23

J.P. Chanoine[x], J.J. Body[x], G. Van Vliet, F. Delange.
Depts. of Pediatrics and Radioisotopes, St Pierre Hospital, Dept.of Medicine, Inst. J Bordet, Children Hospital, Free University of Brussels, Belgium.

MONOMERIC CALCITONIN (CT) DEFICIENCY IN PATIENTS WITH CONGENITAL NON GOITROUS HYPOTHYROIDISM (CH) DURING EARLY INFANCY.

CT deficiency has been reported in children and adolescents with CH;but whether it is also deficient in CH patients during infancy has not been investigated. Plasma extraction of CT has much improved the sensitivity and specificity of CT radioimmunoassays for the measurement of the monomeric CT form, the active form of this hypocalcemic hormone. To further analyze CT secretion in early infancy, we measured CT and Calcium (Ca) values in 1) normal infants aged 0-2 yrs (gr. NL-1, n=39) and 2-5 yrs (gr. NL-2, n=12) and 2) CH infants aged 0-2 yrs (gr. CH-1, n=6) and 2-5 yrs (gr. CH-2,n=6) Results are shown in the table (Mean ± SEM):(^{xx} $p<0,01$ as compared to groups NL)

	gr.NL-1	gr.CH-1	gr.NL-2	gr.CH-2
CT(pg/ml)	12.86±1.12	3.23±0.63^{xx}	6.48±1.16	1.25±0.06^{xx}
Ca(mg/dl)	9.73±0.09	9.73±0.20	9.65±0.08	9.57±0.11

The data show that CT values 1) decrease during the first years of life in both normal and CH patients, and 2) are lower in CH than in normal subjects. In conclusion: 1) low but detectable values of CT are present in CH patients, indicating that functional calcitonin secreting cells do exist in these patients; 2) the low CT levels in infants with CH as compared with normal subjects suggest that CT deficiency could have an important pathogenic role in the hypercalcemia occasionally observed in CH patients during the neonatal period.

24

J.Léger*, C.Tau*, M.Garabedian*, P.Czernichow
Pediatric Endocrinology and Diabetes
Hopital des Enfants Malades, Paris, France.

HYPERCALCEMIA IN INFANTS WITH CONGENITAL HYPOTHYROIDISM (CH) RECEIVING 400 iu/d Vit D.

Hypercalcemia has been described in infants with CH before and after treatment with Thyroxine (T4). In a group of 25 infants, hypercalcemia during T4 therapy was related to vit D supplementation (in France 1200iu/d). To study further adequate vit D dosage to maintain normal Ca levels, 2 groups of infants were studied during the first 6 months of life. Group I (n=5) without and Group II (n=10) with 400 iu/d of vit D. Serum Ca (mg/dl +SEM) and 25OHD were measured at diagnosis (<1month) before treatment, and at 2, 4 and 6 months of life.

Group		<1	2	4	6 months
I	Ca	10.4±.3	10.1±.4	10.4±1.3	10.0±.1
II	Ca	10.5±.1	10.6±.2	*10.8±.1	10.6±.1 *p<0.05vs group I

In group I, Ca was normal and 25(OH)D was: 15+5, 7+4, 9+2 ng/ml at 2, 4 and 6 months. In 1 case however, hypocalcemia and low 25(OH)D occured at 3 months of age and necesssitated vit D administration. In group II, Ca was moderately elevated with a significant difference between the 2 groups at 4 months. 25(OH)D levels were 17+2, 21+6, 15+2 ng/ml at 2, 4, 6 months, within the normal range in France.
In conclusion: in infants with CH, low dosage of Vit D is associated with hypercalcemia whereas infants receiving no vit D are at risk of hypocalcemia. Vit D supplementation should be given with caution to infants with CH up to the 6th month of age and carefully controlled by serum Ca measurement.

25

C.Mengreli, E.Sarafidou*, S.Pantelakis*
Institute of Child Health, Athens, Greece

METABOLISM OF a-FETOPROTEIN IN CONGENITAL HYPOTHYROIDISM

a-Fetoprotein (a-FP) levels are increased in congenital hypothyroidism (CH) for unknown reasons. To explore this, we studied the half-life of a-FP during the first month of life in neonates with CH and neonates with transient hyperthyrotropinaemia (TH), which we considered as the control group. Between the 3rd and 7th day of life a-FP was measured in 60 cases with CH with a mean gestational age of 39.9±1.5 weeks and in 184 cases with TH with a mean gestational age of 39.3±1.9 weeks. The mean log a-FP levels in the two groups were 4.35±0,39ng/ml and 3.97±0.36ng/ml respectively ($p < 0,01$). Levels of a-FP were also measured in 61 cases with CH at a mean age of 29.8±12.9 days and in 37 cases with TH at a mean age of 36.5±13.1 days. The respective mean values of log a-FP were 3.84±0.46ng/ml and 2.71±0.55ng/ml,after adjustment for conceptional age differences ($p < 0,001$). The half-life of a-FP was 15.7 days for the CH group and 7.7 days for the TH group. The half-life of a-FP was also calculated in each of 39 cases with CH and 8 cases with TH for which there were serial measurements of a-FP. The half-life of a-FP in the two groups was 12 days and 4.9 days, respectively. We conclude that catabolism of a-FP is delayed in CH group, resulting in inceased serum levels of a-FP. The lack of thyroid hormones, and especially of T3, is probably responsible for that.

