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Insulin reserves in children with impaired glucose tolerance(IGT) and subsequent development of diabetes mellitus (DM).

The validity of the maximum stimulation test (MIST) and oral glucose tolerance test(OGTT) as screening procedures for the development of DM was studied in 33 children with IGT. They were administered MIST(p.o.glucose;i.v.tolbutamide and glucagon) and OGTT on 2 consecutive days.Insulin response was compared with the development of DM for up to 5½yrs.MIST was a better indicator of the chance to develop DM:3 non-obese subjects with poor MIST insulin response (glucose/insulin ratio> 4)developed DM. One child who was on Orinase at the time of studies,progressed to DM despite a good MIST insulin release.All others had a good MIST insulin response and did not develop DM.The predictive value for the development of DMwith a poor MIST insulin response was 75%.The predictive value for non-development of DM with a good MIST insulin response was 96.2%.In contrast,OGTT elicited poor insulin responses in 9 of 30 children;only 3 of them progressed to DM.The predictive value for development of DM with a poor OGTT insulin response at 1 hr was 33.3% and the predictive value for non-development of DM with a good OGTT insulin release was 100%.Thus, the ability to release insulin during MIST may be a better prognostic indicator of the chance to develop DM in children with IGT,whereas OGTT may help in assessing the decreased risk of DM.

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Fetomaternal transfer of glucose in human placenta: Relation to fetal blood pressure.

Apparently carbohydrates are transported across the placenta by a carrier system. The influence of both altered pressure and flow in the fetal vascular system and of insulin in the maternal circulation upon the maternofetal transport of glucose were studied. Segments of five placentas were studied by an open dual perfusion system. 1.) Using a maternofetal glucose gradient (range 266 - 425 mg/100 ml), augmented fetal flow by increased blood pressure did not alter the relative glucose transfer rate (mean 0.0894 mg/min./g placenta, SEM ± 0.03 for a glucose gradient of 100 mg/100 ml) from maternal to fetal system. 2.) Without any glucose gradient, an influence of fetal pressure variation on the transfer of glucose could not be demonstrated. 3.) Insulin infusion to maternal circulation does not change the glucose transfer. - The assumed carrier complex for the facilitated diffusion of glucose will not be altered by blood pressure in physiological range and by the maternal insulin concentration.

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24 hour cortisol profiles demonstrate exaggerated nocturnal rise in diabetic children.

To identify altered patterns of cortisol (F) secretion and metabolism in diabetic (D) children, plasma F was measured every 20 min. for 24h in 12 normal (NL) and 11 insulin dependent,non-ketotic D's on a single daily insulin dose.The diurnal pattern of secretion was identical. The mean 24h plasma F was similar in both groups (NL = 5.4±1.6, D=6.6±2.0 µg%; mean ±SD): but significantly elevated in the D's between 5 a.m. and 9:20 a.m., the main secretory period of the day in both groups (NL = 8.1±1.8, D=12.2±3.2 µg%; mean ±SD, p<.001). Peak F averaged 15.5±3.8 in the NL's vs. 19.6±4.1 µg% in the D's (mean ±SD; p<.02). 24h urinary excretion of 17OHCS, free cortisol (FF), and 6B-hydroxycortisol (6βOHF) measured in 11 NL's and 19 D's showed increased excretion of FF and 6βOHF, but not of 17OHCSs in the D's.

	*FF (µg/d)	*6βOHF (µg/d)	*17OHCS (mg/d)
NL	50 ± 13	244 ± 65	4.3 ± 2.2
D	106 ± 64	620 ± 322	4.7 ± 2.5
P	<.01	<.001	NS *per g/creat.±SD

These results demonstrate an exaggerated nocturnal rise in plasma F in D children not reflected by increased 17OHCS excretion, but evidenced by elevated urinary FF and 6βOHF, more sensitive tests for hypercortisolemia. These abnormalities might be corrected by twice daily insulin therapy to improve nocturnal insulinization.

