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ENDOCRINE FUNCTION IN PATIENTS WITH THALASSEMIA MAJOR. N.Saka, M.Şükür, R.Bundak, B.Zülfikar, O.Neyzi. Istanbul University, Medical Faculty of Istanbul, Istanbul, Turkey.

Endocrine function was investigated in 44(22 female, 22 male) transfusion dependent and deferoxamine treated thalassemic patients between 2.9 and 21.3 years(mean:10.9 yrs) of age. Pretransfusion hemoglobin ranged from 6.5 to 9.2 g/dl and serum ferritin from 375 to 11000 ng/ml. 17 patients were growth retarded and 25 of 38 patients had delayed bone age. Of the 16 patients (11F,5M) over 13 years of age, 14 had delayed puberty (in onset or progression). Hypoparathyroidism was present in two patients and diabetes in one patient. All patients had normal basal serum T_4 and cortisol levels. Basal serum TSH was elevated in one subject. TSH response to TRH was exaggerated in 7 of 21 patients. GH response to stimulation (insulin and L-dopa) was subnormal in 4 of 20 cases. While 13 of 16 patients had decreased cortisol response to hypoglycemia,only 1 of 6 patients had decreased response to ACTH. Three of 9 patients over 13 years and with delayed puberty had no LH,FSH response to GHRH. Oral GTT showed chemical diabetes in one of 8 cases. The results suggest that endocrine abnormalities are common in patients with thalassemia major treated with frequent transfusion and chelating therapy.

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DNA ANALYSIS IN PRADER-WILLI SYNDROME (PWS) WITH MATERNAL UNIPARENTAL DISOMY AND EXTRA INVERTED DUPLICATED CHROMOSOME 15. L.Sills, R.Rapaport, J.Wagstaff, L.Suslak, H.Aviv, K.Skuza, L.Goode, L.Y.Shih, and F.Desposito. Division of Endocrinology and Genetics, Children's Hosp. of NJ, Newark, NJ and UMD-NJ Medical School, Newark, NJ 07107; Children's Hosp., Division of Genetics, Boston, MA 02115

PWS has been associated with deletion of paternal 15q11-13 or maternal uniparental disomy of chromosome 15 (chr 15) (imprinting). We describe a boy with PWS with maternal uniparental disomy of chr 15 and an extra inverted duplicated chr 15 in 70% of the cells. The patient had a history of hypotonia and poor feeding as an infant, mental retardation, and hyperphagia. At age 13 yrs his height was 147 cm (10th%), weight 102 kg (>99th%), and growth rate 4.6 cm/yr. He had a narrow bifrontal diameter and no acromicria. He was prepubertal and had right cryptorchidism. Serum LH and FSH were low. Testosterone was low and did not change with HCG stimulation. By DNA analysis, 8 polymorphic loci on the patient's chr 15 (7 in 15q11-13) were identical to the mother's and different from his unaffected brother's. Southern blot hybridization of the inverted duplicated segment indicated additional copies of 1 of 4 loci (D15S18) in the 15q11-13 region, proximal to the minimal critical PWS deletion region. Analyses of the parental origin of this segment are in progress. This patient appears to represent a new class of PWS with maternal disomy for chromosome 15 and an additional chromosome 15 derivative that does not contain the PWS critical region.

Thyroid

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LONG-TERM NEURODEVELOPMENTAL CORRELATES OF TREATMENT ADEQUACY IN SCREENED HYPOTHYROID CHILDREN. J.F. Rovet, R.M. Ehrlich, E. Donner, Department of Pediatrics, The Hospital for Sick Children, Toronto, Ontario M5G1X8 Canada.

To assess the later effects of treatment adequacy in children with congenital hypothyroidism (CH) diagnosed by newborn screening, we correlated performance on neurobehavioural and psychoeducational tests with T4 levels and dosage L-thyroxine at diagnosis and specific intervals throughout childhood. Of our original cohort of 108 screened CH children followed since birth, 95 were available for testing at 7 years and 70 at 9 years and the third grade; controls consisted of siblings and classmates (school data only). Tests included standardized age-appropriate measures of cognitive abilities, behaviour, school achievement, and class performance based on teacher report. Compared with controls, CH did more poorly on tests of visuospatial ability, arithmetic, reading comprehension, auditory memory, class learning, and attention. Correlations revealed that (i) initial disease severity was associated with subsequently poorer verbal, visuoperceptual, and graphomotor abilities; (ii) higher starting dosage of L-thyroxine with better spatial, numerical, and auditory processing skills; (iii) higher dose in infancy and early childhood with greater hyperactivity and less adequate memory and attention but not with poorer cognitive abilities; (iv) high concurrent T4 values with poorer memory and attention, arithmetic, graphomotor skills, and class behaviour. These results suggest that while a higher dose may be necessary during the newborn period when the brain is undergoing rapid development, subsequent levels should be monitored closely to minimize behaviour problems and less adequate attention, memory, and arithmetic achievement associated with high serum T4 values.

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SECONDARY HYPOTHYROIDISM IN PEDIATRIC CARDIAC SURGERY PATIENTS. M.Bettendorf, U.Tiefenbacher, S.Schmidt-Ott, K.Schmidt, H.-P.Adams, R.Schmidt, M.Klett, D.Schönberg. Children's Hospital, Department of Pediatric Endocrinology, University of Heidelberg, 6900 Heidelberg, Germany.

