

The daily administration of 300 mg of sulfanilamide was found to be definitely toxic for the infected guinea pig. This was shown by the fact that the control animals survived longer than those treated. The toxicity of the compound was greatest for pure-white guinea pigs.

Conclusions. Under the conditions of the experiment it was found that sulfanilamide had an inhibitory effect upon the development of tuberculosis in the guinea pig if the drug was administered before the infection was given. When the infection had been present 17 to 24 days, treatment with sulfanilamide did not alter the macroscopic appearance of the tuberculous process. The development of sensitivity to tuberculin was unaltered by sulfanilamide therapy.

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Analysis of Insulin Response of Rabbits After Injection of Diabetic Serum.

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Since the measurement of substances antagonistic to insulin is not possible by direct chemical methods, various indirect physiological methods have been tried. For this purpose De Wesselow and Griffiths¹ used the response of rabbits to insulin before and after the injection of plasma from diabetic patients. Their results suggested that insulin-sensitive and insulin-insensitive types of diabetes might be differentiated in this manner. Our efforts to use this method have led to inconclusive results. An analysis of these results is presented which illustrates the difficulties in interpreting this test. It is probable that equal caution is necessary in appraising any other test where the response to insulin is used. For purposes of comparison the diminution in the response to insulin produced by pituitary extracts has been included.

The fall in the blood sugar of rabbits after insulin was observed before and after the injection of serum from diabetic patients. The test was carried out as described by De Wesselow,¹ except that 10 cc of fresh serum was used instead of 10 cc of plasma. Three

¹ De Wesselow, O. L. V., and Griffiths, W. J., *Lancet*, 1936, **230**, 991.

hours after the subcutaneous injection of the serum, the fasting blood sugar was taken. Insulin (0.2 unit per kg) was then given intravenously and the blood sugar observed every 15 minutes for one hour. The difference between the initial blood sugar and the lowest blood sugar obtained during the test has been expressed as the percent fall from the initial level.

The alteration of the insulin response in rabbits after the injection of crude saline extract of anterior pituitary (beef) was observed. The pituitary extract was injected in doses ranging from the equivalent of 1.5 g of fresh anterior pituitary given 3 hours before insulin to doses several times this amount given daily from 3 to 5 days. In a few of the experiments with daily injections no extract was given

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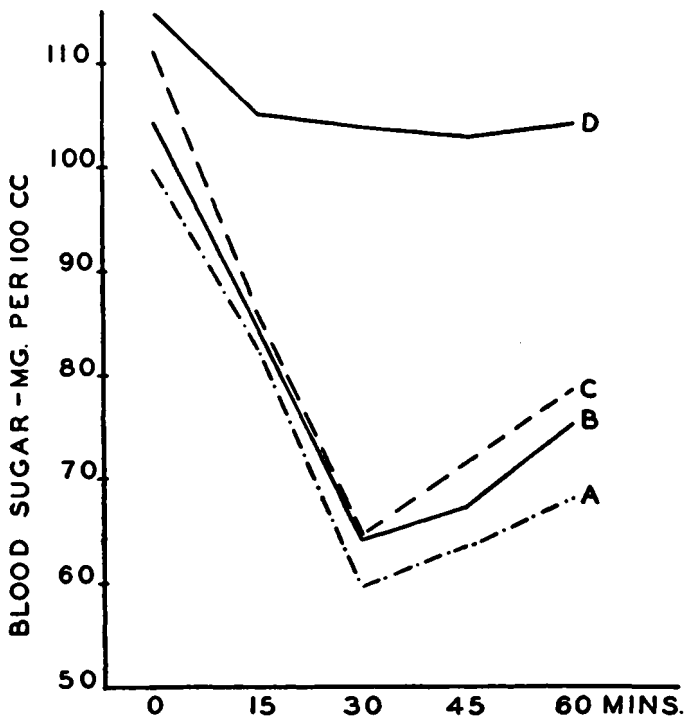


FIG. 1.

