Effect of Alloxan on Feed Consumption and on Replacement Therapy With Graded Levels of Insulin in Rats.* (31180)

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It has been shown that when alloxan was injected intraperitoneally at a level of 15 mg/100 g BW to induce chronic diabetes, feed consumption declined to a level 67% below the control period, then began to increase. The feed intake increased 36% from day 7 to 12, and 56% from day 13 to 18 per 100 g BW over the control period(1). When alloxan was administered to lactating animals, feed consumption was greatly reduced for a day or two after treatment but then increased rapidly so that during the first 6 days, feed consumption was greater than in control lactating rats(2).

The object of the present study was to determine the effect of alloxan diabetes upon feed consumption and to determine the effect of graded levels of insulin upon feed consumption.

Materials and methods. Twenty-nine nulliparous mature female rats of the Sprague-Dawley-Rolfsmeyer strain were placed in metabolism cages constructed so as to prevent coprophagy and feed wastage. Temperature was maintained at 78 ± 1°F and the rats were artificially illuminated during daylight hours. Purina Lab. Chow with an energy value of 4.41 calories/g and 23.4% total protein was fed during a preliminary period of 10 days to determine the mean daily feed consumption of each animal in the group. The normal feed consumption of the animals prior to alloxan administration and replacement therapy with insulin is considered the control value since there was no change in feed consumption during a comparable period in the previous experiments(1).

The rats were given a single intraperitoneal injection of alloxan (reagent) at a level of 15 mg/100 g BW to induce chronic diabetes (1). During the first 6 days of treatment a total of 5 rats died. The sugar in the urine was estimated by the use of "Tes-tape" (urine sugar test tape, Lilly). Six rats did not show chronic diabetes, so were discarded. The remaining 18 rats were replaced with graded levels of Protamin Zinc Insulin, starting with 1 unit of insulin daily for 6 days and with 1 unit of insulin increment up to 4 units. The feed consumption was measured daily.

Results. The 18 normal rats weighing initially a mean of 235 g during a period of 10 days consumed a mean of 13.07 g/day and 5.18 g/100 g BW (Table I). Then alloxan was given and a period of 18 days was allowed to induce chronic diabetes. Then feed consumption was estimated from day 19 to 29. The 18 rats weighing a mean of 237 g consumed a mean of 22.13 g of feed/day and 9.46 g/100 g BW, an increase of 69% and 83%, respectively, over normal feed consumption. When 1 u insulin was given for a period of 6 days, the feed consumption increased slightly; whereas, at 2 u a nonsignificant decrease was observed. At 3 u/day feed consumption showed a non-significant decrease of 10%; whereas, /100 g BW a significant 20% decrease was observed. Two rats died at this level. At the 4 u level the daily feed consumption decreased 12%; whereas, /100 g BW there was a highly significant decrease of 23%. At this level 5 rats died. The urine was negative for sugar at 3 and 4 u levels.

Discussion. The effect of the removal of the pituitary, adrenals and the thyroparathyroid glands and the production of alloxan diabetes on feed consumption has been reported(1,3,4). The removal of these glands resulted in a gradual decline in feed consumption up to about 30%; whereas, alloxan diabetes increased feed consumption up to 56%. It has been shown that in diabetic rats injected with ovarian hormones plus 3 u of insulin mammary gland DNA was increased slightly above the normal value(5). It was observed that 2 u of insulin was the

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TABLE I. Effect of Alloxan Diabetes and Replacement Therapy with Insulin on Feed Consumption in Rats.

Treatment	No. of rats	Mean body wt (g)	Mean feed intake (g) Per day	% Diff.	Per 100 g body wt	% Diff.
Normal control (10 days)	18	253	13.07 ± .24		5.18 ± .99	
19 to 29 days after alloxan injection	18	237	22.13 ± 1.01[1]		9.46 ± .57[4]	
Successive 6 days. Replacement therapy						
1 unit insulin	18	243	23.73 ± 1.46	7	9.98 ± .76	6
2 units "	18	256	21.81 ± 1.05	— 1	8.61 ± .50[5]	— 9
3 " "	16	263	19.98 ± 1.04[2]	—10	7.61 ± .40[6]	—20
4 " "	11	268	19.55 ± 1.27[3]	—12	7.27 ± .43[7]	—23

Student's "t" probability
1 *vs* 2 = .4 > P <.2
1 *vs* 3 = .1 > P <.05
4 *vs* 5 = P <.5
4 *vs* 6 = .02 > P <.01
4 *vs* 7 = .005 > P <.001

optimal level for chronic-diabetic lactating rats to return lactation to normal(2). It has been shown that adrenalectomy caused a reduction in thyroid hormone secretion rate (TSR) and replacement therapy with 150 μg hydrocortisone acetate plus 1% NaCl was sufficient to return TSR to a normal level(6).

In this study, 1 u of insulin did not reduce feed intake in diabetic rats, whereas 2 u had a slight effect. Higher levels (3 and 4 u) of insulin decreased feed intake significantly compared with the diabetic levels. The mortality increased when higher levels of insulin were administered. It will be noted that feed consumption did not return to the normal level during the administration of graded levels of insulin. It is possible that an approach to the normal feed level would have been observed on the lower levels if the duration of replacement therapy had been lengthened. However, on the higher levels of insulin feed intake in normal animals has been shown to increase(7).

Summary. Alloxan diabetes was induced in a group of 18 female Sprague-Dawley-Rolfsmeyer rats weighing a mean of 237 g. Prior to treatment they consumed a mean of 13.07 g/day and 5.18 g/100 g BW. Following treatment they consumed a mean of 22.13 g/day and 9.46 g/100 g BW of Purina Lab. Chow daily during a 10-day period, an increase of 69%/day and 83%/100 g BW. Graded levels of insulin (1 to 4 u) were administered during 6-day periods. On 2 u/day, feed consumption decreased 9% (non-significant), on 3 u 20% (significant) and at 4 u a highly significant decrease of 23%/100 g BW was observed. At the 3 and 4 u level, 2 and 5 rats died.

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