Normal thyroid function is vital for growth and nervous system myelinization. The number of myocardial ß-adrenergic receptors and the rate of synthesis and use of myocardial high-energy phosphates are thyroid hormone dependent. Abnormal thyroid function may occur after cardiac surgery; we therefore assessed perioperative thyroid hormone secretion in children. 82 patients (age range 2 days to 16 years) with congenital heart disease were studied before and after surgery (day 1,3,5,7). Plasma TSH,T3,T4,fT4,TG and urinary iodine excretion were measured. Results are expressed as mean ± SEM. Statistical analysis was performed by ANOVA (preoperative vs. postoperative) and a general linear models procedure (SAS).

Results	preop.	day 1	day 3	day 5	day 7	ANOVA
TSH µE/ml	2,0±0,1	0,7±0,1*	1,7±0,2	2,4±0,3	2,7±0,7	
T3 ng/ml	1,5±0,05	0,5±0,03*	0,7±0,04*	0,9±0,05*	0,7±0,07*	*p ≤ 0,01
T4 µg/dl	8,9±0,3	4,5±0,2*	4,9±0,3*	6,7±0,4*	5,1±0,8*	

There was also a significant fall of fT4 and TG. T3/T4 ratio remained unchanged. Plasma hormone values failed to reach preoperative values within 7 days. This effect was statistically independent of age, cardiopulmonary bypass and iodine contamination.TSH(R=0,43),T3(R=0,74),T4(R=0,56),fT4(R=0,42),TG(R=0,42) were significantly lower in dopamine treated patients compared to children not receiving dopamine infusion. We conclude, that secondary hypothyroidism was present in all patients. T3 replacement therapy has to be strongly considered in pediatric patients after cardiac surgery, especially when treated with dopamine. T3 may serve as a positive inotropic agent and reduce inotropic support (catecholamines). Whether this therapy will influence the postoperative intensive care course of these patients in general and will reduce recovery time from surgery is under investigation.

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A CASE OF CONGENITAL EUTHYROID GOITER WITH IMPAIRED THYROGLOBULIN (TG) TRANSPORT : IMMUNOHISTOCHEMICAL EVIDENCE OF INTRACELLULAR TG IODINATION. Y.Ohyama*[1], S.Nakamura*[1], K.Kazahari*[1], K.Shibayama*[1], Y.Yokota*[1], T.Kameya*[2], N.Suzuki*[3], and T.Hosoya*[3],*[1]Departments of Pediatrics and *[2] Pathology, Kitasato University School of Medicine and *[3]Faculty of Pharmaceutical Science, Chiba University, JAPAN

Thyroglobulin (Tg) is believed to be iodinated immediately after secretion of Tg into the follicular lumen. In recent years, however, Tg has reportedly been suggested to be iodinated in follicle cells on the basis of biochemical studies. We encountered a boy with goiter diagnosed at the age of 5.5 years, the pathogenesis of which was considered to be Tg deficiency because of Tg secretion failure in blood. Results: 1. The Tg level in the patient's thyroid tissue was very low, about 10% of the normal level according to SDS-PAGE. The main band was 19S Tg, and was almost the same as that of the normal control in terms of molecular weight, immunological aspect and electrophoresis. 2. There was no abnormality in the H_2O_2 generating system, and thyroid peroxidase activity was higher than that of the normal controls. 3. Electron-microscopic findings: the rough endoplasmic reticulum was markedly dilated. 4. Immunohistological findings: There was homogenous, positive staining for Tg and T_4 in the cytoplasm of the follicle cells and follicular cavity in the normal thyroid, while Tg and T_4 staining were seen only in the cytoplasm of the folliclar cells in our patient. In conclusion; 1)These observations are compatible with a defect in Tg transport from the cell into the lumen. 2)It might suggest that direct production of T_4 from Tg is achieved by intracellular iodination of Tg. Consequently, this patient was considered to have been clinically maintained in a euthyroid state.

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BRAIN MRI IN CONGENITAL HYPOTHYROID INFANTS AT DIAGNOSIS.

Cerebral atrophy with sella turcica alterations have been found in adult patients with primary hypothyroidism, who started replacement therapy after one year of age. Only one report described demyelinating processes in a 14 months old untreated girl, that presented a development delay.

The aim of our study was to investigate the CNS morphology and myelination with Magnetic Resonance Images (MRI) in congenital hypothyroidism (CH) detected by neonatal screening before replacement therapy.

We studied 7 CH infants, 5 girls and 2 boys, mean age 21 days, 4 agenetic and 3 ectopic. Beclard's nucleus was absent in 2 patients, mean T4 concentration at diagnosis was 22.2 ng/mL (n.v.: 50-115 ng/mL). As normal controls 22 term newborns (38-41 weeks of gestational age) were studied.

MRI studies were performed with a 1.5 T magnet, extremity coil, T1 - weighted and heavily T2 - sequences. In all patients and controls a complete set of T1 and T2 - weighted axial sections were obtained. No sedation was needed for the MRI studies.

Brain MRI examination was normal in all patients compared to controls. In particular no differences in the myelination patterns of the brain were observed between normal subjects and patients with hypothyroidism. The ventricles and the subarachnoid spaces showed a normal size.

Our study shows no morphologic brain abnormalities in CH infants detected by neonatal screening before replacement therapy. Perinatal hypothyroidism seems to have no effect on CNS structures.