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Effects of Diabetes on Development of Small Intestinal Enzymes of Infant Rats (42636)

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Abstract. The effect of streptozotocin (SZ) on the development of small intestinal enzymes in postnatal rat pups was studied. SZ was injected ip on Day 10 and, if necessary, again on Day 12. On Days 15, 18, and 21, one pup from each group (including a vehicle-injected control (C) group) was decapitated under conditions which minimized stress. Plasma glucose, insulin (IRI), and corticosterone were measured, as were pancreatic IRI, liver glycogen, and liver membrane binding of IRI. Small intestinal segments were processed and analyzed for sucrase, lactase, maltase, and ileal acid β-galactosidase activities. Our results indicate that plasma glucocorticoid levels remained virtually constant in both SZ and C groups, while the ontogenic profiles of sucrase and maltase in SZ rats were shifted toward an earlier appearance and a precocious maturation. Circulating levels of IRI were not reduced significantly by SZ despite the fact that pancreatic IRI was decreased 95%. Jejunal lactase, unlike data reported for adult diabetic rats, was not affected by SZ diabetes. Also, acid β-galactosidase was unaltered in the SZ rat pups. It is concluded that possibly the elevated disaccharidases seen in diabetic postnatal rat pups are the direct effect of elevated blood glucose. If so, the SZ rat pup model may be a useful tool with which to study effects of glucose on intestinal enzymes in the absence of changes in plasma insulin.

The effects of diabetes on intestinal brush-border hydrolases in adult rodents are well documented. Both total and specific activities of sucrase, maltase, and lactase increase several days after induction of diabetes with alloxan or streptozotocin (1–4). The effects are prevented or markedly diminished by insulin therapy, suggesting that they are the result of insulin deficiency and not a direct effect of the agent used to produce diabetes. Interestingly, exogenous insulin administration also increases sucrase, lactase, and alkaline phosphatase activity in adult nondiabetic rats (5). Intestinal disaccharidase activities are also elevated in genetically diabetic mice; however, lactase appears to be a lone exception in this regard (6). In contrast to the many reports in adult rats, the effect of diabetes in infant rats, especially on the development of small intestinal enzymes, has not been examined.

Rat small intestinal enzymes which are involved in carbohydrate hydrolysis undergo major developmental changes accompanying the process of weaning (7). The developmental changes are characterized by two groups of enzymes. The first group of enzymes, represented by sucrase and maltase, increases in activity during the third postnatal week (8, 9). The second group of enzymes, represented by lactase and acid β-galactosidase, decreases in activity during the third postnatal week (8, 10). The hormones corticosterone and thyroxine have been implicated as regulators of many of these enzymatic changes (7, 11). The role of insulin in the ontogeny of intestinal brush-border disaccharidases has been recently studied on intestinal explants *in vitro* and *in vivo* in suckling mice by Menard's group (12–15). A premature appearance of sucrase activity and an increase in both maltase and lactase activities were observed in 8-day-old mice injected with insulin. A direct, stimulatory effect of insulin was observed in explanted tissue. This effect of exogenous insulin is in apparent contradiction with the expected effects of insulin deficiency induced by diabetes on intestinal disaccharidases in adult rats. That is, it would not necessarily be expected that both insulin excess in young (12, 15) and old (5) rodents and insulin deficiency in diabetic adult rodents (1–4) would increase small intestinal hydrolase activity. Thus, the goal of the current investigation was to determine the effect of diabetes on the development of small intestinal enzymes of infant rats.

