

A COMPARISON OF THE CHEMICAL ALTERATIONS IN
THE BLOOD OF RATS INFECTED WITH PATHOGENIC
AND NON-PATHOGENIC TRYPANOSOMES

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In a recent study (1) of some of the factors involved in acute infections with *Trypanosoma equiperdum* in rats it was found that the CO₂ capacity of the serum was lowered, the lipoid phosphorus, and lecithin, increased, and the liver glycogen greatly diminished or absent. The blood sugar, on the other hand, remained at a normal level until late in the disease. Cholesterol remained unchanged in amount, while the non-protein nitrogen and uric acid increased only subterminally with the partial breakdown of the kidneys.

It seemed of interest to investigate the factors which had proved to be influenced in the pathogenic infection, in infections due to the non-pathogenic *Trypanosoma lewisi*, to determine a possible injurious effect of this parasite. The blood sugar in rats infected with this organism has already been reported upon *in extenso* (2), and found to remain normal.

The methods are those that were used in the previous work. The results for the lipoid phosphorus, the calculated lecithin, and the liver glycogen, are given in Table I. Table II summarizes the experiments for the determination of the CO₂ capacity, and Table III contains a comparison between the fatal and the non-fatal infections, in respect to these three factors.

The data for the 21 animals in Table I are arranged to illustrate the rise and fall in number of the trypanosomes throughout the infection. The determinations were made from animals with increasing numbers of trypanosomes up to 450,000 per cubic millimeter (No. 11): the remaining animals were those in which the crisis was passed. The lipoid phosphorus was determined, and the lecithin calculated,

in normal animals before the infection was given, and again when the infection had reached the stage indicated by the trypanosome counts. The percentage of variation between the two determinations is also given.

This variation is positive in 9 cases and negative in 4. The normal range for lecithin, based on the results of this and the previous paper, seems to lie in the rat between about 170 and 250 mg. per 100 cc. of blood. In 4 of the animals only a single determination was made, and all of these lie within the normal range (Nos. 5, 12, 14, and 19). In one animal (Rat 6) the upper limit is transcended, and the variations throughout, both positive and negative, are relatively slight and without the marked upward trend which is apparent in the infections with *T. equiperdum*. These figures for rats are slightly higher than those for human blood as determined with this method by Rosen and Krasnow (3); they found the range to be from 160 to 240 mg.

The figures showing the amount of liver glycogen, calculated as glucose per gram of liver, are also included in Table I. This arrangement does not imply any connection between the two factors. Glycogen is found to be present in significant amounts in every case, and does not vary with the rise and fall of the parasites. This finding is in contrast with the results of Regendanz and Tropp (4). These workers have published figures for 4 rats infected with *T. lewisi*, which show, they believe, that the glycogen is significantly lowered. Their animals had been splenectomized in order to increase the number of organisms in the blood. It is impossible to tell, however, to what extent such an increase has actually occurred, since they do not publish any trypanosome counts; nor are their figures for the glycogen content much lower than "normal," especially in view of the great variations to which this constituent is subject.

Table II presents the CO₂ capacities of the serum of 12 infected rats. All of these animals were taken for study at the time when the parasites were in the stage of rapid increase. The values found are all within the normal range. They show that the rats do not suffer from an acidosis during the infection, although acidosis is present from an early stage in infections with *T. equiperdum*.

TABLE I
Lipoid Phosphorus, Lecithin, and Liver Glycogen, as Glucose, in Rats Infected with Trypanosoma lewisi

Rat No.	Before infection		After infection		Percentage variation	No. trs. per cu.mm.	Glucose. Mg. per gram of liver
	Lipoid p. Mg. per 100 cc. blood	Lecithin. Mg. per 100 cc. blood	Lipoid p. Mg. per 100 cc. blood	Lecithin. Mg. per 100 cc. blood			
1						50,000	12.3
2						75,000	12.0
3	8.9	222.5	10.1	252.5	+13	92,500	
4	8.1	202.5	8.5	212.5	+5	125,000	17.6
5			8.65	216.2		140,000	13.3
6	9.85	246.2	11.6	290.0	+18	150,000	8.1
7	8.25	206.2	10.0	250.0	+21	167,000	8.0
8						200,000	18.0
9	8.6	215.0	9.9	247.5	+15	317,500	7.1
10	9.05	226.2	9.9	247.5	+9	342,000	4.8
11	9.1	227.5	9.0	225.0	-1	450,000	9.8
12			9.5	237.5		200,000	11.0
13	8.9	222.5	8.65	216.2	-3	130,000	35.0
14			8.3	207.5		125,000	9.5
15	8.6	215.0	8.3	207.5	-3	105,000	6.6
16	9.2	230.0	9.3	232.5	+1	100,000	20.4
17	9.15	228.7	8.6	215.0	-6	100,000	
18						100,000	15.5
19			9.05	226.2		62,500	6.1
20	8.8	220.0	9.8	245.0	+11	62,500	
21	7.35	183.7	7.75	193.7	+5	25,000	

