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Influence of Previous Diet on Insulin Tolerance.*

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A number of workers have studied the relationship of diet to insulin tolerance.[1-6] The results obtained have been quite contradictory due to the fact the food intake was in no case equal and adequate for all groups of experimental animals. In the present experiments we applied to this problem the method of stomach tube feeding previously described by Reinecke, Ball and Samuels.[7] We have been able to demonstrate that shifting a large proportion of the dietary calories from carbohydrate to fat, keeping the total calories constant, results in an increased tolerance to insulin.

Methods. Adult male rats, obtained from Sprague-Dawley and weighing 250-300 g, were used. All animals were first force-fed a diet prepared by mixing equal amounts of the high fat and high carbohydrate diets described in Table I. Four days later, when the rats had become accustomed to feeding by stomach tube, they were separated into 2 groups having similar ranges of weight. One group was fed the high carbohydrate diet (83% of the calories as carbohydrate, 2% fat, 15% protein); the other group was given the high fat diet (85% of the calories as fat, 15% protein). The amounts fed were calorically equal in both groups, and were sufficient to maintain or increase body weight.

TABLE I.
High Fat and High Carbohydrate Diets Fed in Equi-Caloric Amounts by Stomach Tube.*

Constituent	High fat	High Carbohydrate
	Amount	
Lactalbumin (Labco No. 15-42)	15 g	15 g
Osborne-Mendel Salt Mix.	4 "	4 "
Celluflour (Chicago Dietetic)	10 "	10 "
Vitamin B Complex, Lederle	1 capsule	1 capsule
Percomorph Oil	1 drop	1 drop
Corn Oil	37.5 g	1 g
Dextrin, Merck's N.F.V.	0	83 "
Gum Ghatti	3.6 "	0
Water to make a total volume of 180 cc in each		

* Valuable aid in the development of these diets was furnished by Dr. R. M. Reinecke.

Adequate vitamin and mineral supplements were present in both diets.

After 6 weeks on this regime, the animals were fasted 36 hours and their sensitivity to exogenous insulin determined. The dosage of insulin (Lilly's Iletin) used was 0.16 U. per 100 g body weight injected intraperitoneally. Samples of blood, 0.05 ml in amount, were taken from the clipped end of the tail just before insulin injection and at intervals thereafter. Protein was precipitated by 5 ml of Folin's dilute tungstic acid reagent. Blood sugar determinations were made in duplicate on 2 ml aliquots of the tungstic acid filtrate by a modification of the Folin-Malmros micro-method. The procedure was similar to that described by Jeghers and Myers,[8] somewhat modified and adapted to the Evelyn photoelectric colorimeter.

Results. Fig. 1 illustrates the effect of previous diet on the insulin tolerance of the adult male rat. It is evident that after a 36-hour fast, blood sugar levels are similar

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1 Abderhalden, E., and Wertheimer, E., *Pflugers Arch.*, 1924, **205**, 547.

2 Bainbridge, H. W., *J. Physiol.*, 1925, **60**, 293.

3 Himsworth, H. P., *Clinical Science*, 1933, **1**, 1.

4 Himsworth, H. P., *J. Physiol.*, 1934, **81**, 29.

5 Himsworth, H. P., *Clinical Science*, 1935-36, **2**, 67.

6 Hynd, A., and Rotter, D. L., *Biochem. J.*, 1931, **25**, 457.

7 Reinecke, R. M., Ball, H. A., and Samuels, L. T., PROC. SOC. EXP. BIOL. AND MED., 1939, **41**, 44.

8 Jeghers, H. J., and Myers, V. C., *J. Lab. and Clin. Med.*, 1930, **15**, 982.

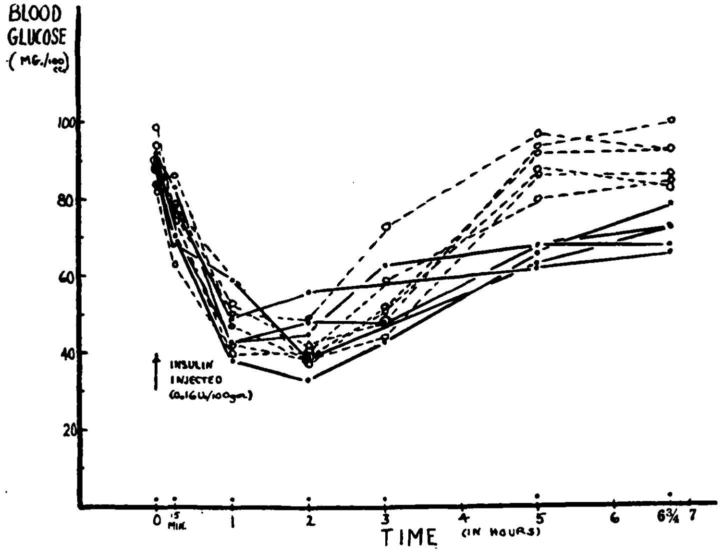

FIG. 1.
Diet and Insulin Tolerance of Normal Rats.
Blood sugar curves of normal adult male rats injected with 0.16 U. of insulin per 100 g after 36 hours fast. These animals had previously been fed by stomach tube for 6 weeks equi-caloric amounts of the special diets:
High carbohydrate diet •————•
High fat diet ○------○
Each curve represents one insulin test in one rat.

in both carbohydrate-fed and fat-fed animals. Likewise, the degree of depression of the blood sugar level by injected insulin is about the same. The recovery rates are, however, quite different. Animals previously force-fed the high fat diet show a consistently more rapid recovery from hypoglycemic levels.

Discussion. The above results show that the insulin tolerance of rats previously fed a high fat diet is greater than that of high carbohydrate-fed animals, after a 36-hour fasting period. Samuels, Reinecke and Ball[9] have shown that fat-feeding has a sparing action on liver glycogen disappearance during fasting. After 33 hours fasting, the liver of fat-fed animals contained much more glycogen than that of carbohydrate-fed animals. It seems likely then, that the difference in insulin sensitivity noted is a result of the difference in fasting levels of liver glycogen.

When insulin was injected, a rapid and equal depression of the blood sugar level occurred in both groups, indicating that the action of insulin in increasing carbohydrate utilization was unaffected by previous diet. In response to hypoglycemia, the liver liberated sugar by glycogenolysis. Since more glycogen was available in the fat-fed animals after the period of fasting used here, the rate of recovery from insulin hypoglycemia was more rapid.

Summary. Adult male rats, previously force-fed a high fat diet by stomach tube in amounts sufficient to maintain body weight, were less sensitive to the action of injected insulin than similarly-treated animals previously force-fed equi-caloric amounts of a high carbohydrate diet. The decreased sensitivity manifested itself primarily as a markedly increased rate of recovery from insulin hypoglycemia. The most likely direct cause of the increased insulin tolerance in the fat-fed animals is the higher level of liver glycogen after a 30-36 hour fasting period.

9 Samuels, L. T., Reinecke, R. M., and Ball, H. A., PROC. SOC. EXP. BIOL. AND MED., 1942, **49**, 456.