Materials and Methods. *Chemicals.* Streptozotocin, bovine serum albumin, thi-

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merosal, Trizma, bacitracin, 5'-adenosine monophosphate, glucose 6-phosphate, anthrone, dextran, α-lactose, maltose, *p*-chloromercuribenzoic acid, *o*-nitrophenol-β-D-galactopyranoside, *o*-nitrophenol, and unlabeled corticosterone were obtained from Sigma Chemical Co. (St. Louis, MO). Ethylenediamine tetraacetate disodium salt, sucrose, and activated charcoal (neutral Norit) were obtained from Ames Company (Elkhart, IN), and glucose reagent (glucose oxidase) kits were obtained from Boehringer–Mannheim Co. (Indianapolis, IN). ^{125}I-insulin (porcine) and [1,2,6,7-^{3}H]corticosterone were obtained from New England Nuclear (Boston, MA). Unlabeled rat insulin and unlabeled porcine insulin were obtained from Eli Lilly Co. (Indianapolis, IN). Guinea pig anti-rat insulin serum was obtained from Linco Research, Inc. (Eureka, MO). Goat anti-guinea pig gamma globulin was obtained from Antibodies, Inc. (Davis, CA). Normal carrier serum (guinea pig) was obtained from Kew Scientific, Inc. (Columbus, OH). Trasylol was from Bayer, Italy. All other chemicals were reagent grade.

Animals. Timed-pregnant Sprague–Dawley rats (Charles River Crl:CD[SD]BR) were obtained from Charles River Breeding Laboratories (Wilmington, MA) and were housed in animal quarters under a 12-hr light/dark cycle with food and water available *ad libitum*. On the due date, rats were checked twice daily for births. The birth date was regarded as Day 0. Approximately 24 hr following birth, litters were reduced to nine rat pups per dam.

On postnatal Day 10, pups from the same litter were divided into two pair-weighted groups, i.e., three pups in the control group (C) and six pups in the streptozotocin (SZ) treatment group. Diabetes was induced in the SZ group pups by intraperitoneal injections of SZ (75 mg/kg body wt). Control pups received an equivalent volume of buffer (0.1 *M* citrate, pH 4.5). Glucose in urine was tested daily from the date of first injection by using Clinitrix reagent paper strips. Pups were reinjected with the same dose of SZ on Day 12 if necessary to establish persistent glycosuria.

Assay of plasma glucose, insulin, and corticosterone. On Days 15, 18, and 21, one pup from each group (C, SZ) of each litter was sacrificed by decapitation using conditions designed to minimize stress (8). Trunk blood was collected in heparinized test tubes which contained 1000 U Trasylol/ml of blood to inhibit insulin degradation. The blood was centrifuged at 3000 rpm for 15 min at 4°C. Plasma was stored at −20°C. One aliquot of plasma was analyzed for glucose concentration.

Immunoreactive insulin (IRI) was measured in plasma and tissue by a double-antibody radioimmunoassay (16). The buffer used in the RIA was 1% BSA, 50 m*M* NaH_2PO_4, 0.9% NaCl, 0.025% thimerosal, and 0.025 *M* EDTA. On the first day of assay, the rat insulin standards (from 8 to 0.1 ng/ml) or plasma sample and guinea pig anti-rat insulin serum (GPAIS) were added in the assay tube. The final concentration of GPAIS in the assay tube was 1:50,000. The reaction mixture was kept at 4°C for 24 hr. On the second day the tracer (porcine ^{125}I-insulin, sp act 100 μCi/μg) and normal guinea pig serum (1:200) were added to the assay tube. The final concentration of tracer in the assay tubes was 50–100 pg of ^{125}I-insulin. The reaction mixture was left at 4°C for another 24 hr. On the third day, goat anti-guinea pig serum (P4 1:100) was added to the assay tubes. The reaction mixture was stored at 4°C overnight. On the last day, the reaction mixture was centrifuged at 3000 rpm for 30 min. The supernatant was aspirated and the precipitate was counted.

Another aliquot of plasma was analyzed for total corticosterone by an established competitive binding assay (17).

Assay of pancreatic insulin content. The pancreas was dissected out at the time of sacrifice. It was homogenized in 2 *N* acetic acid and heated at 100°C for 5 min to inactivate proteases. After centrifugation, the supernatant was stored at −20°C for assay of pancreatic insulin content. At the time of assay, the supernatant was neutralized with 1 *N* NaOH and then diluted from 1:200 to 1:10,000. Radioimmunoassay as described above was used to measure the pancreatic IRI (insulin) content. Hormone content is reported as nanograms of hormone per milligram of tissue wet weight.

