

The Experimental Treatment of Trypanosomiasis in Animals.

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(Communicated by Professor R. Boyce, F.R.S. Received April 8,—Read May 11, 1905.)

Numerous drugs have been tried in endeavouring to find a therapeutical agent which would cause trypanosomes to disappear from the blood. Of all those tried, arsenic and trypan red are the only ones exhibiting a marked influence on the parasites.

On account of the liability of the appearance of toxic symptoms, the proneness to sloughing at the site of inoculation, and the oftentimes considerable disturbance which occurred after the subcutaneous administration of sodium arseniate, I decided to try if other compounds would be more satisfactory in the treatment of trypanosomiasis. The arsenic preparation which has given the best results is a compound of arsenic and aniline $C_6H_5NO_2As$ (meta-arsensaure anilid, atoxyl), a preparation which has of recent years been used intravenously and subcutaneously in the treatment of skin diseases and anæmia.

The effect of this preparation in the treatment of trypanosomiasis has been observed in an extensive series of experiments during the last 10 months.

Strains used.

T. gambiense.—Five strains. A very virulent one obtained from one of my cases of Sleeping Sickness—this strain exhibited nothing abnormal in its direct passage through a monkey, but after infecting a baboon (*Cynocephalus babuin*), and then passing into a rabbit, it became abnormally virulent.

T. evansi.—Surra. *T. equinum*.—Mal de Caderas. *T. brucei*.—Nagana. *T. equiperdum*.—Dourine. *T. dimorphon*.—Gambian horse.

No animal was treated until a large number of parasites were observed in the blood and definite signs of anæmia and loss of weight determined. Many of the animals were not treated until several months after infection had occurred.

Four methods of treatment were adopted—

- (a) Atoxyl—high doses at intervals of a week.
- (b) Atoxyl—high initial dose and then reduced amounts administered three times a week.

(c) Atoxyl and trypan red combined.

The arsenic preparation given first and then followed in 36 to 72 hours with high doses of the dye subcutaneously.

(d) Trypan red alone.

All of these methods of treatment were continued over a period of several weeks to three months, or until a decided improvement in the general condition of the animal was noticed, especially increase of weight, rise in hæmoglobin and number of erythrocytes, with absence from the blood of the parasite.

In nearly all cases controls were used. In every case the treated animals have survived their controls. From time to time blood was taken from the treated animals and susceptible animals were inoculated. After a varying length of time treatment was discontinued, and some of these animals, after a period of one to three months without treatment, were bled to death, and the whole blood injected into healthy animals. Such control animals have remained uninfected.

RESULTS.

Treatments A and B.

T. gambiense.—Rabbits, guinea-pigs, and rats after one and a-half to three months' treatment have survived. Treatment discontinued four to five months ago.

T. evansi.—One rabbit, two guinea-pigs are alive three months after stopping treatment. It is now seven months since the guinea-pigs were infected.

T. brucei.—Four guinea-pigs, three months after treatment, were bled, and rats inoculated with whole heart blood have remained uninfected during one and a-quarter months. Rabbit two months treated, one month later still well. Twenty rats have survived four months. One rat infected on fifth day of disease when parasites were present, 150 or more to a field, living, and blood negative 84 days later.

T. equinum.—One rabbit, treatment begun only when characteristic discharge from eyes, nose, etc., appeared—treatment for two months—discontinued one month, animal apparently well. Two guinea-pigs have survived three months without treatment. Rats, so far, 101 days.

T. equiperdum.—Pups, one has died from over dose, other negative and general condition better.

T. dimorphon.—Results not so good. Animals have lived a far longer time than controls, but no apparent cure can be recorded.

Treatment C.

With this method animals require treatment for a shorter period, but many have died from toxic effects of the dye; this is especially the case with dogs, pups, and kittens.

T. dimorphon.—Results of combined treatment far more favourable. Experiments in progress. Trypan red alone.

Results with *T. equinum*, rats have lived 197 days.

Effects on animals infected with *T. gambiense*, *T. evansi*, *T. brucei*, *T. dimorphon*, *T. equiperdum*, are in accordance with Laveran's experiments. No definite curative powers remarked.

Experiments with the sodium arseniate treatment of animals infected with the various trypanosomes have given less favourable results. Greater tendency is noted for toxic symptoms and sloughing to occur. High doses cannot be tolerated for a prolonged period. *In my hands the arsenic-aniline compound has given far better results than treatment with sodium arseniate. The advantages of its administration intravenously or subcutaneously in high doses over a length of time, namely, its less toxic properties, the absence of all tendency to cause sloughing, and the apparently longer action of the drug, make me believe that the employment of this compound is indicated in the treatment of human trypanosomiasis.*

The combination with trypan red is worth trying in small doses per os, but the appearance of any indication of nephritis or other toxic symptoms should cause the treatment to be immediately stopped. I have administered in pill-form six to eight grains three times a week for a period of three and a-half weeks without any untoward symptoms. The case was a native suffering from trypanosomiasis; the parasites lessened in number, and by the end of the third week were hardly ever seen.

Ehrlich and Shiga found that they could protect animals if trypan red was administered (either subcutaneously or per os). After five to seven days such animals could be injected with virulent blood containing trypanosomes without infection occurring.

I have injected a goat with increasing doses of trypan red, and, after a time, used its serum. Mice infected with the Mal de Caderas parasite were injected with small quantities of this serum. In four cases the animals lived 31 to 48 days. Experiments in progress.
