

CHEMOTHERAPY IN ANIMAL TRYPANOSOMIASIS
IN SOUTHERN RHODESIA.

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The first employment of Trypanocidal drugs in this Colony was in 1909 by L.E.W. Bevan, when, after a visit to the Pasteur Institute at Paris, he introduced a method of treatment with alternating doses of antimony and arsenic. He later established that it was the antimony salt which was the main effective element in the treatment. Thereafter antimony potassium tartrate was employed as the stock treatment and it was claimed in 1928 that "during the past eighteen years antimony had saved the lives of thousands of animals". In 1928, experimentation to establish Nagana tolerant animals by inoculating with a *Tr. congolense* strain, standardised in sheep, controlling the resulting infection with antimony to produce a pre-immune state, did not prove successful as challenge of such animals with gross 'fly' resulted in heavy natural infection with *T. vivax*.

In 1932 - 35, an experimental station was established in the Golden Valley 'fly' area where it was proved practicable to maintain cattle in a fit condition for work, milk production and breeding, provided a proper system of management combined with early detection of Nagana cases and immediate antimony treatment was adopted.

The use of antimony potassium tartrate continued and Antimosan, having proved equally effective, was also used to a limited extent until these drugs were superseded by the Phenanthridinium compounds.

The first use of Phenanthridinium was in 1946 when small quantities of 897 were used in the Eastern Districts. Affected cases treated with this drug showed little improvement and infection persisted despite injections at monthly intervals. These were cleared of apparent infection with 1553 - Dimidium Bromide - intravenously,

but clinically showed little improvement. In 1948 the first major trial of Dimidium Bromide was carried out in Mkota Reserve when 'block inoculation' of herds wherein infection had been confirmed was first practiced. In 4,723 cattle, smears of 10% had revealed a 9.3% infection and 121 head had died of Nagana in the ten weeks previous to block inoculation. The first survey carried out four months later showed that only five head had died in the intervening period and only two of these were confirmed Trypanosomiasis cases.

From these results it was concluded that the value of this method of control in an area which could not be regarded as a permanent fly habitat was high, no adverse results being recorded and mortality being materially reduced.

The Dimidium Bromide was injected as a freshly prepared three per cent solution at the rate of 1 c.c. per estimated 50 lbs live weight, by the intravenous route.

With the spread of infection to Chikwizo and Urungwe Reserves, greater use was made of the drug in 1949 and 1950. A total of 11,300 head was block inoculated, mortality being immediately arrested and no ill effects as described elsewhere were observed. 300 injections were performed on European farms only one case of a mild photosensitisation being reported in a Friesland cow. Seventy-three per cent of these cases were caused by *T. congolense*, twenty per cent by *T. vivax* and seven per cent showed mixed infection of *T. congolense* and *T. vivax*.

Further spreads in 1951 lead to the wide spread use of Dimidium Bromide, approximately 20,000 head being inoculated, still with no adverse results. In Mkota Reserve, drug therapy was combined with hand spraying of stock with D.D.T. insecticides but doubt was being expressed as to the future efficacy of the block inoculation in view of so little being done to prevent the Tsetse fly itself becoming fully established in the areas concerned.

In 1952, a major deterioration was recorded within the Colony with spreads of the disease in many areas. Approximately 40,000 head were block inoculated with Dimidium Bromide and photosensitisation was only reported in about 20 head. Despite block inoculations in Urungwe and Mkota Reserves at monthly intervals, it was obvious that drug treatment could not maintain the cattle in the presence of increasing fly density. In Urungwe mortality had mounted to over 3,000 head, and in Mkota only 1,700 head survived out of 4,723. It was decided to evacuate a total of 5,600 head from Urungwe by slaughter. The better conditioned animals were brought in alive for slaughter at the Cold Storage Commission Abattoirs in Salisbury, arrangements being made for all such cattle to be treated with antrycide methyl sulphate and sprayed with insecticides prior to movement. The idea was that should the trypanosomes which they might be harbouring be resistant to Dimidium Bromide these would be eliminated by antrycide, a drug which had not been previously used in Southern Rhodesia. Eight hundred and ninety two smears were prepared from these animals at slaughter and, in spite of the fact that they had been treated ten days or up to a few weeks previously, a hundred and eighteen cases of *T. congolense*, forty of *T. vivax* and one of a mixed *T. congolense* and *T. vivax* infection were discovered, i.e. over 17%. From this it appeared that little if any or even as much benefit could be expected by switching from the use of Dimidium Bromide to Antrycide.

In 1953, despite about 8,000 inoculations with Dimidium Bromide, it was apparent that where fly occurred to a detectable extent, drug treatment had failed miserably. In Mkota Reserve where surviving cattle only totalled 254 out of a total of 4,723 in 1948, it was obvious that repeated inoculations had lead to the production of a resistant trypanosome - many animals had been inoculated 25 to 30 times at 14 day intervals and still showed positive smears. Even in the European occupied blocks, e.g. Karoi, where 'fly' infestation was so light that it could not be demonstrated, some losses from trypanosomiasis occurred

and relapses were not infrequent, despite an intensive system of control by Veterinary Officials. In an effort to overcome this apparent drug fastness and the comparatively high relapse rate, the dosage was increased from 1.3 mg/kilo to 2 mg/kilo and greater attention was paid to accurate weight assessment of the affected cattle. Even so, relapses continued to occur at intervals of approximately a fortnight in many cases.