Assay of liver glycogen. A piece of liver was

taken at the time of sacrifice, placed on dry ice, and then stored at −32°C for assay of liver glycogen content. At the time of assay, liver tissue was digested in 30% KOH and the glycogen content was measured by the anthrone method of Seifter *et al.* (18).

Assay of intestinal disaccharidases and acid β-galactosidase. Small intestine (from the ligament of Treitz to the ileocecal junction) was removed from the decapitated rats. The proximal half of this length is defined as jejunum and the distal half is defined as ileum. The two segments were flushed thoroughly with ice-cold saline and stored separately at −10°C for assay of jejunal disaccharidases and ileal acid β-galactosidase.

Jejunal disaccharidases were assayed according to the method described by Henning (8). The homogenates of jejunal mucosa were used directly for the sucrase and lactase assay but were diluted further for the maltase assay. Glucose produced from sucrose, maltose, and lactose was measured with glucose reagent kits. Protein was determined by the method of Lowry et al. (19). Acid β-galactosidase was assayed in the ileum by the methods described by Henning and Leeper (20), which is a modification of the original method of Koldovsky and Sunshine (21). Enzyme activities were expressed as micromoles glucose per hour per milligram of mucosal protein.

Statistical evaluation. All results are presented as means ± SE. Statistical analysis was performed by Student's *t* test for nonpaired samples (two-tailed). Comparison was made with the appropriate control group. *P* values of 0.05 or less were accepted as significant.

Results. *Effects of streptozotocin.* Two days after the first injection of SZ, i.e., on Postnatal Day 12, less than 10% of the injected pups were glycosuric. A second dose of SZ was injected into the aglycosuric pups. On the next day (Day 13), glucosuria appeared in 60–70% of the SZ-injected pups. Some of the remaining 30–40% of the SZ-injected pups were glycosuric only for a few following days; some never became diabetic. The pups with persistent glycosuria were included in the SZ group and sacrificed on Days 15, 18, and 21. Figure 1A shows that body weight increased from Day 15 to Day 21 in control rats. As compared with control

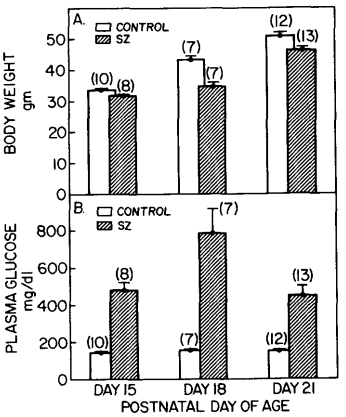

FIG. 1. Effects of streptozotocin (SZ) on body weight (A) and plasma glucose (B) of newborn rats sacrificed at three postnatal ages. Open bars are control rat pups, shaded bars are experimental (SZ) rat pups, vertical bars are SEM, and number in parentheses = number of observations for each group.

rats, the body weight of SZ pups was significantly lower on all 3 days of sacrifice ($P < 0.05$).

The effect of SZ on plasma glucose is shown in Fig. 1B. The basal levels of plasma glucose of control rats were constant with age, approximating 150 mg/dl. The plasma glucose of SZ pups on Day 15 averaged 485 ± 51 mg/dl, which was threefold higher than that of control pups ($P < 0.01$). On Day 18, hyperglycemia peaked in SZ pups. The plasma glucose of SZ pups was 791 ± 138 mg/dl, which was almost five times that of the control rats ($P < 0.01$). The large standard error of the SZ group indicated the variation in response of individual pups to the β-cytotoxin. On Day 21, the remaining SZ pups appeared to be in much better physical condition than on Day 18. The plasma glucose decreased to 455 ± 8 mg/dl, but was still significantly higher than that of the control pups ($P < 0.01$). Hyperglycemia and glycosuria both indicated that the SZ had an established diabetic lesion.

The effect of SZ on liver glycogen content also was examined on Days 15, 18, and 21 (data not shown). Liver glycogen content of SZ pups was only 10% that of the controls on Day 15 and 60% on Days 18 and 21 ($P < 0.01$, 0.05, and 0.01, respectively).

