

THE PITUITARY AND THE INSULIN CONTENT OF PANCREAS

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BEST, HAIST & RIDOUT [1939] have shown that the insulin content of the pancreas of rats is reduced by fasting or by feeding fat. In view of the fact that certain pituitary extracts produce a definite change in the insulin content of this gland [Best, Campbell & Haist, 1939] it was of interest to determine the effect on the insulin content of (1) removal of the pituitary, and (2) fat feeding or fasting in hypophysectomized animals.

METHODS

The methods used were essentially those described by Best, Haist & Ridout [1939]. Female rats were used. Animals weighing between 100 and 200 g. were hypophysectomized, using the retropharyngeal approach. Some of the operations were performed by Dr Jane Russell and some by the author. After operation these rats were kept in individual cages and given as much of a balanced ration and of a 10% sucrose solution as they desired. The daily caloric intake in the control animals was kept as nearly as possible the same as that of the hypophysectomized rats. All of the hypophysectomized animals and some of the "paired-fed" controls lost weight, while some of the latter group made a slight gain.

RESULTS

The results of the first experiment are shown in Table I. The average normal value for rats fed *ad libitum* was 26.5 units of insulin per group of ten rats. This was the average value obtained on eleven groups of normal rats in a previous experiment. It is evident from these results that while the hypophysectomized rats have a lower average insulin

content than intact animals fed *ad libitum*, the insulin content of their pancreases does not differ significantly from that of the "paired-fed" control group.

TABLE I. The effect of hypophysectomy on the insulin content of pancreas

Group	Days after hypophysectomy	Days paired-fed	No. of rats	Weight			Insulin content of pancreas	
				Initial g.	Final g.	Units/group of 10 rats	Units/1000 g. initial weight of rats	
Hypophysectomized	26	—	9	1395	1259	20.2	13	
Paired-fed controls		7	9	1393	1335	21.4	14	
Hypophysectomized	27	—	8	1230	1193	21.4	14	
Paired-fed controls		13	8	1214	1217	18.8	12	
Hypophysectomized	38	—	10	1713	1550	17.1	10	
Paired-fed controls		28	10	1800	1778	19.8	11	
Hypophysectomized	52	—	8	1398	1296	20.6	12	
Paired-fed controls		42	8	1447	1500	20.9	12	
Hypophysectomized	66	—	7	1217	1108	22.7	13	
Paired-fed controls		56	10	1783	1847	19.6	11	
Average for hypophysectomized rats						20.4	12	
Average for paired-fed control rats						20.1	12	

The effect of feeding fat was studied. Fat actually constituted 90% of the diet by weight. Agar and vitamins A, B₁, and D made up the remainder. It should be pointed out that the mortality rate of the hypophysectomized animals in these fat-feeding experiments was high. The results are shown in Table II.

TABLE II. The effect of fat feeding on the insulin content of pancreas in hypophysectomized rats

Group	Days after hypophysectomy when fat started	Feeding before fat started	Fat feeding (7 days)	No. of rats	Weight			Insulin content of pancreas	
					Before operation g.	Before fat feeding g.	Final g.	Units/group of 10 rats	Units/1000 g. initial weight of rats
Hypophysectomized	39	<i>ad lib.</i>	<i>ad lib.</i>	8	1296	1206	947	6.0	3.7
Control	—	<i>ad lib.</i>	<i>ad lib.</i>	8	1256	1637	1298	7.6	4.8
Hypophysectomized	26	<i>ad lib.</i>	<i>ad lib.</i>	8	1399	1270	1070	5.9	3.4
Control	—	Paired-fed	Paired-fed	8	1424	1273	1071	9.4	5.3
Hypophysectomized	32	<i>ad lib.</i>	<i>ad lib.</i>	10	1515	1381	1177	8.4	5.5
Control	—	Paired-fed	Paired-fed	10	1508	1544	1344	9.6	6.4
Average for hypophysectomized rats								6.8	4.2
Average for control rats								8.9	5.5

These indicate that in hypophysectomized animals feeding fat causes a fall in the insulin content of pancreas to a level even lower than that of the "paired-fed" controls. The difference in the appearance of the adrenal glands in the two groups is shown in Fig. 1. This is a photograph of the adrenals from one hypophysectomized and one control group. This finding, along with the failure to gain weight and the absence of any visible pituitary tissue, on careful inspection at autopsy, supports the conclusion that the removal of the pituitary was complete.

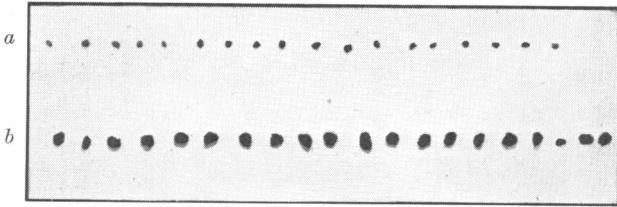


Fig. 1. Photograph of fresh adrenal glands. a, adrenals from hypophysectomized rats fed fat for 7 days. b, adrenals from control "paired-fed" rats fed fat for 7 days.

