IX. ON DRUG AND SERUM-FASTNESS IN A STRAIN OF TRYPANOSOMA EQUIPERDUM USING ALBINO RATS AS HOSTS

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Trypanosoma equiperdum of equine dourine, when injected into rats, exhibits a continuous and progressive infection; that is, the trypanosomes, from the time they enter the peripheral blood, increase in number at a constant rate until the rat dies. These same trypanosomes when injected into some other laboratory animals, such as rabbits, dogs, coyotes, etc., showed infections characterized by irregular increases and decreases in number. The periodic decreases, when the parasites more or less suddenly disappear from the blood, are spoken of as crisis, while their return to the blood is termed relapses. The period of their absence from the blood following a crisis is spoken of as the latent period.

Most of the work reported on trypanocidal antibodies has been worked out by using **in vitro** methods. Schilling (1902) probably first observed that the serum from some infected animals lysed the same species of trypanosomes. Lingard (1904 and Franke (1904) also noted the trypanolytic properties of serums. Ehrlich and Shiga (1904) noted that a mouse cured of an infection with a pathogenic trypanosome is refractory for about twenty days to a second infection with the same strain. Ehrlich (1909), Ehrlich, Roehl and Gulbransen (1909), Rosenthal (1913), and Ritz (1914) showed that relapse strains arrising in infected mice incompletely cured were biologically different from the original strain.

Observations on the trypanolytic property arising in untreated infections have been made by Rodet Vallet (1916), Massaglia (1907), Levaditi and Mutermilch (1910), Leger and Ringenbach (1911), and Ritz (1916).

Very few observations have been made on **in vivo** trypanolysins. Following this type of observations, Diesing (1905), Kleine and Mollers (1906) found that serum made from asses after recovery from infections with **T. togolense** would bring about artificial crisis in mice previously infected with the same species of trypanosomes.

The strain of trypanosomes (**T. equiperdum**) used in these studies was obtained from the late Dr. A. S. Loevenhart of the University of Wisconsin.

The results of these experiments are shown in Tables X and XI. Table X shows the effect of giving rats infected with T. equiperdum a series of treatments with antisera upon each return of the parasites to the peripheral blood following crises. It may be seen that there is little or no effect on the ability of the antisera to produce a second, third, or even a fourth crisis following relapses.

The same general results were obtained using a series of treatments with a standard amount of crystal violet. (See Table XI.) The results as shown in this table were obtained by injecting the amount indicated in the external jugular vein. Each injection was made on the second day of the reappearance of trypanosomes in the peripheral blood. The figures shown are the averages taken from ten rats.

Many workers have found rapid and marked responses taking place in trypanosomes when they are subjected to changed environments. Thus, Ehrlich and others produced drug and serum-fast strains by subjecting them to antisera or trypanosidal drugs. That is, when a crisis had been once produced by the use of a certain drug or antiserum, that particular strain of trypanosomes, the relapse strain, was no longer affected by that particular drug or antiserum.

TABLE No. X

Antiserum from blood of	1st Crisis (in hours)	2nd Crisis (in hours)	3rd Crisis (in hours)	4th Crisis (in hours)
Human	156	134	168	120
Rabbit	144			
Coyote	144	120	144	
Human and Coyote mixed	120			
Averages	141	127	156	120

TABLE NO. XI

Crystal Violet	1st Crisis (in hours)	2nd Crisis (in hours)	3rd Crisis (in hours)	4th Crisis (in hours)
0.30 c. c.	125	126	164	144

Ritz (1914) reported a case of particular interest. Working with mice, he produced seventeen immunologically different relapse strains from an indivdual that had been incompletely cured. In over six hundred mice he found twenty-two immunological strains.

Strange to say, no tendency toward drug or serum-fastness was encountered in these studies. This is difficult to explain, since drug and serum-fastness has been so widely observed. Reference to the above tables shows that rats were treated repeatedly, with the same serum or drug producing a crisis each time. At no time did human serum or crystal violet fail to product a crisis on a relapse strain from previous treatment with these lytic agents.

It seems possible that the effectiveness in these cases may be due to the manner of treatment (intravenous injections) which brought the antiserum or drug immediately and suddenly in contact with the trypanosomes; whereas, with intraperitoneal or subcutaneous injections, contact would be

brought about much more slowly and, therefore, their effectiveness as trypanocidal agents reduced. Furthermore, the fact that parasites living in the tissues at the time of intravenous injections of lytic agents might easily survive to find their way into the blood stream and repopulate it after the lytic qualities of the antiserum or drug had been destroyed by the blood.