The effect of diabetic serum and anterior pituitary extract on response to insulin in the rabbit.

A. Average of 48 control tests. Insulin given intravenously in dose of 0.2 units per kg.

B. Average of 20 tests after the injection of serum from diabetics over 49 years old.

C. Average of 14 tests after the injection of serum from diabetics under 49 years old.

D. Average of 14 tests after the injection of anterior pituitary extract.

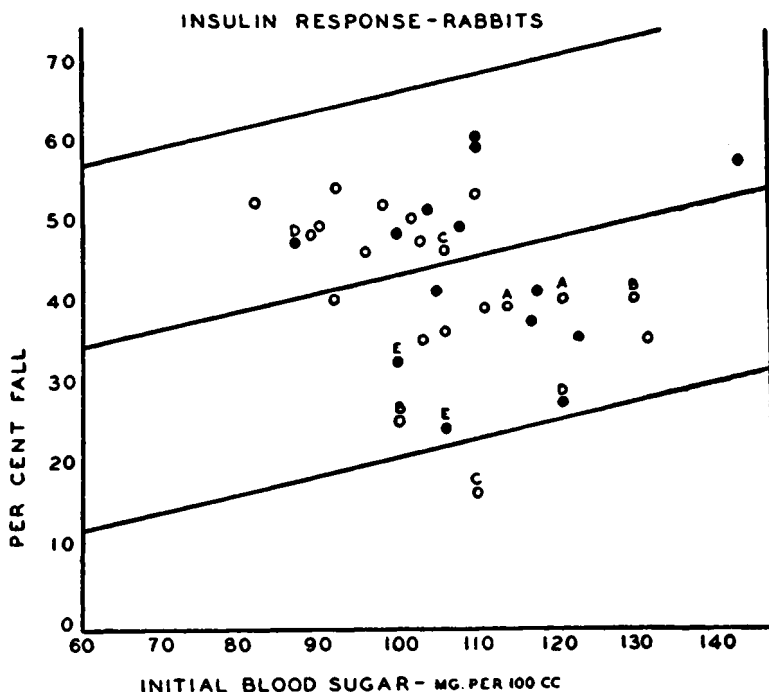


FIG. 2.

○ Injected with serum of diabetics over 49. A, B, C—each tested twice with same sera.

● Injected with serum of diabetics under 49. D, E—each tested twice with same sera.

Middle line is regression line of 48 control rabbits injected with insulin only. Upper and lower lines indicate twice the standard deviation of the control series.

on the day of the insulin test. Insulin (0.2 units per kg) was given intravenously and blood sugars taken at 15-minute intervals as in the animals given diabetic serum. In all, 14 tests were performed.

The results of 48 insulin tests in 40 normal rabbits were analyzed. The mean initial blood sugar was 100 mg per 100 cc and the average fall was 44% of initial value. The percent fall increased with the increase in the initial blood sugar level. This finding is statistically significant and is in close agreement with the results obtained by Hemmingsen and Marks² in 2900 rabbits. The standard deviation of the percentile falls in our small series was ± 11.4 , a figure comparable to that in Culhane's³ series of more than 1500 tests. In the few of our rabbits in which repeated tests were performed there was

² Hemmingsen, A. M., and Marks, H. P., *Quart. J. Pharm.*, 1932, 5, 245.

³ Culhane, K., *Quart. J. Pharm.*, 1928, 1, 517.

