The hypersensitive state induced in rabbit by intracutaneous vaccination with R and S forms of pneumococci may persist for at least 4 months—the longest period so far tested. Moreover, it has been found, in a number of instances, that, after all evidences of the ophthalmic reactions have disappeared, the intravenous injection of nucleoprotein may cause the reappearance of the eye reaction.

A study of the development of hypersensitiveness in animals following experimental infection is in progress. The evidence at present indicates that rabbits surviving a slowly progressive but localized infection in the skin become hypersensitive to pneumococcus protein and that this state may appear as early as 12 days after the onset of the lesion.

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Lactic Acid Content of Blood of Trypanosome Infected Rats.

I. J. KLIGLER AND A. GEIGER.

From the Department of Hygiene, Hebrew University, Jerusalem.

Experimental trypanosome infection in rats presents one of the simplest pictures of a protozoan blood infection. After an incubation period of about a week (depending upon the dose injected) there is a period of uncertainty when host and parasite become alternately dominant. Then the trypanosomes become definitely established in the peripheral circulation and increase in numbers progressively until death. Parallel with the increase in the number of trypanosomes there is a progressive decrease in the number of red cells. The significant features of the infection are: (1) An increase of the trypanosomes to a constant number which seems to be characteristic of the species; (2) Anemia, which is variable, ranging between 30% and 50% of the original cell count; (3) Sudden death with symptoms of dyspnea within 10 to 36 hours after the trypanosomes have reached the maximum concentration. There are no toxic symptoms and the injection of large numbers of trypanosomes or a large amount of serum taken from an animal shortly before death do not produce any symptoms of intoxication.

This picture raised 2 problems: (1) The reason for the cessation of the multiplication of trypanosomes; was it due to an inhibiting substance or to exhaustion of the substrate? (2) The actual cause of death. If the cause of death could be ascertained in this simple type of infection, the findings might throw light on the pathology

of the disease in animals in which the course of infection is more complex and hence the cause of death more difficult to establish.

To elucidate these problems we decided to study the changes in the blood chemistry during the course of the infection. Kurt Schern[1] has shown that glucose has a protective effect on trypanosomes and that there was a reduction in the fermentable substances in the liver of trypanosome infected animals. It seemed likely, therefore, that during the infection the available glycogen and glucose reserve was used up by the trypanosomes to the point of exhaustion and that at the same time lactic acid was produced which caused progressive exhaustion of the alkali reserve; this depletion ultimately resulting in the death of the animal. Our first attention was directed to the production of lactic acid.

Rats 150 to 180 gm. in weight were infected with *Tr. evansi* and killed at various stages of the infection. Blood was taken from the carotid artery and the lactic acid content determined by the method described by Freedmann, Cotonio and Shaffer.[2] Care was taken to anesthetize the animals slowly in order to avoid a sudden increase in the lactic acid as a result of excessive muscular activity. The animals were placed under an inverted beaker containing cotton soaked with ether and left there until they were dead.

The results of one series of tests are shown in the following table. Similar results have been obtained in other series. Normal control rats were killed each time for comparison.

TABLE I.

Concentration of lactic acid in trypanosome infected rats at different stages of the infection.

Serial No.	No. of tryps. per cu. mm. blood at time of test	Lactic acid: mgm. per 100 cc. of blood		Ratio increase in lactic acid over normal control
		Infected	Control	
1	2,000	28.5	29.4	0.00
2	2,000	29.8	30.1	0.00
3	300,000	43.0	27.7	1.55
4	300,000	36.0	26.0	1.40
5	668,000	48.2	29.5	1.64
6	1,180,000	106.0	29.0	3.66
7	1,080,000	103.0	35.0	2.94

It is evident from the table that there is a progressive rise in the lactic acid concentration in the blood which runs parallel with the increase in the number of trypanosomes in the blood stream.

[1] Schern, K., *Cent. f. Bakt., Orig.*, 1926, xcvi, 356.

[2] Freedmann, T. E., Cotonio, M., and Shaffer, P. A., *J. Biol. Chem.*, 1927, lxxiii, 335.