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INSULIN BINDING TO THE HL-60 HUMAN PROMYELOCYTIC CELL LINE.

The HL-60 cell line derived from a patient with promyelocytic leukemia may be grown in liquid suspension cell culture. It binds [^{125}I]-iodoinsulin in a highly specific, rapid, reversible, temperature and pH dependent manner. The pH maximum is approximately 7.8 and binding is maximal after 80 min at 22C with virtually 90% specific. Specific binding is linear with cell number over the range of 10^7 to 10^8 cells. The displacement of bound [^{125}I]-iodoinsulin by unlabeled insulin yields curvilinear Scatchard plots at 22C. Using a 2 site model the insulin binding characteristics may best be defined by a "high" affinity site (n_1=8.7±2.6(SD)·10^3 per cell; k_1=2.7±0.55·$10^8 M^{-1}$) and a "low" affinity site (n_2=1.12±0.32·10^5 per cell; k_2=7.8±3.6·$10^6 M^{-1}$). To determine insulin release from its receptor, cells were exposed to [^{125}I]-iodoinsulin for 90 min at 22C. Aliquots were diluted 100-fold in binding buffer or buffer plus 1.67·10^{-6}M insulin. The excess unlabeled insulin accelerated the dissociation of labeled insulin at 22, 30 and 37C, but did not at 4 or 15C. Displacement of [^{125}I]-iodoinsulin by vertebrate insulins and modified porcine insulins is in agreement with their known biological activities. Purified multiplication stimulating factor was less than 1 percent as effective as porcine insulin. These data indicate that the HL-60 cells maintain specific, high affinity insulin receptors. The release of insulin is accelerated by unlabeled hormone above 22C but not below 15C.

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HbA1 and beta cell function in cystic fibrosis (CF).

The increase in the longevity of patients with CF appears to have been accompanied by a rise in the frequency of glucose intolerance. HbA1 blood conc. is an objective mean to assess carbohydrate homeostasis. HbA1 conc. were examined in 34 CF patients aged 1½-20½ years. In 11 oral glucose tolerance tests (OGTT) were performed and glucose and insulin conc. were measured. The mean HbA1 conc. in CF children (n=34) was 7.97±0.2 (mean±SEM) and significantly higher than that in normal children - 6.8±0.13 (n=40) (mean±SEM), although there was no difference in the fasting blood glucose between the two groups.

8 children had a normal, while 3 children had an impaired OGTT. These latter 3 children had a delayed peak response in insulin levels, while there was a decrease in the level of the insulin response in all the children. No correlation was found between HbA1 conc. and the age of the patients, nor between HbA1 and the clinical status (Shwachman score).

In summary, severe insulinopenia in children with CF is not always accompanied by an increment in HbA1, although serial determinations of the level of HbA1 may reveal deterioration in glucose tolerance.

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The relationship between the degree of blood glucose regulation and psychological factors in diabetic adolescents.

52 white, middle class, insulin dependent diabetic adolescents (13 years to 19 years), who had diabetes at least 5 years, and their mothers completed questionnaires designed to assess anxiety, locus of control, personality traits, self concept and adjustment to diabetes. The hemoglobin Alc (HbAlc) value was used to measure the degree of blood glucose regulation. The HbAlc value of 9.5% was used to arbitrarily divide the subjects into a high and low HbAlc group. There was a disproportionately greater percent of females having high HbAlc values (70%) compared to males with high values (38%). Two way ANOVA (with sex and the level of blood glucose regulation as independent variables) found no significant differences attributed to the level of blood glucose regulation and some significant differences attributed to sex. Females had significantly higher scores for anxiety, feeling unhappy and feeling less confident because of their diabetes, greater independence in managing their diabetes but females were more likely not to follow their meal plan if upset. Since our results indicate that psychological factors as measured in this study may not be of major importance in blood glucose regulation, greater emphasis should be directed to the effects of metabolic and genetic factors on blood glucose regulation.