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HYPERTHYROID GOITRE DUE TO INAPPROPRIATE TSH SECRETION SUCCESSFULLY TREATED WITH DEXTRO-THYROXINE.

J.A., a 6 year-old girl with small goitre had elevated levels of T4, T3 as well as TSH. Her high and weight were at the 10th percentile, bone age was delayed about 2 years but clinically she was euthyroid. Treatment with t.h. resulted in TSH suppresion but sings of hyperthyroidism appeared. During the next 3 years without any treatment T4, T3 and basal TSH were still elevated and TRH stimulated TSH increased to the hypothyroid range. At the age of 9 years clinical symptoms of hyperthyroidism were evident. Hypothalamo-pituitary studies were normal, there was no evidence for pituitary tumor. A partial selective pituitary resistance to t.h. was supposed. Since 1980 the patient was treated with D-T4 in a dose of 0.5mg/d. Gradual decrease of TSH levels was accompanied by reduction in the size of goitre and amelioration of clinical symptoms of hyperthyroidism, confirmed by normalisation of BMR. Temporary interruption of D-T4 therapy resulted in the increase of all clinical and biochemical abnormalities. To our knowledge this is the first case of hyperthyroidism due to inappropriate TSH secretion treated with D-T4.

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SERUM THYROID MICROSOMAL ANTIBODIES(MCHA)AND THEIR PREDICTIVE VALUE OF OVERT THYROID DISEASE IN DIABETIC CHILDREN:A LONGITUDINAL STUDY.

Whilst the last 10 years'literature unanimously points out the increased prevalence of serum MCHA in children and youngsters with insulin-dependent diabetes mellitus (IDDM), the predictive value of overt thyroid disease of such a biohumoral marker in these patients widely varies according to the different Authors:frequently >40% in US reports, generally <10% in European reports. We followed for a 5-yr period 12 MCHA positive IDDM children (12/99 vs a prevalence of 6/197 found in an age-matched control group, $\chi^2=9.5$, $p<0.005$), who underwent semestral clinical and biochemical (T4, T3, FT4, FT3, TSH, TSH response to i.v. TRH) assessments of thyroid function. Results: a) during the whole follow-up period, the MCHA titers have been fluctuating up and down in all patients, with no effects on thyroid function tests; b) no patient has been showing goiter or other clinical signs of thyroid dysfunction; c) no patient has been exhibiting persistent or even transient changes in thyroid function tests suggestive of hypothyroidism or hyperthyroidism; d) in 4/12 cases the first TRH-test elicited a TSH hyperresponse suggestive of subclinical hypothyroidism, but such a pattern was not confirmed at the next tests.
Conclusions: based on a longitudinal study, our data confirm that the increased prevalence of MCHA in IDDM children is not associated to high risk of overt thyroid disease, at least in Europe.

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CONTINUOUS SUBCUTANEOUS GLUCAGON INFUSION IS AN EFFECTIVE MEAN OF INCREASING BLOOD GLUCOSE (BG) IN HYPERINSULINEMIC INFANTS.

Hyperinsulinemic infants develop severe hypoglycemia due to a major suppression of glucose production by the liver. Treatment of this condition is made difficult in a subset of patients by the limited efficacy of drugs, such as diazoxide or corticosteroids. The need for maintaining a large supply of glucose in these patients requires continuous nasogastric feeding and sometimes prolonged peripheral or central venous catheterization. We have used the subcutaneous infusion of glucagon via a small insulin pump in an attempt to maintain BG within normal limits in 5 hypersinulinemic infants previously treated with 15 mg/kg.d diazoxide. Glucagon was infused continuously as a 1 mg/ml 0.5 N saline solution at a rate of 0.37±0.17 mg/kg.d during the 2-12 weeks preceeding subtotal pancreatectomy. No side effects were detected. BG increased from 50±28 to 110±57 mg/dl ($p<0.001$), with a consistent effect in all treated children. Less than 6±4% BG values fell below 45 mg/dl versus 41±14% ($p<0.025$) under previous therapy. Mean insulin values were as expected unchanged (10±7.3 versus 18±13 µU/ml before). During this period, feeding could be discontinued and diminished down to 0.65±0.1 g carbohydrates/kg.h; versus 0.93 ±0.1 g/kg.h before. Because of its simplicity and reliability, we propose that the subcutaneous continuous infusion of glucagon should be largely employed for the control of hypoglycemia in infants developing severe hyperinsulinism and/or resistance to diazoxide therapy.