Figure 2A shows the effect of SZ on

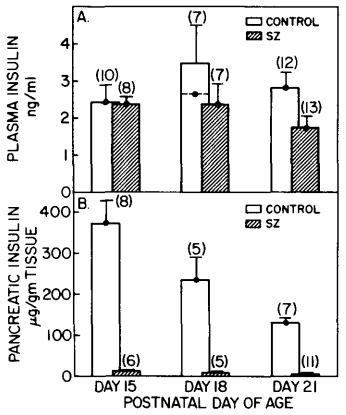

FIG. 2. Effects of streptozotocin (SZ) on plasma insulin levels (A) and pancreatic insulin concentrations (B) in newborn rats sacrificed at three postnatal ages. Other legend details are identical to those of Fig. 1.

plasma insulin (IRI) of the SZ pups. There was no statistically significant difference between plasma insulin of SZ pups and that of the control pups at the ages studied. However, there was a strong tendency of decreasing plasma insulin of SZ pups on Day 21. One observation in the control group on Day 18 was quite deviant from the average value (8.8 ng/ml). If excluded from this group, the mean and standard error would be 2.6 ng/ml, as indicated by the dashed line.

Because of the apparently "normal" circulating concentration of IRI in SZ pups, immunoreactive pancreatic insulin content also was measured to confirm the diabetogenic effect of SZ. Figure 2B shows that the pancreatic IRI content of the SZ pups was only 4% ($P < 0.01$) that of the control pups on Day 15, 5% ($P < 0.01$) on Day 18, and 5% ($P < 0.01$) on Day 21. Thus, it was observed that SZ is an effective B-cell toxin in this rat pup system.

Despite the metabolic derangements of the SZ pups, the circulating level of total corticosterone was not elevated within the experimental observation period. It was 1.8 ± 0.2 µg/dl for SZ pups versus 2.1 ± 0.7 µg/dl for control pups on Day 15, 4.3 ± 1.3 µg/dl versus 4.8 ± 1.5 µg/dl on Day 18, and 6.0 ± 1.0 µg/dl versus 4.6 ± 0.9 µg/dl on Day 21.

Effects of diabetes on the developmental patterns of small intestinal enzymes in SZ-injected rat pups. The effects of diabetes on the small intestinal enzyme activities of infant rats were examined on Postnatal Days 15, 18, and 21. Figure 3A presents the developmental pattern of sucrase activity of SZ pups and control pups. Sucrase activity was almost undetectable in the control pups on Day 15, but was readily measured in the diabetic littermates ($P < 0.01$). On Day 18, sucrase activity was increased in the controls, but it was more than twofold higher in the diabetic pups ($P < 0.01$). The difference between sucrase activity of diabetic pups and that of the controls was diminished to a level below that of statistical significance on Day 21 because the activity increased steeply in the control pups between Days 18 and 21.

A similar pattern was observed for maltase activity (Fig. 3B). On Day 15, maltase activity was already present in the control pups, but it was elevated twofold in the diabetic littermates ($P < 0.01$). This difference was still statistically significant on Days 18 and 21 ($P < 0.01$).

Data for two enzymes which display declining activities during postnatal development are presented in Fig. 4. Lactase activity (Fig. 4A) was not significantly different in diabetic and control pups at any age studied. Similarly, ileal acid β-galactosidase (Fig. 4B)

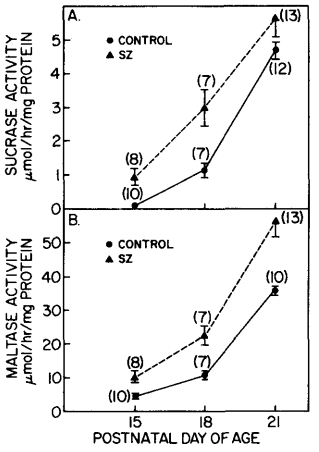

FIG. 3. Effects of streptozotocin (SZ) on intestinal sucrase activity (A) and maltase activity (B) of newborn rats sacrificed at three postnatal ages. Assays were done on the proximal half of the small intestine distal to the ligament of Treitz. Other legend details are identical to those of Fig. 1.

