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191 ECTOPIC ACTH SYNDROME AND "TUMOR HYPERCALCEMIA" DUE TO A HEPATOBLASTOMA.

We are reporting the first case of combined ectopic ACTH syndrome and "humoral hypercalcemia of malignancy" in a child with a liver tumor: A 6 9/12 y o girl presented with Cushing's syndrome, hypercalcemia and a large liver tumor. Serum CRF was undetectable. ACTH ranged from 184 to 819 pg/ml and was unresponsive to CRF and dexamethasone (2 and 8 mg). All urinary steroids, except for THAldo, were greatly elevated. By contrast, serum multisteroid analysis revealed high levels of only cortisol, corticosterone and DHAS, whereas progestins (Prog, 17-OHProg) and mineralocorticoids (DOC, Aldo) were normal. Serum Ca was 14.2 mg/dl, P 2.2 mg/dl, 1,25-$(OH)_2$D 61 pg/ml (normal: 20-40), urinary cAMP 6.7 nmol/dl GF (normal: 1.6-4.9) and P reabsorption 1.6 mg/dl (normal: 4.5-6.8). Serum PTH(44-68), 25-(OH)D, AP, osteocalcin and urinary Pro-OH were normal, and PTH(intact) was suppressed, suggesting the presence of a PTH-like factor distinct from PTH. The tumor was surgically removed and proved to be a hepatoblastoma. Extraction yielded 8.3 ng/gm of ACTH and 0.04 ng/gm of CRF. Histochemical staining was positive for ACTH and CRF. By electron microscopy, multiple hormone granules were demonstrated in individual tumor cells. Postoperatively, ACTH and Ca levels rapidly reverted to normal. 4 m later, basal and CRF- and ITT-stimulated ACTH and cortisol results were normal, and the girl was clinically doing well.

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192 INTACT PTH LEVELS IN HEALTHY TERM NEONATES (HTN) AND IN EARLY NEONATAL HYPOCALCEMIA (ENH).

We employed a new IRMA intact PTH assay (Allegro, Nichols Institute), which is able to detect the biologically active form of the hormone, in order to evaluate the secretory pattern of PTH in normal newborns and in preterm infants with ENH. Intact PTH levels were low in cord serum (n.v. in chidren 38.0 ± 12.5 pg/ml) in both HTN and in ENH. In HTN we found a significant rise of PTH levels with a peak at day 1° (+7.5 fold) and a slight fall at day 5° (Table). In ENH intact PTH values increased more (+19 fold) than in HTN and showed a decrease when normal calcium levels were achieved (Table).

	n	cord	1°d	2°d	5°d
HTN	10	4.5 ± 2.3	33.7 ± 6.4°	30.8 ± 7.3°	25.0 ± 7.1°
ENH	15	3.7 ± 1.5	70.5 ±19.0*	59.6 ±14.8*	38.2 ± 8.6°

Values as mean ± 1SD.°significantly different from birth ($p<0.001$);*significantly different from birth and HTN ($p<0.001$).

Our data showed that in ENH intact PTH levels rose in first hours of life when calcium decrease as in HTN demonstrating a normal responsiveness of parathyroid glands to hypocalcemia also in preterm infants.

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193 EFFECTS OF KETOCONAZOLE ON 1,25(OH)Vit D LEVELS AND ON URINARY CALCIUM EXCRETION IN IDIOPATHIC ABSORPTIVE HYPERCALCIURIA.

Idiopathic absorptive hypercalciuria (AH) may be due to an intestinal hypersensitivity to normal 1,25(OH)Vit D levels or a primary intestinal hyperabsoption of calcium. Recent study showed that the antimycotic agent ketoconazole induce inhibition of 1-alpha-hydroxylase. To detect the role of 1,25(OH)Vit D in the genesis of AH we tested the effects of ketoconazole (K) (3 mg/Kg/daily in three doses for a week) on 1,25(OH)Vit D levels (n.v. 38.2 ± 7.5 pg/ml) and 24 hours urinary calcium excretion (24h UCa) (n.v. < 4 mg/Kg/daily) in a child (M, 5 yrs) with diagnosed AH. Results were as follows: before K: 1,25(OH)Vit D: 61.6, 24h UCa 10.8; 6 days after K: 1,25(OH)Vit D 40.7 (- 34 %), 24h UCa: 3.8 (- 65 %); 2 days after suspension of K: 1,25(OH)Vit D: 58.2; 24h UCa: 13.7. There was no effect of K on serum levels of Mid-Mol PTH, 25-OH-D, calcium, phosphate, magnesium and alkaline phosphatase.

