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Diabetes unresponsive to subc. but responsive to I.V. insulin: Biphasic behavior.

Six female diabetics, 14 to 31 years of age, had erratic control for years and developed resistance to subc. insulin (2.5-30.0 units/kg/day) but had normal response to I.V. insulin (0.35-0.9 units/kg/day). Three patients required continuous I.V. insulin infusion for 6 mos to 1 year. Euglycemia was achieved, when aprotinin (a protease inhibitor) and regular insulin (0.7-1.4 units/kg/day) was given subc. Plasma levels of free insulin rose and ketonuria subsided. Four patients had episodes of spontaneous severe hypoglycemia, before and during aprotinin therapy, requiring I.V. glucose for 2 to 60 days. Days and weeks after the last sub . injection of ins. hypoglycemia and hyperinsulinemia (50 to 2000 μU free insulin/ml) persisted, C-peptide was <0.5 ng/ml; counterregulatory hormones were normal; in one patient fat biopsy insulin (1090 μU/gm) and glutathione-insulin transhydrogenase in leukocytes and subc fat were higher than in 2 controls; ^{3}H-insulin was absorbed and degraded normally during the hypoglycemic phase and not absorbed during the resistant phase. The findings suggest that insulin is sequestered (and may be degraded) at the injection site during the resistant phase and released during the hypoglycemic phase.

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Hyperinsulinism in Infants and Children: Response to Diazoxide.

Early diagnosis and treatment of hypoglycemia in children of any age is important. Prompt treatment with diazoxide of infants or children with documented fasting hypoglycemia is effective. In addition, the blood glucose response to diazoxide is an important diagnostic test for hyperinsulinism along with confirmatory metabolic and hormonal studies. Longitudinal growth, neurologic and metabolic data of 17 infants and children (< 2 years at the time of diagnosis) with hyperinsulinism treated with diazoxide will be presented. The blood glucose of 13 of the 17 patients responded to diazoxide (5-10 mg/kg) within 48 hours. Ten of these children have continued to require low dose (< 5 mg/kg) treatment for symptomatic or laboratory evidence of hypoglycemia (mean duration 4 years, 1-11 years). Hyperinsulinism, although asymptomatic, is still present in the 3 children who have been able to discontinue treatment. The pathological diagnosis of the 4 infants whose blood glucose failed to respond to diazoxide were islet cell adenoma (2) and nesidioblastoma (2). Two of these infants died; the 2 who survived required total pancreatectomies and subsequent treatment with insulin and pancreatic enzymes. Hypertrichosis was evident in all children treated with diazoxide and was dose related. One child developed reversible leukopenia. Neurologic sequellae in most children surviving are surprisingly minimal and unrelated to the age of onset, the degree or duration of hypoglycemia.

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Optimal glucose control can be achieved in the young diabetic.

Recent studies indicate that glucose control may be improved in adult diabetics with intensive insulin (II) Rx (using either infusion pumps or multiple injections) and home blood glucose monitoring. To examine the efficacy of these Rx strategies in children, we examined whether near normal glucose levels could be achieved in 8 young (age 10-15 yrs) diabetics given II Rx (6 pump, 2 multiple injections) for 2-6 mos. Control was assessed by HbA_1 (nl 5-8%) and glucose measurements of blood samples mailed from home (HG). Glycemic excursions (MAGE) were determined from inpatient glucose profiles (IG). Effect of II Rx on glucose levels (mg/dl) is shown below (¶ $p < 0.01$).

	HG(premeal)	HG(postmeal)	IG	MAGE
Pre-II Rx	246±18	312±21	256±18	153±13
II Rx	109±8 ¶	128±8 ¶	113±6 ¶	92±6 ¶

HbA_1 levels fell significantly after 2 wks (12.7±1.0 to 9.3±0.7%) and was further reduced by 4-8 wks. (7.6±0.1%, $p<0.005$). Glycosuria was virtually eliminated (81±20 vs 3±1 gm/day). Insulin dose increased by 50% with II Rx (to 1.4 U/kg/day). However, hypoglycemia symptoms were mild and none required IV glucose. Conclusions: Near normal glucose control can be achieved in the outpatient management of children and adolescents with diabetes. The comparative efficacy of insulin pump vs multiple injections needs to be determined.

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Prolactin, TSH, T3, T4, fT3, fT4, TBG and reverse T3 in Turner's Syndrome.

In 18 girls with Turner's S. basal plasma values of T3, T4, fT3, fT4, TBG and reverse T3 were assessed and a TRH-test carried out to assay prolactin and TSH. The results were studied bearing in mind the cariotypes, the presence or absence of ovarian dysgenesis and the pubertal stage. Patients with Turner's S. whose bone age was < 11yrs had a significantly higher prolactin pituitary reserve than 12 normal prepubertal girls. The hypothalamo-pituitary-thyroid function showed some significant differences which can be related to the different cariotypes. In patients with Turner's S. and bone age > 11yrs prolactin and thyroid hormones do not seem to be significantly different compared with 5 pubertal females. It would appear from these preliminary data that in prepubertal females ovarian activity involves a negative feed-back, which becomes positive at puberty. The frequent changes in the hypothalamo-pituitary-thyroid axis are also confirmed.

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THYROXINE (T_4), TRIIODOTHYRONINE (T_3) AND REVERSE TRIIODOTHYRONINE (rT_3) CONCENTRATIONS IN CHILDREN WITH TYPE I DIABETES (IDD).

Measurements of T_4, T_3 and rT_3 were done by means of a radioimmunoassay in 22 children (age 3,6 - 13,8 yrs., 13 boys, 9 girls) with newly diagnosed type I diabetes. In 17 patients, rT_3 values were significantly elevated (mean 57 ng/dl) as well as the rT_3/T_3 ratio (mean 0,92). T_3 concentrations were low or low normal in 18 children (mean 72,2 ng/dl). Only in 4 patients, T_3 and rT_3 were in the normal range. TSH (basal) was normal in all children. There was no significant correlation of the T_3 and the rT_3 concentrations with the time since onset of symptoms of diabetes, the blood glucose values, the HbA_{1c} concentrations and the parameters of diabetic ketoacidosis. 4 weeks after onset of therapy, T_4, T_3, rT_3 and TSH concentrations were normal in all children. Our results suggest that peripheral monodeiodination of T_4 in untreated diabetic children results in an increased production of rT_3 while that of T_3 is reduced. This inverse relation of degradation changes to normal shortly after onset of therapy.

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HLA typing and congenital, primary hypothyroidism.

An association has been demonstrated between HLA-antigens and thyroid diseases such as Graves' disease, Hashimoto's thyroiditis and subacute thyroiditis.

The significance of HLA types in the pathogenesis of congenital hypothyroidism has not been clarified. Recently, a study from Japan showed an increased frequency of HLA-Aw24 in congenital hypothyroidism (N Engl J Med 1980; 303:226). An American study did not confirm this finding, but could not exclude the possibiloty that HLA-B18 may be increased in patients with congenital hypothyroidism (N Engl J Med 1980;303: 1177).

In a study of HLA-A, B and C types in - so far - 24 Danish patients with congenital hypothyroidism we did not find any association between the HLA types and the congenital dysplasia of the thyroid gland. In particular, the frequencies of Aw24 and B18 antigens were both lower in the patients than in the controls.