6477

Apparent Increased Resistance of Vitamin B-Deficient Rats to an Acute Infection.

L. REINER AND J. B. PATON. (Introduced by C. S. Leonard.)

From the Burroughs Wellcome and Co. Experimental Research Laboratories, Tuckahoe, N. Y.

Most recent investigations emphasize the fact that avitaminosis tends to decrease the resistance to infection. However, in a long series of experiments on trypanosome infection of rats *(Trypanosoma equiperdum)* just the opposite effect was produced. The lack of vitamin B complex appeared to increase the resistance. This unexpected phenomenon seems to be worthy of note although a satisfactory explanation has not yet been found.*

The effect was first noticed when one group of infected experimental animals was accidentally kept on a diet low in vitamin B complex and died irregularly and somewhat later than the controls. In further experiments rats were kept on a diet deficient in B complex for as long a period of time as possible. They were then infected with trypanosomes and control rats, receiving the same diet made complete by addition of the vitamin B complex, were infected at the same time with the same emulsion of trypanosomes. The controls survived the infection with a few hundred thousand trypanosomes approximately 4 days and died all within a half day interval. The infected vitamin-deficient rats lived one, 2, or even 6 days longer. No difference was found in the development of the disease since the trypanosomes appeared at the same time and multiplied apparently at the same rate in the controls and in the vitamin B complex deficient rats, but the latter lived for a comparatively long time with a great number of trypanosomes in the blood stream; this number, however, did not surpass that found in the blood of controls at the time of their death.

Rats kept on a vitamin B_1 free diet (recommended by the U.S.P. Vitamin Conference, January, 1932) but receiving vitamin G (B_2) in the form of autoclaved yeast, showed the increased survival almost to the same extent as those which received neither vitamin B_1 or G. Those which received rice polishings extract (B_1) but no autoclaved yeast (G) occasionally lived longer than the controls. If

* Solazzo (*Z. f. Immunitäts.*, 1929, **60**, 239) claims to have lowered the resistance of pigeons against *Trypanosoma brucei* by keeping them on a diet deficient in vitamin B and in an environment of low temperature.

the latter effect was not accidental, then vitamins B_1 and G may be considered, at least from the point of view of the phenomenon discussed in this paper, as "related" vitamins.

It is obvious that in a large group of rats kept on vitamin B deficient diet all will not have reached the same degree of depletion at a definite time (the time of inoculation†) and hence it was not to be expected that all would show uniform effects of avitaminosis on trypanosome infection. Therefore, the statistical average of the survival of the vitamin-deficient animals subtracted from that of the controls was taken as a measure of the effect observed. This difference was 0.99 days with a probable error of ± 0.07 days,‡ an average value which was obtained from the results of 11 independent experiments comprising 165 rats, 108 of which were deficient in vitamin and 57 were controls. The number of trypanosomes injected constituted the only difference between the various experiments Other experiments with over a hundred rats gave essentially identical results but these were not used in calculating the above averages because the experimental conditions were varied. The data from a typical experiment are given in the table.

A few experiments have been made attempting to explain the effects described. Although they did not solve the problem, they do exclude some explanations which one would have supposed were the most likely. We first thought that the protozoa depend upon the vitamin content of the rat organism, just as much as do the cells of the host itself. However, feeding of the vitamin from the time of inoculation until death did not noticeably change the course of the infection, although the symptoms of the deficiency (polyneuritis) improved even during the first day.

In one experiment a group of control rats was kept starving. The trypanosomes appeared in the blood stream somewhat later than in the animals kept either on deficient or complete diets. These rats died of starvation before the infection was fully developed. This may indicate that starvation also affects the course of the infection but in a different way from the lack of vitamin B complex; more data are required to settle this point definitely.

Moreover, animals kept on a diet deficient in vitamin A may be

† The rats were inoculated when it was believed from previous experience that the most depleted rats could not survive longer than the expected course of the infection.

‡ Thus the observed effect is 14.1 times greater than its probable error and by Gauss' Law of Error the probability that the effect is real and not due to error is greater than 10^{10} to 1. Rietz and Mitchell, *J. Biol. Chem.*, 1910, **8**, 297.

TABLE I.

Effect on Trypanosomiasis of Diet Free from Vitamin B Complex or Components.

No.	Av. Wt. in gm. Initial	Final	% Gain or Loss	Depletion Period Days	Days After Inoculation, No. Rats Which Died 4	4½	5	6	6½	7	7½	8½	10½	Av. Time Survival Days	Stand. Devia.	Av. Time of Surviving Controls	% Rats Surviving Controls
840-845																	
3♂, 3♀ B_1 (no G)	36.8	81	+120	42	3				1		1	1		6.25	1.91	1.75	50
852-857																	
3♂, 3♀ G (no B_1)	38.5	96.5	+150	42		3	1	1	1					5.1	0.80	0.6	50
861-866																	
3♂, 3♀ No B_1 or G	59.3	51.3	— 13.4	20*		4	1				1			5.08	1.10	0.58	33
891-896																	
3♂,† 3♀ No B_1 or G	46	43.8	— 5	20	1		1	1		1			1	6.6	2.27	2.1	80
834-839																	
3♂, 3♀ Controls	34.3	131.3	+282			6								4.5	0.25		

* Started later because deprived of both B and G.

† One died before inoculation.

considered just as much in a state of starvation as those deprived of vitamin B, yet rats lacking vitamin A were found to die even earlier in trypanosomiasis than those on a complete diet as far as can be judged by experiments on a small group of animals (7).

The methylene blue reduction rate of trypanosomes suspended in the blood serum of B deficient animals was the same as the rate of those suspended in normal rat serum.

Finally, mechanical factors were considered. The viscosity of the blood of B deficient rats is increased and the entire organism is dehydrated. It is conceivable that this damages the vitality of the trypanosomes. However, the medium in which the trypanosomes move is really the plasma and therefore the viscosity of the plasma rather than that of the entire blood is the factor which may influence their motility. The citrate plasmas of the 2 B deficient animals tested did not have a higher viscosity than that of the controls.

These experiments suggest that the delayed death of vitamin B deficient rats infected with trypanosomes may be due to some secondary change in the intermediary metabolism of these deficient animals.

Summary. 1. Albino rats kept on vitamin B complex-free diet survived on an average longer after infection with *Trypanosoma equiperdum* than controls kept on a complete diet. 2. Lack of vitamin B_1 seems to be the important factor although a slight effect was also observed with animals receiving B_1 but no G. 3. No change was found in the plasma of deficient animals which could account for the phenomenon observed. 4. Although feeding of vitamin B, after the injection of trypanosomes cured polyneuritis it did not restore the normal reactivity towards the infection before death. 5. Rats kept on a vitamin A free diet and infected with *Trypanosoma equiperdum* apparently died somewhat earlier than controls kept on a complete diet.