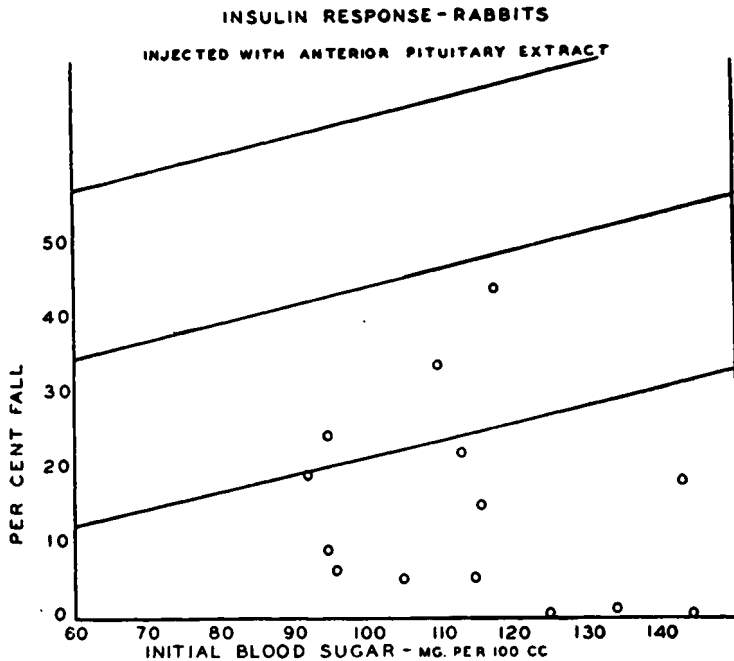


Fig. 3.

○ Response to insulin of rabbits after injection of anterior pituitary extract. The lines have the same significance as in Fig. 2.

a wide range of response in spite of the care taken to make the tests uniform.

The results of 34 insulin tests in rabbits previously injected with serum from diabetic patients are shown in Figs. 1 and 2. Although the curves (Fig. 1) show a slight difference between the normal and the injected rabbits this apparently is not significant when the results are further analyzed (Fig. 2). An arbitrary age grouping has been made in Figs. 1 and 2, since De Wesselow found that insulin-insensitive diabetics were more numerous among older patients. In this series the separation of juvenile diabetics did not reveal any greater difference than that shown in Fig. 1 where the age 50 was selected.

On the other hand a pronounced inhibition of the insulin response was obtained (Fig. 1, curve D, and Fig. 3) following the injection of anterior pituitary extract. It should be emphasized that these results were secured only after obtaining pituitaries frozen on removal from the steer. Before this was done 18 tests, using various crude and commercial extracts, were performed. Of these only 2 showed the least evidence of suppression of insulin action, a fact

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which suggests that the non-specific effect of tissue injections is not responsible for the results.

The rabbit test proposed by De Wesselow and Griffiths¹ to differentiate insulin-sensitive and insulin-insensitive diabetics has failed to do this in our hands. While differences in technic may explain this, it appears that there are more fundamental difficulties to be overcome before a clinical assay of contra-insular mechanisms by this method is possible. The nature of these difficulties has been fully discussed by De Wesselow and Griffiths⁴ in relation to the use of glucose and insulin in diabetics.

The confirmation of the insulin antagonistic action of whole pituitary extracts in rabbits needs no comment.^{5, 6} It is so definite that it suggests a contrast rather than a similarity between these experiments and clinical diabetes.

Summary. The response of rabbits to insulin before and after the injection of diabetic serum has not, in our experience, afforded a means of distinguishing different types of diabetes. The inhibition of the response of the blood sugar to insulin in rabbits after the injection of pituitary extract has been confirmed.

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Infection with *Trypanosoma lewisi* in the Hypophysectomized Rat.

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Trypanosoma lewisi is a natural parasite of the blood of wild rats, and can be transferred easily to laboratory rats. After inoculation to normal adult rats, it produces a blood stream infection of considerable intensity, although only rarely does the infected animal die. At the end of a patent period ranging from a few day to several weeks, the animals usually clear themselves of the infection and thereafter wholly resist reinfection with this parasite.¹ In the pres-

⁴ De Wesselow, O. L. V., and Griffiths, W. J., *Quart. J. Med.*, 1938, **7**, 17.

⁵ Cope, O., and Marks, H. P., *J. Physiol.*, 1934, **83**, 157.

⁶ Young, F. G., *J. Physiol.*, 1936, **87**, 13P.

¹ Taliaferro, W. H. "The Immunology of Parasitic Infections," New York, Century, 1929.