26

A. Ilicki*, A. Larsson, W. Mortensson*.
Departments of Pediatrics, Uppsala University, and Pediatric Radiology,, Karolinska Institutet, S:t Göran's Children's Hospital, Stockholm, Sweden.

METHODS FOR BONE MATURITY ASSESSMENT TO EVALUATE PRENATAL HYPOTHYROIDISM.

Delayed skeletal maturation in newborn infants with congenital hypothyroidism (CH) is considered to reflect the degree of intrauterine hormone deficiency. Bone development was assessed by X-ray during the first month of life in 63 infants who had positive screening tests for CH. Serum hormone analysis confirmed the diagnosis in 46 infants while the remaining 17 infants were euthyroid at follow-up. Therapy was initiated in CH patients at the same age as radiograms were taken: 14.5±5.7 (x±SD) vs 15.0±5.5 days. Five radiographic methods to assess skeletal development (including Sénécal et al. (Arch Fr Ped. 34 (1977) 424) were tested for their capacity to distinguish CH patients from euthyroid infants. The various methods involved assessment of the shape and size of ossification centers in the knee and ankle regions. All five methods revealed statistically significant retarded bone maturity in CH infants (Mann-Whitney U test: $p<0.001$) and can be use to distinguish CH patients from euthyroid neonates. However, one of the tested methods, based on assessment of bone centers in the knee region only, has the advantage of convenience and is therefore to be recommended for routine use.

27

J.Alm*(Introd. by M.Ritzén).
Department of Pediatrics,Karolinska Institute, St Görans Children's Hospital, Stockholm, Sweden.

THYROXIN (T4) EFFECTS ON GROWTH AND HEPATIC EPIDERMAL GROWTH FACTOR RECEPTOR (EGF) ONTOGENY IN MICE WITH CONGENITAL HYPOTHYROIDISM (CH).

The effects of thyroid hormones on growth and development are probably mediated by specific growth factors as EGF. We have studied the effects of thyroxine on growth and hepatic EGF receptor ontogeny in a mouse strain with an inherited form of CH.
Hypothyroid mice (h/h) were treated with T_4 between day 20 and day 40 postnatally, h/h nontreated mice and euthyroid (+/+) mice served as controls. Animals were killed at day 20 or day 40 postnatally. Serum thyroxine was measured by RIA and EGF receptor binding in a liver plasma-membrane homogenate. Up to 20 days of age all mice showed the same weight gain and EGF hepatic receptor binding were low and not significantly different between h/h and +/+ mice. From day 20 h/h mice had a significantly lower growth rate than +/+ mice, a growth retardation that were normalised by T_4 treatment.

40 day old mice:	*Mean body weight(g)*	*B max (EGFng/mg prot)*	*Ka l/mol(10^8)*
h/h female/male	9.9/9.0	ND/<0.1	ND/1.8
h/h+T_4 - " -	12.5/14.0	0.17/1.9	4.1/4.6
+/+ - " -	13.7/15.7	0.30/2.6	5.4/8.3

Early postnatal growth (day 0-20) in mice is thyroid hormone independent and resembles in that respect late prenatal growth in humans. In contrast, between day 20 and 40 postnatally thyroid hormone is necessary for normal growth and for the increase in hepatic EGF binding observed in mice. Our results indicate that an altered ontogeny of Epidermal Growth Factor receptors might be involved in the growth and developmental retardation found in CH.

28

J.Léger* and P.Czernichow
Pediatric Endocrinology and Diabetes
Hopital des Enfants Malades, Paris, France.

ECTOPIC THYROID TISSUE IS STILL SECRETING AFTER 5 YEARS OF LT4 TREATMENT

Old data seems to indicate that ectopic thyroids involuate after several years of TSH suppression by T4 treatment. This work was undertaken to study the secretion of thyroid hormone (TH) and thyroglobulin (Tg) by remnant thyroid tissue. In 16 children with congenital hypothyroidism (CH) due to ectopic gland, aged 7.1±0.5 yrs (range 5-11.5 yrs), serum TSH, FT4, FT3 and Tg were measured under adequate LT4 therapy (phase I) and after 4 weeks of LT4 deprivation (phase II). Informed consent was obtained from the parents.

Phase	TSH mU/l	FT4 pmol/l	FT3 pmol/l	Tg ng/ml
I	5.6±1.5	26±1	7.4±0.3	8±2
II	90.4±9.6*	8±1*	3.7±0.3*	25±3*

(* $p < 0.001$ vs period I)
In phase I Tg was detectable in 8/16 patients which indicates that some thyroid secretion occurs in treated patients. Tg levels increase in phase II (range 6 to 50 ng/ml) which demonstrates in all cases the presence of actively secreting remnant tissue responsive to TSH stimulation. The low levels of FT4 and FT3 may indicate some thyroid hormone production in patients off therapy for one month.
In conclusion: Ectopic thyroid doesn't involuate during the 5 first years of life. Tg measurement is an efficient tool to evaluate remnant thyroid tissue if the patient are investigated under appropriate TSH stimulation.