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Effect of Alternating Periods of Underfeeding and *Ad libitum* Feeding on Insulin Sensitivity of Rats.* (23280)

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Prolonged underfeeding (4-6 weeks on 10 g of diet daily) followed by a 24 hr fast causes an increase in the hypoglycemic response to insulin in adult male rats(1). In the present study fasting insulin sensitivity of a group of rats was examined after a period of undernutrition, during a subsequently instituted *ad libitum* feeding regimen, and in the course of a second period of undernutrition.

Materials and methods. Seven male Sprague-Dawley rats, serving as their own controls, were used. The mean initial weight of the group was 281 ± 4 (S.E.) g. All insulin sensitivity determinations were undertaken after a 24 hr fast. One tenth U of insulin (Iletin-Lilly) per kg was injected i.p. Blood sugar levels were ascertained as in our previous study(1). The first insulin sensitivity measurement (Fig. 1, A) was performed 5 weeks after the initiation of a restricted feeding regimen (10 g ground Rockland diet daily), the second (Fig. 1, B) after 3 weeks and the third (Fig. 1, C) after 6 weeks of subsequent *ad libitum* feeding of the same diet. Following the third determination daily food rations were again reduced by 2 g daily from

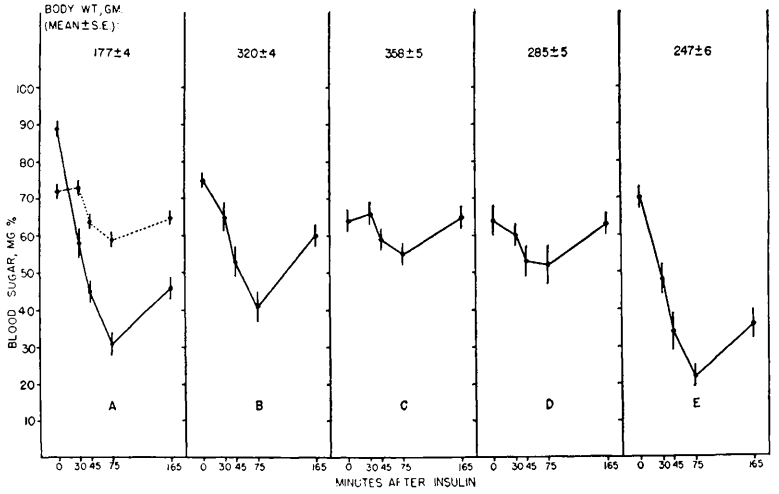

FIG. 1. Blood sugar levels before and after insulin in fasted rats after prolonged undernutrition (A), during *ad libitum* feeding (B and C) and renewed undernutrition (D and E). Details in text. Dotted line: values in 23 *ad libitum* fed-fasted rats of a previous study(1). Vertical lines: stand. errors of the mean.

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18 to 10 g daily, and the next 2 insulin sensitivity measurements were made after the animals had consumed 10 g food/day for 4 weeks (Fig. 1, D) and 9 weeks (Fig. 1, E) respectively.

Results. Prolonged undernutrition led to relatively high fasting blood sugar levels and increased insulin sensitivity (Fig. 1, A). Nutritional rehabilitation was accompanied by progressive lowering of fasting blood sugar titers and gradual return of normal insulin sensitivity (Fig. 1, B and C). A second period of underfeeding at first did not lead to any change (cf. Fig. 1, C and D). However, upon further prolongation of undernutrition marked insulin sensitivity returned, although it was not accompanied by fasting blood sugar levels higher than those found in *ad libitum* fed rats (cf. Fig. 1, A and E).

Discussion. These findings demonstrated that *ad libitum* feeding abolished both the relative hyperglycemia and hypersensitivity to insulin in the fasted state which are characteristic of underfed rats, and that return of normal insulin resistance was not due to immunity to insulin which had arisen because of its repeated administration, since during a second period of underfeeding excessive insulin sensitivity again developed, although less rapidly than in the course of initial undernutrition. Systematic studies of the influence of age on fasting glycemia and insulin sensitivity and on the effects of underfeeding on these aspects of carbohydrate metabolism remain to be done. However, in our previous study(1) we have not noted any consistent differences in these regards among rats whose weight ranged from 180 to 350 g at the inception of underfeeding or, if the animals were fed *ad libitum,* at the time of determination of insulin sensitivity.

Summary. The characteristic fasting insulin hypersensitivity of chronically underfed rats is gradually abolished by subsequent prolonged *ad libitum* feeding and slowly returns during repeated undernutrition.

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Influence of Adrenergic Blockade and an Amine Oxidase Inhibitor on Reserpine Hypotension. (23281)

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The hypotensive effect of intravenous reserpine in anesthetized dogs requires 2 hours to become significant(1). Recent evidence which indicates that reserpine releases a sympathetic neurohumoral agent by Holzbauer and Vogt(2) and Maxwell *et al.*(3) suggests that this agent might be acting to mask a rapid onset of reserpine action. We have tested this hypothesis by determining the effect of adrenergic blockade and amine oxidase inhibition on the onset of reserpine hypotension. The following is a report of our findings.

Methods. Twenty-five dogs anesthetized with 30 mg/kg sodium pentobarbital intraperitoneally and a continuous intravenous infusion of 0.1 mg/kg/minute of sodium pentobarbital were used. Femoral arterial pressures were recorded with the Anderson glass capsule manometer(4). All drugs were administered intravenously. Phentolamine HCl was administered over a 15-30 minute period to minimize its hypotensive effect. Observations on hypotension produced by reserpine were limited to the first half hour after reserpine administration. Choline p-tolyl ether bromide, an amine oxidase inhibitor first reported by Brown and Hey(5) was employed in these experiments.

Results. Reserpine phosphate on blood pressure. In 6 dogs 0.5 mg/kg intravenous reserpine phosphate produced no significant