TABLE II
Carbon Dioxide Capacity of Serum in Rats Infected with Trypanosoma lewisi

Rat No.	Trypanosomes per cu.mm.	CO ₂ capacity. Vol. per cent
1	100,000	56.0
2	137,000	56.0
3	150,000	64.6
4	175,000	71.1
5	180,000	60.7
6	200,000	63.6
7	200,000	69.1
8	225,000	68.3
9	230,000	69.1
10	237,500	62.6
11	250,000	58.8
12	275,000	64.4

DISCUSSION

Table III gives a comparison of the pathogenic and non-pathogenic infections. In *T. lewisi* rats the lecithin varies from the normal -6 per cent to +21 per cent, and shows an average increase of +6.5 per

TABLE III
Percentage Variations of Lecithin, and Average Liver Glycogen Content, as Glucose, throughout Infections with *Trypanosoma lewisi* and *Trypanosoma equiperdum*

	Lecithin	Glucose. Mg. per gram of liver
<i>T. lewisi</i>	-6 per cent to +21 per cent avg. + 6.5 per cent (9 increases, 4 decreases)	12.6 mg. (no negative cases)
<i>T. equiperdum</i>	+8 per cent to +99 per cent avg. 35.6 per cent (11 increases, no decreases)	1.8 mg. (7 negative cases out of 11)

Variation in CO₂ Combining Capacity at Various Concentrations of *Trypanosoma lewisi* and *Trypanosoma equiperdum* per Cubic Millimeter of Blood

	No. trypanosomes	CO ₂ combining cap. Vol. per cent
<i>T. lewisi</i>	137,500	56.0
<i>T. equiperdum</i>	137,500	37.0
<i>T. lewisi</i>	200,000	69.1
<i>T. equiperdum</i>	200,000	13.6
<i>T. lewisi</i>	237,500	62.6
<i>T. equiperdum</i>	225,000	45.0
<i>T. lewisi</i>	275,000	64.4
<i>T. equiperdum</i>	275,000	35.0

cent; 9 of the animals showed increases and 4, decreases. With *T. equiperdum* all the animals showed increases, ranging from +8 per cent to +99 per cent, and averaging +35.6 per cent. The same difference is shown in the comparison of the glycogen. With *T. lewisi* this constituent was present to an average extent of 12.6 mg. of glucose per gram of liver, and no animals were found in which it could

not be demonstrated; in the livers of *T. equiperdum* animals, on the other hand, it was absent in 7 out of the 11 cases, and averaged for the series 1.8 mg. per gram of liver. The CO₂ capacities are contrasted in 4 sets of animals in which the concentrations of trypanosomes per cubic millimeter were similar. In each case the *T. lewisi* animals show a normal, and the *T. equiperdum* animals an abnormal, capacity.

In general, the table, together with the others in this and the previous paper, shows that the action of *T. equiperdum* on these three factors is not due to the influence of its numbers, since equal numbers of *T. lewisi* are without effect, but to some action which it has upon the host. To apply the term "toxin" to this effect is simply a begging of the question, since no completely acceptable evidence for the existence of such a substance has ever been adduced.

The possibility must be kept in mind that counting the trypanosomes in the peripheral blood may not be a valid method of comparing the extent of the two infections, since large numbers of the pathogenic organisms might be retained in, and have their effect upon, the inner organs. Work now in progress shows that such an "inner action" does occur when guinea-pigs are infected with *T. equiperdum*, in that a severe anemia appears in these animals relatively long before the parasites are demonstrable in the blood stream, or while their concentration is extremely low.

By the study of the factors here discussed it should be possible to determine whether "pathogenic" strains of *T. lewisi* exist. At present, the evidence for the pathogenicity of this organism is not convincing; especially is this so since Marmorston-Gottesman and Perla (5) have shown that death of normal animals infected with *T. lewisi* may really be due to a concomitant infection with *Bartonella muris*.

SUMMARY

Blood samples from rats infected with *Trypanosoma lewisi* give normal values for lipoid phosphorus, lecithin, CO₂ combining capacity, and liver glycogen.

When these results are compared with the results of similar experiments with *T. equiperdum* infections, on the basis of the concentration

of trypanosomes in the blood, it is found that the pathogenicity of the latter organism does not depend upon its numbers as affecting the blood, but that it must be in some other way injurious to the host. Whether the injury is due to a true toxin, an endotoxin, or mechanical interference is not yet known.

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