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167

DECREASED GROWTH VELOCITY DURING EARLY WEEKS OF LIFE IN INFANTS WITH CONGENITAL HYPOTHYROIDISM.

Infants with congenital hypothyroidism (CH) have a normal size at birth.Growth during the first weeks of life has not yet been studied although CH offers a model to describe the effect of thyroid hormone on growth during early infancy. Thyroid scan and thyroglobulin determination were performed in 47 infants with CH allowing classification into the following groups: athyreosis n=13, ectopic n=25 and eutopic gland n=9. Infants were measured at birth, at diagnosis (less than 1 month of age) and 2, 4, 8 weeks after therapy. Height was expressed in standard deviation score and corrected for gestational age according to intra and extra-uterine growth standards of Largo et al. Bone age was retarded at birth and at diagnosis, epiphyseal surfaces of the knee were correlated with plasma T4 values. By contrast, height (mean ± SD) at birth was normal (0.3 ± 0.8 SD) with identical distribution among the 3 subgroups. At diagnosis it was at -0.1 ± 0.6 SD, a value significantly different from the value at birth ($p<0.05$). After 2 weeks of therapy a continuous decline in growth velocity was observed, reaching -0.2 ± 0.7 SD at 6 weeks of life ($p<0.02$ vs size at birth). Growth retardation was correlated with the intensity of thyroid deficiency. Mean height after 2 weeks of therapy was at -0.6, -0.1, 0.1 SD in patients with respectively athyreosis, ectopic and eutopic gland. Catch-up growth was observed thereafter, height reaching 0.3 SD at 12 weeks for the entire group.

In conclusion: A significant decreased height velocity was observed in CH before therapy and was more pronounced in severe hypothyroidism. In contrast to fetal period, thyroid hormone play an important role on growth during early weeks of life. This system is operating immediatly after birth.

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168

ALPHA-FETOPROTEIN (α-FP) MEASUREMENT IN DRIED BLOOD SPOTS:A DISCRIMINATING FACTOR BETWEEN TRANSIENT HYPERTHYROTROPINAEMIA AND CONGENITAL HYPOTHYROIDISM.

α-FP was measured in dried blood spots obtained between the 3rd and 7th day of life by heel-prick from newborns within the operation of the Greek screening programme for congenital hypothyroidism (CH) in newborns, in order to check, if this analyte could serve as a second biochemical index in addition to thyrotropin (TSH) measurement for discriminating newborns with CH from those with transient hyperthyrotropinaemia (TH). α-FP was measured by a RIA method. We studied 60 newborns with CH and 184 newborns with TH. The mean gestational age (GA) of CH group was 39,9±1,5 weeks (mean±SD) and of TH group 39,2±1,9 weeks.Discriminant analysis was used after logarithmic transformation of α-FP values, in order to find the linear combination of α-FPand GA, which best discriminates between CH and TH cases. The mean±SD of α-FP in CH group was 32,6±31,1µg/ml, whereas the corresponding figure for TH group was 13,8±16,0µg/ml, difference statistically significant ($p<0,001$). The discriminant function of $\log \alpha$-FP and GA was $35,57(\log \alpha\text{-FP})+4,89(GA)-341,91$. This equation classifies a case to the CH group if it has a positive value and to the TH group otherwise. The misclassification rate is about 26%. In conclusion α-FP values in dried blood spots are significantly higher in CH newborns than in TH ones and the measurement of α-FP in CH screening programmes could offer a diagnostic aid in differentiating CH from TH newborns, especially those with border line TSH values.

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169

GONADOTROPHIN, GROWTH HORMONE AND PROLACTIN SECRETORY DYSFUNCTION IN PRIMARY HYPOTHYROIDISM.

We have studied 5 prepubertal girls (age 6.7 - 12.3 yr) and 2 boys (age 13.3 and 14.2 yr) in early puberty (stage 2 genitalia) with primary hypothyroidism. Overnight serum hormone profiles (15-minute sampling) were performed at diagnosis and after 3 and 6 months of replacement therapy (Thyroxine 100µg/m²/day).

Pre-treatment, the girls had peak TSH levels 850-4800 mU/l with FSH concentrations raised (peak 3.9-19.5 U/l) above the LH levels (peak 1.8-3.7 U/l) which were non-pulsatile. Pelvic ultrasound showed small numbers of ovarian cysts without a multicystic morphology. Prolactin concentrations were elevated and pulsatile (peaks 800-4600 mU/l). Progressive falls in TSH, prolactin and FSH occurred during treatment. LH levels were unchanged in 3 girls but increased, becoming pulsatile in the 2 older girls, who also progressed to breast stage 2 by 3 months. GH pulse amplitude increased during treatment.

