

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 univariate 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 genetic and 3 idiopathic. Beckard'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 MRI studies were performed with a complete set of T1 and 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. Perhaps hypothyroidism seems to have no effect on CNS structures.

DIAGNOSIS.
MR IN CONGENITAL HYPOTHYROID INFANTS AT
Scientific Institute H San Raffaele, University of Milan, Italy.
 Department of Pediatrics, Endocrine Unit, Department of Neurology,
 V. Silingua, F. Thümler, G. Weber, S. Boffelli, G. Scotti, and G. Chiumello.

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LONG-TERM NEURODEVELOPMENTAL CORRELATES OF
PRETREATMENT AND POST-TREATMENT HYPOTHYROID CHILDREN.
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To assess the later effects of treatment adequacy in children with congenital hypothyroidism (CH) diagnosed by newborn screening, we correlated performance on neurobehavioral and psychosocial tests with T4 levels and dosage of L-thyroxine at diagnosis and specific intervals throughout childhood. Our original cohort of 108 screened CH children followed the third grade, 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, visuospatial, 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 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

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Thyroid

DNA ANALYSIS IN PRADER-WILLI SYNDROME (PWS) WITH MATERNAL UNIPARENTAL DISOMY AND EXTRA DUPLICATED CHROMOSOME 15.
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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 acromegaly. 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 paternal's chr 15 (7 in 15q11-13) were identical to the mothers' 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.

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(70) TRANSFORMER: IMMUNOHISTOCHEMICAL EVIDENCE OF INTRACELLULAR Tg
 IODINATION. Y. Ohya, S. Nakamura, K. Kazehara, T. Shibayama, Y. Yokota, T. Kameyama, N. Suzuki, and T. Hosoya. Department of Pediatrics and Pathology, Kitasato University School of Medicine and 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 follicular 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 195 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 H2O2 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 homogeneous, positive staining for Tg and Tg in the cytoplasm of the follicle cells and follicular cavity in the normal thyroid, while Tg and Tg staining were seen only in the cytoplasm of the follicular cells in our patient. In conclusion, these observations are compatible with a defect in Tg transport from the cell into the lumen. 2) It might suggest that direct production of Tg from Tg is achieved by intracellular iodination of Tg. Consequently, this patient was considered to have been clinically maintained in a euthyroid state.

Results	preop.	day 1	day 3	day 5	day 7
TSH (pmol/L)	2.0(0.1)	1.7(0.2)	2.4(0.3)	2.7(0.7)	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)
T4 (ng/dl)	8.9(0.3)	4.5(0.2)	4.9(0.3)	6.7(0.4)	5.1(0.8)

*p ≤ 0.01 ANOVA

Normal thyroid function is vital for growth and nervous system myelination. The number of myocardial β-adrenergic receptors and the rate of synthesis and use of myocardial high-energy phosphates are thyroid hormone dependent. A normal myocardial function may occur after cardiac surgery, we therefore assessed preoperative 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 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 model procedure (SAS).

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SECONDARY HYPOTHYROIDISM IN PEDIATRIC CARDIAC SURGERY
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ENDOCRINE FUNCTION IN PATIENTS WITH THALASSEMIA
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Endocrine function was investigated in 44(22 female, 22 male) transfusion dependent and deformed treated thalassemic patients between 2.9 and 21.3 years (mean: 10.9 yrs). 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 T4 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 (control) 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.