43 COMBINED PITUITARY FUNCTION TESTS BY SIMULTANEOUS INJECTION OF SEVERAL RELEASING HORMONES.

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With the discovery of hpGRF and hCRF pituitary function can be assessed by the use of four physiologic releasing hormones.
After a rest of two hours to reach basal cortisol levels, healthy young male volunteers received a bolus of the following releasing hormones: 1) GRF (100 µg) + CRF (50 µg) + TRH (200 µg) + LHRH (100µg) 2) GRF + TRH 3) CRF + TRH 4) LHRH + TRH 5) each releasing hormone alone (n=5 in each group). During the following two hours, GH, ACTH, cortisol, TSH, LH, FSH and prolactin were measured every fifteen minutes. The combination of the four releasing hormones resulted in a rapid rise of all measured hormones with the following peak values: GH: 20,6 ± 3.8 ng/ml, ACTH: 81 ± 7 pg/ml, cortisol: 112 ± 8 ng/ml, TSH: 17.6 ± 2.2 µU/ml, LH: 143 ± 25 ng/ml, FSH: 582 ± 132 ng/ml and prolactin: 39 ± 7 ng/ml (x ± SEM). The peak level of TSH in the combined test was nearly twice the level in single TRH-tests (TSH max: 10,2 ± 1,3 µU/ml, Students' t-test, $p < 0.05$). Exaggerated TSH-response to TRH was shown to be entirely due to additional GRF administration, CRF in combination with TRH had no additional effect on TSH release. For all other measured hormones we found no significant differences between application of a single releasing hormone and the combinations studied (analysis of variance). We conclude that: 1) The combined injection of four releasing hormones provides a valuable test for anterior pituitary function. As there are practically no side effects, application in children is favored. 2) In this test increased TSH-response is to be considered.

44 AN ALGORITHMIC APPROACH TO HYPOGLYCEMIA.

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In order to facilitate the diagnostic efforts of the different etiologies of infantile hypoglycemia, we have devised an algorithm. This algorithm contains a systematic approach to enable the physician to reach the final diagnosis in a logical and goal oriented way without subjecting the children to unnecessary and possibly hazardous investigations. The algorithm is based on the following measurements tailored to each individual patient: concentrations of blood glucose, lactate, ketone bodies, ammonia and of glucose regulating hormones. These measurements will be performed in the fasting stage and after loading tests (glycerol, galactose and alanine) as needed. If required enzymatic test will be performed to establish the final diagnosis. 18 children aged from one month to seven years who suffered from persistent or recurrent hypoglycemia have been investigated according to this decision tree. The following diagnosis were made:Hormonal deficiencies 3; Glycogen Storage Disease (I and III) 7; Beta oxidation defect 3; Ketotic Hypoglycemia 3; Maple Syrup Urine Disease 1; Hereditary Fructose Intolerance 1; and Fructose-1,6-diphosphatase deficiency 1. The correct diagnosis was arrived at in 17 patients. The diagnosis was not reached in one neonate who suffered from Glucose-6-Phosphatase deficiency and who presented initially without lactic acidosis. Once he developed lactic acidosis he fitted perfectly into the algorithm.

45 CONGENITAL GH- AND ACTH DEFICIENCY: NEONATAL HYPOGLYCEMIA ASSOCIATED WITH MICROPENIS.

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A fullterm male infant admitted for symptomatic neonatal hypoglycemia (H) and micropenis was found to have abnormal GH-response to fasting and insulin-induced H (peak: 1.4 ng/ml; normal 6) and low somatomedin C levels (0.1 U/ml; normal 0.1-1). This plus an inadequate response of plasma cortisol and ACTH (94.6 nmol/L → 102 and 12 pg/ml → 13, respectively) to H,as well as abnormal urinary 17-hydroxycorticosteroid response to metapirone (basal 0.5 mg/24 hrs → 0.5; normal> 3-fold rise] suggested both, GH- and ACTH-insufficiency. Plasma T4 (5.4 µg/dl), TRH+ test (TSH: 3.2 → 21.4 µg/ml) and LH-RH-test (LH: 4.7 → 7.8 mU/ml) were normal. No or only a minute response to H noted for ß-hydroxybutyrate (235 µMol/L → 220), free fatty acids (0.1 → 0.3 mval/L), alanine (77 µMol/L → 80) associated with low plasma C-peptide levels (0.11 → 0.16 nmol/L) suggest substrate deficiency as the primary cause of H.

At age of 5 months a HCG stimulation resulted in a 5-fold rise of plasma testosterone (T)(0.09 → 0.39 ng/ml) and a 2-fold increase of dihydrotestosterone (DHT)(0.15 → 0.32 ng/ml). A biopsy specimen from scrotal skin revealed in comparison to control patients of similar age a decrease of cytosolic binding sites (*) for T and DHT receptors (28 vs 150 fmol/mg protein and 30 vs 200, respectively). The specific receptor affinity however was normal (Cyt-T-R: Kd=1.05 / Bmax=28; Cyt-DHT-R: Kd=0.65 / Bmax=117). We postulate, that the micropenis in patients with GH-deficiency is associated with an androgen receptor defect.