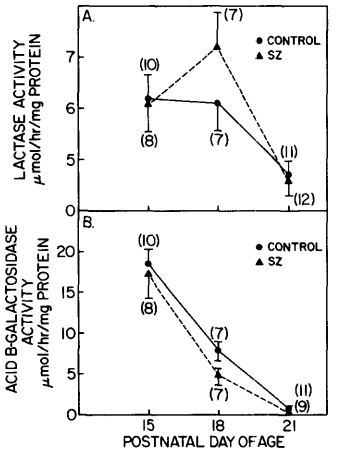

FIG. 4. Effects of streptozotocin (SZ) on intestinal lactase activity in proximal half of small intestine (A) and acid β-galactosidase activity in the distal half of the small intestine (B) of newborn rats sacrificed at three postnatal ages. Other legend details are identical to those of Fig. 1.

declined at the same rate in the SZ group as in the control pups.

Discussion. The purpose of this study was to examine the effect of diabetes on the development of small intestinal enzymes of infant rats. The ontogenic profiles of sucrase and maltase in SZ-induced diabetic pups were shifted toward an earlier appearance and precocious maturation (Fig. 3). This effect followed the same trend as that reported for diabetic adult rats (1–4, 6). The magnitude of the increase in sucrase and maltase activities of diabetic pups as compared to control pups was twofold and thus similar to the observations reported in adult rats (1, 2). Elevation of circulating glucocorticoids has previously been shown to cause precocious increases of both sucrase and maltase activities (7). Thus, it was important to determine whether SZ treatment caused plasma concentrations of corticosterone to be increased. As no such increases were found, it is concluded that the precocious maturation of these enzymes in pups receiving SZ was not mediated by glucocorticoids.

Somewhat to our surprise, plasma IRI levels in diabetic pups were found to be insignificantly lower than those of the control pups (Fig. 2A), while the pancreatic IRI content in SZ pups was reduced by 94–96% of that of the control pups (Fig. 2B). Although this finding is inconsistent with what is established in literature for adult rats, it is in agreement with Bonner-Weir *et al.* (22), who reported that in diabetic pups injected with SZ at 2 days of age, plasma IRI levels did not differ significantly from controls until after the third week of life. Still, pancreatic IRI content was markedly depleted. It appears that an extrapancreatic source of insulin may exist which is impervious to SZ. It has been demonstrated that circulating insulin persists after evisceration, suggesting that sources other than the pancreas can supply insulin to plasma (23). Alternatively, and despite our use of an homologous assay system, the IRI data presented here may represent immunologically related, cross-reacting substances. In order to explain the existing hyperglycemia and hepatic glycogenolysis in face of normal plasma insulin levels, one must consider the possibility that the SZ-diabetic pups were insulin resistant. Investigation of such a possibility would necessitate binding studies employing membranes prepared from the major insulin target sites, namely liver, skeletal muscle, and adipose tissue. Preliminary data with liver membranes did not indicate that any binding differences existed between diabetic and nondiabetic pups. Also, because of the documented difficulty in preparing satisfactory rat skeletal muscle preparations (24), this experimental avenue was not pursued further.

In view of the fact that circulating concentrations of IRI were not reduced by SZ, the precocious increase of sucrase and maltase activities must be due to one of the other metabolic derangements induced by SZ. The two most likely candidates would be plasma glucagon and glucose. Although the former was not measured in this study, it would certainly be expected to be elevated. However, previous studies have shown exogenous glucagon to have no effect on sucrase development (25). Thus, we predict that the results observed in this study are a direct result of the elevated plasma glucose. This prediction is consistent with the reports that high carbohydrate diets cause elevation of jejunal sucrase and maltase in suckling and weanling rats (26, 27) and that addition of sugars to the culture medium of intestinal explants from

suckling rats results in increased activities of these enzymes (27).

Although jejunal sucrase and maltase activities were precociously increased in infant rats, such increases were not observed in jejunal lactase activity (Fig. 4A). This is inconsistent with the observations reported in adult diabetic rats in which all three intestinal disaccharidase activities were elevated to about the same extent (2). Some caution should be exercised in the interpretation of the SZ or alloxan diabetic data in adult rats because other reports indicate that the nature of the diabetic lesion may influence greatly the results obtained. Thus, in the genetic-obese mouse model so frequently employed in studies of Type II diabetes, intestinal lactase activity per segment increases, but when expressed as per unit DNA or total protein, the diabetic state appears to be without effect (28, 29). The mechanisms for regulating this small intestinal enzyme, therefore, may differ according to the nature of the diabetic lesion.