In the report of Best, Haist & Ridout [1939] it was shown that feeding a balanced diet to rats starved for 1 week led to a restoration of the insulin content of pancreas to a normal value. Table III shows

TABLE III. Animals fed fat for 7 days, then balanced diet for 7 days

	Hypophysectomized rats	Paired-fed controls
Days after operation	32	—
No. of rats	8	8
Weight (g.):		
Before operation	1193	1229
Before fat feeding	1143	1303
After fat feeding	991	1171
Final	1018	1168
Insulin content of pancreas:		
Units/group of 10 rats	29.5	26.8
Units/1000 g. initial weight of rats	19	18



the effect of feeding a balanced diet to hypophysectomized rats that had previously been fed fat only, for 1 week. The hypophysectomized animals were first fed fat for 7 days as in the previous experiment and then were given a balanced ration plus 10% sugar solution *ad libitum* for 7 days. The control group received as nearly as possible the same diet and the same caloric intake as the hypophysectomized group before and during the test. At the end of 7 days on the balanced diet the pancreases were removed. It is evident that feeding a balanced diet

restores the insulin content of pancreas. Actually, the final value is similar to that of the normal intact animal and is slightly higher than the level in the hypophysectomized group prior to the fat feeding.

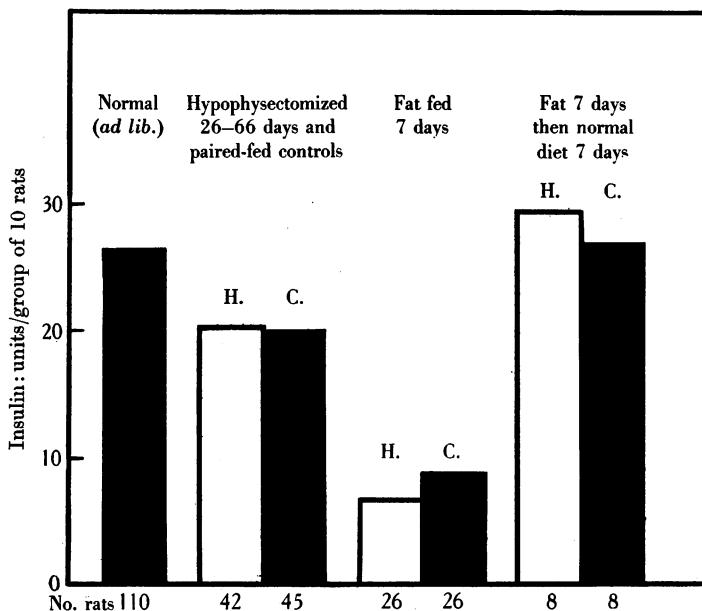


Fig. 2. Hypophysectomized rats. Average results.

DISCUSSION

The results we have obtained in hypophysectomized animals are well illustrated in Fig. 2. From this it is apparent that hypophysectomy leads to a slight fall in the insulin content of pancreas when the values are compared with those of controls fed *ad libitum*. The values obtained, however, are similar to those in the control animals which received the same caloric intake. It shows also that the fall in insulin content which occurs when fat is fed can be obtained in hypophysectomized animals, and that the feeding of a balanced diet after such a period of fat feeding will restore the insulin content of the pancreas of these animals to normal values.

Chambers, Sweet & Chandler [1935] found that the insulin content of the pancreas of hypophysectomized dogs did not differ from that of normal animals. We have obtained similar results in the rat. They studied the effect of fasting in hypophysectomized dogs and found that after 24-30 days' starvation the ingestion of 25 g. of glucose, gave no

rise in respiratory quotient and a definite hyperglycaemia [Chambers, 1938]. These facts indicate that, in some respects at least, the hypophysectomized animals react to starvation in a manner similar to normal ones. The results of our experiments on the insulin content of the pancreas in hypophysectomized rats add weight to the evidence that the pituitary gland is not essential for the effect of fat feeding or of undernutrition on carbohydrate metabolism. It would appear moreover that, *within a wide range, the pancreas can regulate the production and liberation of insulin according to the need for it, in the complete absence of the pituitary gland.*

SUMMARY

1. The insulin content of the pancreas in hypophysectomized rats is slightly less than in normal animals fed *ad libitum* but is of the same order as that of controls receiving a similar caloric intake.

2. A fall in insulin content is obtained in hypophysectomized rats when fat is fed.

3. When a balanced ration is given to hypophysectomized rats, which have previously received a diet very rich in fat for 1 week, the insulin content of the pancreas returns to normal within 7 days.

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