In contrast, the boys had less severe hypothyroidism. Pre-treatment TSH levels were 210 and 1400 mU/l; prolactin levels were elevated to 1200 and 1700 mU/l. Gonadotrophin profiles showed pulsatile patterns appropriate for early puberty with LH predominating over FSH.

Raised FSH secretion occurs as a spectrum in children with primary hypothyrodism, even in those without abnormal sexual development.

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170

ENDEMIC COGNITIVE AND NEUROMOTOR DEFICIT IN SCHOOLCHILDREN OF IODINE DEFICIENT AREAS.

Mental defects were found by Bender-Gestalt test,Santucci method,in 33/192 (17.1 %) euthyroid schoolchildren born between 1975 - 1980 in an endemic goiter and cretinism area in which goiter prevalence was 79% and daily iodine urinary excretion was 22.3 +/- 16.4 mcg.just in the years in which studied children were born.These defects are variously associated with goiter (36.4%),short stature (15.1),bone age retardation (21.2%) and with minor neuromotor disorders including hyporeflexia (21.2),hyperreflexia/clonus of the rotula and or foot (30%),dyslalia (6.1%).These findings could be considered as minor manifestations of neurological endemic cretinism. It must be noted that these defects are not only the clue of that severe endemia since the extension of the study to another community of 119 schoolchildren living in an area with a goiter prevalence of 59% revealed a 12.6% children with comparable mental and neuromotor defects.Despite an actual sharp decrease in goiter prevalence in both areas (79-44% , 59-26%),these iodine deficiency disorders seem to persist hitherto.If neurological damage is due to iodine deficiency "per se" or to maternal hypothyroxinemia is still unclear.

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171

SERUM THYROXINE (T4) AND THYROTROPHIN STIMULATING HORMONE (TSH) LEVELS IN CHILDREN TREATED FOR CONGENITAL HYPOTHYROIDISM

Between 1981 and 1985 185,723 infants (99.7% of newborn population) born in the South West of England were screened for congenital hypothyroidism using an immunoradiometric assay for TSH.42 infants (16 boys and 26 girls) were diagnosed as having primary congenital hypothyroidism (incidence 1:4400).Treatment and progress were monitored by local paediatricians.

Following therapy TSH remained elevated in 52% of infants at3 months, 33% at 12 months, 24% between 2-3 years and in one at 4 years.Serum T4 was never below the normal range for age throughout the study period but was significantly higher in those children who had normal TSH levels.

Table: Mean T4 levels (nmol/L) during study period

Age yr.	0.25	0.5	1	2	3	4
TSH <10 mu/l	178	198	162	166	199	159
TSH >10 mu/l	120	111	113	93	152	128

There was a wide range of L-thyroxine dosage at all age groups and it was those with the lower doses per Kg body weight who had the raised TSH levels.The clinical characteristics of the group were similar with satisfactory growth and development in all children.

We conclude that a significant number of children treated for congenital hypothyroidism have raised TSH levels in association with T4 levels in the reported normal range during the first 4 years of life.Possible reasons for this will be discussed.

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172

OPTIMAL DAILY DOSAGE OF THYROXINE IN CHILDHOOD: A REAPPRAISAL.

In Britain in 1980 the bio-availability of L.Thyroxine was increased by 11%. Treatment of 13 hypothyroid children (7congenital, 6 juvenile. (3 - 16 years) was reassessed using a highly sensitive assay of T.S.H. T3, T4, Free T3 + Free T4.

At the beginning of the study 12 children had T.S.H. below the upper limit of normal (< 5 MU/L). At intervals of 4 weeks L Thyroxine was reduced by 12.5 ug until the T.S.H. was elevated above normal. The one child with an elevated T.S.H. had L. Thyroxine increased by 12.5 ug at 4 weekly intervals until the T.S.H. fell into the normal range (0.3-5 MU/L). The optimal dose was defined as the minimum dose to maintain T.S.H. < 5 MU/L.

Mean dose at start of study 108.5 ± 4.7 ug/M²/day/3.8 ± .18 ug/kg/day. Mean optimal dose was 92.5 ± 4.0 ug/M²/day/3.24 ± 0.13 ug/kg/day. There was no difference in optimal dosage in congenital or juvenile cases. Optimal dose correlated strongly with both surface area ($r = 0.98$) and weight ($r = 0.97$). Some children had subtle behavioural signs of over-treatment initially; in none was bone age advanced. Mean values for T3, T4, Free T3 + Free T4 all fell at the upper limit of the normal range on both initial and optimal dosage.

We conclude that current dosage recommendations for L. Thyroxine may be too high and highly sensitive T.S.H. assay assist in titration of dosage.