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Clinical and Hormonal Findings in Cases of Congenital Hypothyroidism discovered by Neonatal Screening.

In the Danish nationwide screening for congenital hypothyroidism (measurement of TSH (RIA) in wholeblood collected on PKU-cards) 18 patients were found among 89.000 newborns. At diagnosis, the ranges of plasma concentration of hormone- and hormone-binding proteins were: TSH: 219-1128 mU/l, T_4: 10-74 nmol/l, T_3: 0.32-2,83 nmol/l, TBG: 197-390 nmol/l, TBPA: 2319-4569 nmol/l, Alb: 351-494 µmol/l. The number of clinical signs were negatively correlated with plasma T_3 concentration. The infants were treated with a daily dose of 50-100 µg sodium L-thyroxine. During treatment plasma T_3 reached level of healthy fullterm babies within a few days, plasma T_4 within 1 week and plasma TSH within 3 weeks of treatment. Plasma Alb and plasma TBPA concentrations decreased following 1 week of therapy, plasma TBG concentration increased in some patients. After 1 month plasma Alb was still decreased, whereas plasma TBG and plasma TBPA were above pretreatment levels in half of the patients.

The therapeutical consequences of these findings are open for discussion.

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Measurement of Free Thyroxine (FT4) in the Newborn: A reliable test to confirm euthyroidism in neonates with low T4-values.

Experience in neonatal screening for congenital hypothyroidism has made evident a large overlap between eu- and hypothyroid T4-levels. Concomitant lowering of TBG can explain abnormally low T4-levels only to a certain extent. In order to evaluate the significance of low T4-values, T4/TBG ratio was compared with direct radioimmunological measurements of FT4 in 52 term and 70 preterm infants who had to be retested because of borderline values in our TSH/T4-screening-program. RESULTS: T4 ($\bar{x}$:5,6-12,0 µg/dl), TBG ($\bar{x}$:18,3-27,3mg/l) and T4/TBG ratio ($\bar{x}$:3,2-4,6) increase with gestational age. FT4 ($\bar{x}$: 2,1-2,4ng/dl) is not significantly different in term and preterm infants. Preterm infants with abnormally low T4 (< 4 µg/dl) show FT4-values within the normal range--this in contrast to a decrease of T4/TBG ratio. CONCLUSION: Lowering of T4 and T4/TBG ratio does not indicate a lack in free T4. The contradiction between lowered T4/TBG ratio and normal free T4 may be interpreted as a reduced T4-binding affinity of TBG due to immaturity or severe illness.

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Thyroid hormones and glycosylated hemoglobin (HbA1) in Juvenile Diabetes Mellitus (JDM)

In 60 newly diagnosed children with JDM we measured serum T4, T3, reverse T3 (rT3) and free T4 (FT4) before and serially at 1, 3 and 5 days and up to 6 months during therapy. The mean ± SEM serum T3 before therapy (71 ± 6 ng/dl) was lower ($p<.01$) compared to day 5 (96 ± 5) and the T3 on day 5 was lower than controls (126 ± 9) but was normal by 1 month. Mean serum rT3 before therapy (60 ± 3 ng/dl) was higher ($p<.001$) compared to day 5 (38 ± 2), but day 5 did not differ from controls (32 ± 3). FT4 levels were higher ($p<.01$) than controls and remained unchanged. Serum TSH was normal throughout. Serum T4 was normal and remained unchanged in patients with $^-HCO3 > 15$ mEq/L, but low before therapy when $^-HCO3 < 15$ and increased to normal by day 3. Serum T3 was lower in patients with low $^-HCO3$ before therapy. The elevated rT3 and FT4 were unaffected by low $^-HCO3$. HbAl fell significantly by paired t test ($p<.001$) during the first 5 days of therapy, and further decreased during the ensuing 3 months ($p<.001$). HbAl correlated with rT3 and inversely with T3 during the study period ($p<.001$). We speculate that the metabolic disturbance in untreated JDM resembles the "Low T3 Syndrome" of starvation. The association of low $^-HCO3$ and low total T4 and T3 but normal TSH and high FT4 suggests an impairment of binding to the serum thyroid binding proteins. Correlation of T3 and rT3 with HbAl may reflect their dependency on the severity of the disease.

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Hemoglobin A_{1c}: a predictor for the duration of the remission phase in juvenile insulin-dependent diabetic patients.

Augmented HbA_{1c}-concentrations in diabetics indicate retrospectively a poor metabolic control during the preceding 2-3 months. In the present study attempts have been made to use the HbA_{1c}-concentration at the time of diagnosis as an indicator for the duration of the remission phase in 22 juvenile diabetic children. The regression analysis revealed a significant correlation between the initial HbA_{1c}-concentrations and the duration of the remission phase defined as no glucose excretion and an insulin requirement of less than 0.5 U/kg/day ($r=0.85$ $p:<0.001$). The results suggest that the determination of the initial HbA_{1c}-concentration may serve as a useful indicator to predict the duration of the remission phase in juvenile insulin-dependent diabetes mellitus.

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Carbohydrate Homeostasis in Children With Leprechaunism.

Leprechaunism is a rare congenital disorder characterized by unique clinical features and profound derangements of carbohydrate metabolism. Extensive studies in 3 patients, ages 3 months to 3 years, revealed the following biochemical abnormalities: fasting hypoglycemia < 20 mg/dl and hyperinsulinemia > 50µU/ml; post-prandial hyperglycemia and hypersecretion of insulin (IN) >500 µU/ml in response to all known IN secretagogues including glucose, arginine, glucagon, and tolbutamide; marked resistance to exogenous IN and absence of ketosis were consistent findings. Circadian IN secretion assessed by continuous venous blood withdrawal suggests that the pancreatic B-cell remains responsive in some degree to feeding and fasting albeit at hyperinsulinemic baseline levels. IN was normal as to biological, immunological and chromatographic properties. Glucose turnover studies by stable isotope techniques after a 3-hour fast showed 2H-glucose disappearance to be comparable to normal children with a normal response to glucagon. After prolonged fasting (8-12 hrs.), patients were hypoglycemic and unresponsive to glucagon or epinephrine. IN binding to lymphocyte and RBC receptors were at the lower limits of normal. These derangements of carbohydrate metabolism and IN secretion are consistent with the post-receptor defect hypothesis as a plausible explanation for the disturbance in carbohydrate metabolism seen in leprechaunism.

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Polymorphic changes of rat pituitary FSH depending on sex and maturation.

The existence of various polymorphic forms of FSH has been observed by a number of investigators and the current study focussed attention on the sex and age-dependent nature of this polymorphism in rats. Utilizing very small amounts of pituitary extract on Sephadex G-100 superfine columns it was possible to distinguish various components of FSH with a range of K_{av} values from 0,195 (Component I) to 0,297 (Component VII). Although each group exhibited the existence of all the components, there was a clear predominance of components III and IV (K_{av} 0.233and 0.251) in males and components V and VI (K_{av} 0.268 and 0.281) in femal The castrated animals of both sexes had similar components which lay in between the two sex-linked forms. T pattern of polymorphism was found to be dependent on age as the pubertal animals had components of lower K_{av} in comparison to immature and mature animals. Androgen substitution reversed the castration effects in males and yielded a more male type of component in ovariecto mized females, whereas oestrogen treatment produced no comparable results. Carbohydrate analysis of various components indicates perhaps this polymorphism is related to the carbohydrate moiety.