·5 + 15c.c Antimosan 12 per cent.	B.	—	—	Unsuccessful.
			7. 4.36	,,	B.	—	—	Unsuccessful.
5189	23. 8.35	31. 8.35	18.10.35	2·5	A.	19.10.35	13. 1.36	Unsuccessful.
			19.10.35	2·5	A.			
			9. 3.36	5	B.			
			16. 3.36	5	B.			
			23. 3.36	5	B.	9. 3.36	25. 5.36	Unsuccessful.
			30. 3.36	5	B.			
			7. 4.36	5	B.			
5526	28. 2.36	7. 3.36	11. 3.36	5	B.			
			18. 3.36	5	B.			
			25. 3.36	5	B.	—	—	Trypanosomes failed to disappear.
			1. 4.36	5	B.			Unsuccessful.
			9. 4.36	5	B.			
6026	12. 1.37	21. 1.37	30. 1.37	10	B.			Trypanosomes failed to disappear. Unsuccessful.
			19. 2.37	10	B.	26. 2.37	13. 3.37	Unsuccessful.
			24. 4.37	10	C.	26. 4.37		Sterilized.

TABLE II.

Surfen C Therapy in T. congolense *Infection in Sheep.*

Sheep No.	Date Infected.	Date Trypanosomes Appeared.	Date Treated.	Dose in mg. per Kg.	Batch of Drug Used.	Smear Examination Negative.		Remarks.
						From.	To.	
43349	16.10.35	23.10.35	30.10.35	2	A.	1.11.35	15.11.35	Unsuccessful.
			31.10.35	2	A.			
			22.11.35	2·5	A.	29.11.35	9.12.35	Sheep killed on 24.12.35.
			23.11.35	2·5	A.			
40933	19.11.35	29.11.35	11.12.35	5	A.	14.12.35	—	Sterilized.
			12.12.35	5	A.			
41104	16.10.35	24.10.35	30.10.35	2·5	A.	2.11.35	26.11.35	Unsuccessful.
			31.10.35	2·5	A.			
			11.12.35	5	A.	13.12.35	14. 1.36	Unsuccessful.
			12.12.35	5	A.			
			9. 3.36	5	B.	12. 3.36	31. 3.36	Unsuccessful.
			16. 3.36	5	B.			
			23. 3.36	5	B.			
			30. 3.36	5	B.			
42768	19.11.35	20.12.35	9. 3.36	2·5 + 5c.c Antimosan	B.	10. 3.36	1. 4.36	Unsuccessful.
			2.11.36	10	B.	4.11.36	—	Sterilized.
41029	18. 8.36	29. 8.36	8. 9.36	10	B.	8. 9.36	26. 9.36	Unsuccessful.
			28.10.36	10	B.	—	—	Died on 29.10.36.
45354	22. 3.37	2. 4.37	24. 4.37	10 mg.	C.	26. 4.37	29. 4.37	Unsuccessful.