(*) K Herkner et al. Molecular Biology of Androgen Action: Testosterone/Dihydrotestosterone receptor and Androgen-5α-Reductase in the human foreskin. J Steroid Biochem (in press).

46 PREVALENCE OF MINOR CONGENITAL ANOMALIES IN DIABETIC CHILDREN

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The prevalence of 52 congenital minor anomalies /MCAs/ was determined in lll children with insulin dependent diabetes mellitus /IDDM/, and in lll healthy matched control subjects. The average MCA per person was 1,6o in diabetic children and o,86 in the controls /$p < o,ool$/ The difference was exclusively due to the significantly higher proportion of subjects with 3 or more MCAs in the diabetic group /27,o versus 9,9 per cent, $p < o,ool$/. Malformation type minor anomalies /"mild malformations"/ minor dysplasias, deformations, and phenogenetic variants almost equally contributed to the higher prevalence of MCAs in the patients. No specific MCA characteristic of IDDM was found.

47 RING CHROMOSOME WITH NO MALFORMATION BUT EXTREME SOMATIC RETARDATION:"RING SYNDROME"? A REVIEW OF 206 CASE REPORTS

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Many patients with ring autosomes who had no organic malformation and no or only a few nonspecific dysmorphic stigmata, showed extreme somatic retardation (eSR) the cause of which is not fully understood. Motivated by 4 own patients, the author analysed 206 reports out of about 300 cases with ring autosome known in the literature in order to shed some light upon this phenotype ("ring syndrome"). Cases with no detectable loss of chromosomal material were included only. eSR was defined as height ≥ 3 SD below the mean. Statistics were done by X^2 test. - Out of 206 cases, 114 had no organic malformation, no specific deletion syndrome and no or only a few nonspecific dysmorphic signs. Of these, 40 cases (one fifth of the total), had eSR, while 31 had normal height (NH). The ratio of eSR to NH was greater with high significance among 81 patients with ring of larger chromosomes (No 1-15) than among 33 patients with smaller ones (No 16-22), namely 37:9 and 3:22, respectively, indicating that the greater the chromosome involved, the higher is the probability of severe growth failure. - Cases were analysed according to the frequency of secundary chromosomal aneuploidy (sCA), a consequence of specific ring behaviour during mitosis. Out of 53 cases having sCA in 0-5 % of mitoses ("stable ring"), 13 (24 %) had eSR and 20 (38 %), had NH, while of 84 cases having sCA in more than 5 % of mitoses ("labile ring"), 38 (45 %) had eSR and only 11 (13 %) had NH (for eSR $p < 0.001$). It is suggested that - rather than a loss of specific material prior to ring formation - the specific ring behaviour per se is causing "ring syndrome" in one fifth of cases with ring chromosome.

48 VITAMIN E MALABSORPTION IN GROWING PRETERM INFANTS WITH SYMPTOMATIC ZINC DEFICIENCY.

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Both vitamin E and zinc deficiency continue to be observed in the very low birth-weight infants despite the use of dietary supplements. The interrelationship between vitamin E and zinc nutrition was sequentially evaluated in 58 formula fed growing preterm neonates (birth weight: $\bar{X}$ ± SD, 1043±121g, gestational age: $\bar{X}$ ± SD, 29±0.4 wks). Enteral feeds contained zinc (300mg/100ml) and supplemental vitamin E (to achieve sufficient serum E level of 1-2mg/dl). Three groups of infants were identified on data analyses. Group I (27/58) had sufficient serum zinc (>70mcg/dl) and vitamin E (1-3mg/dl) levels on mean E supplement of 55±10 SD I.U./day. Group II (15/58) were hypozincemic (<70mcg/dl) but had no other evidence of zinc deficiency. These infants had sufficient serum E levels on a mean E supplement of 71±20 SD I.U./day. Group III (16/58) were hypozincemic (<70mg/dl) and had edema and hypoproteinemia. Their mean serum vitamin E level was only 0.8mg/dl±0.4 SD in spite of their having received significantly ($p < 0.001$) higher supplement of vitamin E (162±25 SD I.U./day) than Group I and II infants. Correction of hypozincemia with therapeutic doses of oral zinc was associated with a prompt and striking improvement of serum vitamin E absorption. During the 4 week period of zinc therapy, vitamin E supplements had to be significantly reduced (0-25 I.U./day) to maintain physiologic E levels. These data demonstrate significant but reversible vitamin E malabsorption in preterm neonates with symptomatic zinc deficiency. Concurrent monitoring of both vitamin E and zinc serum levels is recommended.