The concomitant reduction of 1,25(OH)Vit D and 24h UCa after 6 days of K suggests that in AH may be present an intestinal hyperresponsiveness to 1,25(OH)Vit D. This data hypothizes a possible therapy with K in AH. Further studies are needed in other cases.

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194 GLUCOSE INTOLERANCE IN CYSTIC FIBROSIS (CF).

Up to 60% of children with CF develop glucose intolerance (GI). Many CF patients maintain a normal glucose tolerance (NGT) with a low insuline response during the oral glucose tolerance test (OGTT).

We studied 48 CF pts. (aged 2-29 years) without clinical manifestations of diabetes mellitus. Assessment included OGTT, hemoglobin A_{1C}, anti-islet antibodies, pulmonary status and liver involvement. The OGTT was considered abnormal when the 2h serum glucose level was higher than 140 mg/dl. There was no significant difference between the 15 pts. with and the 33 pts.without GI in terms of mean age, wheight index, degree of lung and liver involvement.

Fasting insulin (ins.), peak ins. response, max. ins./max. glucose ratio, and area under the ins.response curve were not different in GI and NGT group. Peak glucose and peak ins. response were significantly delayed in GI vs NGT pts. (99 min and 117 min vs 55 min and 86 min) and Hb A_{1C}. was higher in the former (8,2% vs 7,5%). No circulating anti-islet antibodies were detected in either group.

In conclusion, CF patients with GI differ from those with NGT by a delayed glucose and insuline response to OGTT. Serial Hb A_{1C} levels can be used as a simple and reliable method for the prediction of GI in CF.

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195 EFFECT OF CYCLIC AMP ON GLUCONEOGENIC ENZYMES IN HUMAN PLACENTA

In human placenta, adenylate cyclase is activated by hormones like human chorionic gonadotropin, epinephrine, prostaglandins, luteinizing hormone and vasointestinal polypeptide. For the liver, the resultant second messenger adenosine 2':3'-cyclic monophosphate (cAMP) is known to induce phosphoenol-pyruvate carboxykinase (PEP-CK). So far there have been no reports concerning placental PEP-CK. - METHODS: 600 mg tissue of human term placentae was incubated in Earle's solution and amino acids by gassing with O_2 and CO_2 for 120 minutes. Dibutyryl-cAMP was added to a final concentration of 1 mM. PEP-CK and the other important gluconeogenic enzyme pyruvate carboxylase (PC) were determined in placental tissue by $^{14}CO_2$ fixation method. - RESULTS: 1. The incubation elevated PC activity from 32.9 ± 15.9 uU/mg protein (mean ± S.D.) post partum to 81.6 ± 30.8 (n=6; $p<0.05$) and PEP-CK from 8.65 ± 4.0 to 233.6 ± 88.8 (n=5; $p<0.05$). 2. Dibutyryl-cAMP had no effect on PC (74.9 ± 19.6; n=6), but lowered PEP-CK to 59.1 ± 24.3 (n=5; $p<0.05$). - CONCLUSIONS: 1. Placental PC is not subjected to hormonal regulation which is mediated by cAMP. 2. PEP-CK in placenta showed a pattern different from the liver: cAMP deinduced PEP-CK. This observation is in accordance with our previous findings of epinephrine action on placenta (I.Henrichs et al., Acta endocrin. 114, 36-37 (1987)). - Supported by DFG, He 1107/2.

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196 ACTH INSENSITIVITY, AUTONOMIC NERVOUS SYSTEM DISORDERS AND SENSORY POLYNEUROPATHY

A 10 year old boy is described with a syndrome of adrenal insufficiency due to selective ACTH insensitivity associated with autonomic nervous system disorders and sensory polyneuropathy. Production of glucocorticoids and adrenal androgens were insufficient, but there were no signs of even latent mineralocorticoid insufficiency (after 4 days of low sodium diet-9mEq/L NaCl/day). In addition to achalasia, defective lacrimation, anisocoria and hyperkeratosis of palmes and soles, we also found defective sweating, permanent cutis anserina (impaired function of smooth hair muscles) and electromyographically proved sensory polyneuropathy, which were not previously reported in this rare syndrome.

	Peripheral blood				Urine	
	F ug/dl 8a.m.	DHEA ng/dl	Δ^4 ng/dl	ACTH ng/l 8a.m.	17 OHCS mg/24h	17 KS mg/24h
Before ACTH (Normal)	4 (5-15)	15 (50-250)	10 (20-60)	280-460 (20-80)	1,8-2,6 (3,0-6,0)	0,1-0,2 (1,5-5,0)
After ACTH 0,25 mg i.v. (Normal)	6 (12-30)	20 (180-450)	14 (30-90)			