Being thus faced with drug resistance, consideration had to be given to the use of other drugs. Antrycide obviously had to receive particular consideration but this drug had given most disappointing results previously in the treatment of cattle evacuated from Urungwa Reserve. It had also been widely recorded elsewhere as a drug against which resistance is comparatively easily established under conditions where re-infection takes place. In view of the above, Antrycide was used on only a few cases, too few to constitute a danger and too few from which to draw accurate conclusions. Nevertheless, at least one case of failure of the drug to prevent further relapses was observed.

Most attention was, therefore, given to trials with a new trypanocide, Ethidium bromide. This drug was issued for administration as a 2% solution intravenously after laboratory trials as to dosage etc. and various dosage levels were employed. Persistent Dimidium Bromide relapse cases were selected for the trials, and it was recorded that Ethidium also failed to cure, relapses occurring at about the same rate as had come to be expected with Dimidium.

Arrangements were made to remove four of these persistent relapse cases from all possible re-infection and treat them at higher dosage rates with Ethidium and other drugs. They were put into fly-proof stables at a Research station and kept under continuous observation, including temperaturing and smearing. All four showed *T. congolense* infection on arrival. No. 5 was moribund, No. 6 and No. 88 were in moderate condition. No. 10 is fairly well recovered.

(No.5) was given Ethidium at the rate of 5 mg/kilo and the fairly good conditioned one (No.19) Ethidium at the rate of 2 mg/kilo. One of the other two cattle (No.88) received Antrycide methyl sulphate at the rate of 5 mg/kilo and the other (No.6) 25 c.c. of 5% tartar emetic solution intravenously.

No.5 was killed "in extremis" two days after treatment and although the treatment had, by then, caused a complete disappearance of parasites from the smears, the post-mortem lesions were typical of Trypanosomiasis.

Daily smears from No. 6 (Tartar emetic treated) remained negative from the day after treatment, and treatment was repeated at 5 day intervals until a total of six injections had been given. This animal died within 24 hours of the final injection, death being due to Tartar emetic poisoning.

No.19 remained negative on daily smears till the 59th day following Ethidium treatment, when *T. congolense* was again present in the smears. On the 63rd day it was given Antrycide methyl sulphate at the usual rate of 5 mg/kilo and remained negative thereafter.

No. 88 (Antrycide treated) became negative on smears the day after treatment and remained so thereafter.

It appeared that Antrycide was effective in bringing about cure in cases that showed resistance to treatment with either ethidium or Dimidium Bromide, provided the animals were well cared for. Nevertheless, where re-infection is a probability, i.e. in a tsetse area, there is the fear of establishing Antrycide resistance.

In 1954, over 12,000 Dimidium inoculations were performed and this was the first occasion when a high percentage of photo-sensitisation occurred. About 10% of a herd of 1,765 re-acted following two block inoculations at 14 day intervals.

In 1955, approximately 36,000 inoculations were performed with

Dimidium and actual mortality as well as photo-sensitisation was recorded, particularly in the Eastern Districts. In one block inoculation of 2,326 cattle, 322 deaths were reported with at least 200 severe cases of photo-sensitisation. This area could not be reached due to floods, and investigations unfortunately could not be undertaken. In one area, where about 100 deaths and many more cases of photo-sensitisation were reported, it was postulated that simultaneous grazing on lands where Lantana species was the predominant feed, might have materially added to losses and photo-sensitisation but this seemed dubious in view of our similar losses and adverse results in other Reserves where few or no Lantana species were recorded.

Heavy infection of donkeys in Urungwe Reserve with *Tr. brucei* were reported in 1955, 74 deaths being recorded out of a total of 214. Treatment with Antimosan being unsuccessful, 7% Berenyl was employed at the dosage rate of $2\frac{1}{2}$ c.c. per 50 lb. Most donkeys recovered after one treatment with no relapse. One dog infected with *T. congolense* and one with *T. brucei* were also successfully treated with Berenyl.

During 1955 there was a considerable spread of trypanosomiasis threatening over 17,000 head of cattle. It was considered impracticable to treat these regularly with intravenous injections of Dimidium bromide and it was also feared that such treatment might again fail as it had done in the Urungwe and Mkota reserves should 'fly' density increase. Accordingly it was decided to attempt control with the more easily applied Antrycide prosalt which is also designed to exert a chemoprophylactic effect. This antrycide campaign was started by inoculating 13,591 head, the dosage rate being strictly in accordance with the maker's schedule, but 179 deaths from antrycide poisoning occurred. Representatives of Imperial Chemical Industries visited the area to investigate these losses and decided that under our conditions their dosage rate was too high and recommended the use of

Two further block inoculations have now been carried out without further loss and so far the campaign is giving very good results.

To-date in 1956, 19,275 Dimidium Bromide inoculations have been performed and 13,733 inoculations with Antrycide Prosalt and few adverse results have been reported this year.

It seems to be underlined throughout all our years of drug treatments that if adverse results are to be avoided, block inoculations should be performed when the protein and calcium level of the available grazing is at its highest, when water is easily available and the dehydration factor is absent and that the inoculation of poverty stricken animals, walked long distances to inoculating centres, should be rigorously prohibited.