Since the normal decline of lactase and acid β-galactosidase activities occurs between Day 15 and Day 21 (7, 11), the effects of diabetes on these enzymes may have been offset by the mechanisms which regulate their ontogeny. A likely possibility is that lactase and acid β-galactosidase continue to decline in the SZ-treated pups in response to increasing plasma thyroxine. Thyroxine levels were not measured in the present investigation, but previous studies by others have implicated the developmental rise of circulating thyroxine as the primary regulator of the decline of lactase and acid β-galactosidase activities during the third and fourth postnatal weeks (7, 30). In adult rats, administration of thyroxine has been shown to counteract other treatments which would normally result in an increased lactase activity (31). Analogous counteractions in our system could explain the lack of effect of diabetes on both lactase and acid β-galactosidase. Future work is encouraged to explore this possibility.

If the elevated blood glucose indeed is the cause of the precocious increase of sucrase and maltase activities in the SZ-treated rat pups, there may be an alternative explanation for acid β-galactosidase being resistant to diabetes. Although this enzyme has not been included in the reported studies on the effect of carbohydrates on intestinal enzymes (26, 27), comparison between disaccharidases, alkaline phosphatase, and aminopeptidase has led to the suggestion that the carbohydrate effect is specific to the disaccharidases (27). Previous studies reported by other workers indicate that dietary composition markedly influences the level of intestinal α-disaccharidases but not that of acid β-galactosidase in adult rats (32). Further studies are necessary to confirm the hypothesis that elevated disaccharidases in diabetes are the direct effect of elevated blood glucose. In this regard, the infant rat may provide a valuable animal model because of the unique situation wherein effects on these enzymes are observed in the absence of any change in plasma insulin.

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1. Olsen WA, Rogers L. Jejunal sucrase activity in diabetic rats. J Lab Clin Med **77**:838–842, 1983.
2. Younoszai MK, Ranshaw J. Intestinal disaccharidases in the rat: Effects of pregnancy and diabetes. J Nutr **106**:504–508, 1976.
3. Caspary WF, Rhein AM, Creutzfeldt W. Increase of intestinal brush border hydrolase in mucosa of streptozotocin-diabetic rats. Diabetologia **8**:412–414, 1972.
4. Olsen WA, Perchellet E, Malinowski RL. Intestinal mucosa in diabetes: Synthesis of total proteins and sucrase-isomaltase. Amer J Physiol **250**:G788–G793, 1986.
5. Mahmood A, Pathak RM, Agarwal N. Effect of chronic alloxan diabetes and insulin administration on intestinal brush border enzymes. Experientia **34**:741–742, 1978.
6. Ramaswamy K, Flint PW. Effect of genetic diabetes on enzymes of mouse intestinal brush-border membrane. Amer J Physiol **238**:G114–G118, 1980.
7. Henning SJ. Ontogeny of enzymes in the small intestine. Annu Rev Physiol **47**:231–245, 1985.
8. Henning SJ. Plasma concentrations of total and free corticosterone during development in the rat. Amer J Physiol **235**:E451–E456, 1978.
9. Rubino A, Zimbalatti F, Auricchio S. Intestinal disaccharidase activities in adult and suckling rats. Biochim Biophys Acta **92**:305–311, 1964.