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LONG TERM TREATMENT BY A LONG ACTING SOMATOSTATIN ANALOGUE (SMS 201-995) IN A 4 MONTHS BOY PRESENTING WITH PRIMARY PERMANENT HYPERINSULINISM.

SMS 201-995 was used in a 4 month-old boy presenting hypoglycemic seizures with hyperinsulinism. The dose of SMS 201-995 was rapidly increased during the first week from 10 ug/kg/day to 100 ug/kg/day, and was administrated using continuous subcutaneous infusion (CSI) during 8 months and then 3 or 2 daily subcutaneous infusion per day for 1 month. Capillary blood glucose was measured every 3 hours. Plasma insulin was evaluated twice daily on the first weeks and when blood glucose was lower than 50 mg/dl. Mean blood glucose levels was dramatically and rapidly increased by therapy, frequency of hypoglycemia was strongly reduced, blood glucose/insulin ratio increased, carbohydrate needs were reduced (0.6g/kg/day). CT Scan of the pancreas performed before therapy noticed a global increase of the volume of the gland which was no more observed after one month of therapy. Growth velocity remained in a normal range for age. Measure of plasma GH every 20 min during 5 hours had shown a normal spontaneous GH peak of 50 ng/ml. Neurologic development was normal. Others endocrine functions remained normal. Tolerance of this treatment was good excepted for transient diarrhea and vomiting during the first 2 weeks of therapy and transient moderate increase of Gamma GT. Treatment had been interrupted after one and 6 months of therapy with reccurrent hypoglycemia after 3 and 6 days respectively. 3 or 2 subcutaneous injections resulted in a worstly glycemic control than CSI therapy.

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SOMATOSTATIN TREATMENT OF NEONATAL HYPERINSULINISM DUE TO FOCAL ADENOMATOSIS OF THE PANCREAS

We report the use of somatostatin in a newborn infant with hyperinsulinism due to focal adenomatosis of the pancreas. When administred alone at a rate of 2,5 to 7 µu/kg/h, the natural somatostatin was documented to be short-timed able to prevent hypoglycemia. However the association to glucagon infusion at a rate of 2,5 µu/kg/h allowed successful control of patient's hypoglycemia.
As hyperinsulinism relapsed after a subtotal pancreatectomy, a trial with somatostatin analogue SMS 201-995, which has an expected longer duration of action was performed. It lead to a significant rise in the blood glucose level but failed to prevent safely hypoglycemia even when four injections were performed So, three hours after a subcutaneous injection of 10 µg of the analogue, the blood glucose concentration raised significantly to 5 - 7 mmol./l., but after four to five hours, the level dropped again to 1,8 - 2,2 mmol./l.. The young age of the infant and the cerebral risk of hypoglycemia did not allow us to increase posology and injection's frequency ; then a near total pancreatectomy was performed.

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HYPERINSULINEMIC HYPOGLYCEMIA (NESIDIOBLASTOSIS?). OUTCOME OF 7 CASES TREATED WITH LOW LEUCINE DIET AND DIAZOXIDE.

Mental subnormality in hyperinsulinemic hypoglycemia (HH) of infancy, in the reported series, ranges from 35 to 60%. We report on the outcome of 7 cases. All but one presented with convulsions prior to the age of 9 months. The diagnosis of HH was based on low glucose-insulin ratio (G/I) in random blood samples after limited fasting (6.2±7.1 in HH versus 24.7±14.4 in controls), and after leucine (L) load (1.7±1.5 in HH versus 21.2±13.4 in controls). Random G/I values although lower in infants with HH, as a group, was not diagnostic in individual cases. All subjects were placed on low leucine diet and 6/7 also received diazoxide (10-15mg/kg/day). In all but one child this regimen was effective in raising blood glucose. In one infant, partial pancreatectomy was performed with excellent result. One infant has come off Diazoxide and is well and free of hypertrichosis 30 months later. L. tolerance in children retested while on diazoxide, was normal, while in the child on diet alone sensitivity persisted. All infants have normal IQ now. Side effects: hypertrichosis (all), transient rise in alkaline phosphatase (2) and in uric acid (1). In our subjects, random G/I values were indicative but not diagnostic of HH while post L G/I values established the diagnosis. Strict adherence to diet combined with diazoxide gave the best results and limited the need for pancreatectomy. Either diet or diazoxide alone proved ineffective.