10. Koldovsky O, Palmieri M. Cortisone-evoked decrease of acid β-galactosidase, β-glucuronidase, *N*-acetyl-β-glucosaminidase and arylsulphatase in the ileum of suckling rats. Biochem J **125**:697–701, 1971.
11. Henning SJ. Postnatal development: Coordination of feeding, digestion, and metabolism. Amer J Physiol **241**:G199–G214, 1981.
12. Menard D, Malo C. Insulin-evoked precocious appearance of intestinal sucrase activity in suckling mice. Dev Biol **69**:661–665, 1979.
13. Arsenault P, Menard D. Insulin influences the maturation and proliferation of suckling mouse intestinal mucosa in serum-free organ culture. Biol Neonate **46**:229–236, 1984.
14. Malo C, Menard D. Synergistic effects of insulin and thyroxine on the differentiation and proliferation of epithelial cells of suckling mouse small intestine. Biol Neonate **44**:177–184, 1983.
15. Menard D, Malo C, Calvert R. Insulin accelerates the development of intestinal brush-border hydrolytic activities of suckling mice. Dev Biol **85**:150–155, 1981.
16. Morgan CR, Lazarow A. Immunoassay of insulin: Two antibody system, plasma insulin levels of normal, sub-diabetic and diabetic rats. Diabetes **12**:115–126, 1963.
17. Martin GR, Henning SJ. Enzymic development of the small intestine: are glucocorticoids necessary? Amer J Physiol **246**:G695–G699, 1984.
18. Seifter S, Dayton S, Novic B, Muntwyler E. The estimation of glycogen with the anthrone reagent. Arch Biochem **25**:191–200, 1950.
19. Lowry DH, Rosebrough NJ, Farr AF, Randall RJ. Protein measurement with Folin phenol reagent. J Biol Chem **193**:265–275, 1951.
20. Henning SJ, Leeper LL. Coordinate loss of glucocorticoid responsiveness by intestinal enzymes during postnatal development. Amer J Physiol **242**:G89–G94, 1982.
21. Koldovsky O, Sunshine P. Effect of cortisone on the developmental pattern of the neutral and acid β-galactosidase of the small intestine of the rat. Biochem J **117**:476–481, 1970.
22. Bonner-Weir S, Trent DF, Honey RN, Weir GC. Responses of neonatal rat islets to streptozotocin, limited B-cell regeneration and hyperglycemia. Diabetes **30**:64–69, 1981.
23. Smith SS, Bhathena SJ, Nompleggi D, Penhos JC, Recant L. Studies on persistent circulating immunoreactive glucagon (IRG) and immunoreactive insulin (IRI) found in eviscerated rats with a functional liver. Diabetologia **14**:177–184, 1978.
24. Dubler RE, Whipple JH, Larner J. Characterization of skeletal muscle insulin receptors. Arch Biochem Biophys **236**:119–129, 1985.
25. Buts J-P, DeMeyer R, VanCraynest M-P, Maldague P. Pancreatic glucagon does not alter mucosal growth and maturation of sucrase and thymidine kinase activity in rat small intestine. Biol Neonate **43**:253–262, 1983.
26. Henning SJ, Guerin DM. Role of diet in the determination of jejunal sucrase activity in the weanling rat. Pediatr Res **15**:1068–1072, 1981.
27. Raul F, Kedinger M, Simon PM, Grenier JF, Haffen K. Comparative in vivo and in vitro effect of mono- and disaccharides on intestinal brush border enzyme activities in suckling rats. Biol Neonate **39**:200–207, 1981.
28. Ramaswamy K, Peterson MA. Transport of monosaccharides by the small intestine of genetically diabetic mice. Fed Proc **37**:722, 1978 [Abstract]
29. Lee SM, Bustamante SA, Koldovsky O. The effect of alpha-glucosidase inhibition on intestinal disaccharidase activity in normal and diabetic mice. Metabolism **32**:793–799, 1983.
30. Koldovsky O, Jumawan J, Palmieri M. Thyroxine-evoked precocious decrease of acid hydrolases in the ileum of suckling rats. Proc Soc Exp Biol Med **146**:661–664, 1974.
31. Raul F, Noriega R, Nsi-Emvo E, Doffoel M, Grenier JF. Lactase activity is under hormonal control in the intestine of adult rats. Gut **24**:648–652, 1983.
32. Bustamante S, Gasparo M, Kendall K, Coates P, Brown S, Somawane B, Koldovsky O. Increased activity of rat intestinal lactase due to increased intake of α-saccharides (starch, sucrose) in isocaloric diets. J Nutr **111**:943–953, 1981.

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