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Changes in thyroid economy induced by carbamazepine (CBZ) therapy in L-T4 substituted hypothyroid children.

CBZ treatment is known to decrease serum thyroid hormone titers, without generally affecting TSH levels or the thyroid status. The mechanism for this transiente effect has been not yet defined. In 5 L-T4 substituted hypothyroid children with partial epilepsy serum T4 (µg/dl), FT4 (pg/ml) and rT3 (ng/dl) significantly decreased (table) after (B) 2-mth CBZ therapy (20 mg/kg), whereas an evident diminution of circulating T3 (ng/dl) and FT3 (pg/ml) was found only in the patient n.5. Three subjects had post-treatment serum TSH (µu/ml) wich rose to hypothyroid levels parallely to the T4 decrease. Serum TBG and T3 U values were not minimally modified by therapy. Since in these cases direct effects of CBZ on thyroid can be excluded and on carrier serum proteins as well,the observed changes in thyroid hormone pattern may be due to accelerated T4 clearance, via stimulation of the liver microsomal system.Similar effects are attributed to phentoin(Ann End 44,63A,1983).

	A T4 B		FT4		T3		FT3		rT3		TSH		TBG		T3 U	
1)	13.8	9.2	15.1	12.7	156	189	5.4	6.4	18	16	1.1	1.5	19	18	33	33
2)	12.8	9.9	15.6	10.I	92	113	3.5	4.3	29	15	3.I	2.2	31	32	32	30
3)	11.8	8.2	17.6	10.3	130	122	5.1	4.6	39	14	4.3	I0.0	21	20	32	27
4)	11.4	5.7	12.7	9.2	121	105	5.I	4.4	17	8	3.8	17.8	18	18	38	35
5)	13.7	4.4	16.5	8.0	158	73	6.8	3.7	21	16	1.7	18.5	19	20	36	33

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Changes in Thyroid hormones during surgical stress in healthy infants.

Low T_3 concentration has been reported in non thyroidal illness and after surgical stress in adults, unaccompanied by alterations in TSH values. Changes in thyroid hormones were sought in healthy infants undergoing elective, minor surgical procedures, in an attempt to investigate whether or not in this developmental stage a healthy hypothalamic - thyroid peripheral axis shows analogous alterations. T_3, T_4, TSH were determined by radioimmunoassay, prior to surgery (I), immediately after recovery (II), 24 and 48 hours post operatively in infants with a mean age of 4 mos. All samples from the same subject were determined simultaneously. The results are as follows (mean ±SEM)

	n	I	II	III	IV
T_3ng/dl	17	208 ±9.85	187.2 ±10.97**	145.5 ±7.11**	141.2 ±7.55**
T_4mcg/dl	15	13.84 ±0.85	14.27 ±0.63	14.33 ±0.60	12.70 ±0.62
TSHµU/ml	16	2.6 ±0.28	5.62* ±0.67	2.62 ±0.42	3.56* ±0.45

** $p < 0.001$ from base line
* $p < 0.03$

The data suggest that even short, minor operations in infancy cause a progressive decrease in T_3 concentration, lasting for at least 48 hours. The primary phenomenon seems to be a decrease in T_3 concentration of unknown mechanism wich apparently provokes transient, small TSH rises and no detectable changes in T_4 concentration.

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Comparative study on diagnostic and prognostic value of FT4-level, TRH-test and TSH receptor binding assay in Graves disease (GD).

Twentyfour patients with GD, aged 4 to 18 years, were studied before, during and after antithyroid treatment. FT4-level was determined by Amersham RIA-kit (110 samples), TRH-test was carried out with RELEFACT (Hoechst) using Byk Mallinckrodt TSH RIA kit (56) and TSH receptor binding was detected by the assay of Shewring and Rees Smith (53). The diagnostic values of FT4-RIA and TRH-test were excellent in this material. The TSH receptor antibody results were positive (greater than 15%) in one or more samples of 15 patients out of 24, showing the nature of the disease. The prognostic value of the FT4-RIA is valuable only in short time prognosis: sometimes the relapse was indicated first by increase of the FT4-level. The bad prognosis of GD was predicted better by the TRH-test but good prognosis by the TSH receptor binding assay. The value of TRH-test and TSH receptor binding assay has been poor for choosing the adequate stopping time of antithyroid treatment in 50 % of cases.

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Free T3 levels to monitor lT4 therapy in congenital hypothyroid (CH) children during the first two years of life.

An elevated threshold for TSH suppression has been previously described in children during the first months of replacement therapy. We studied 15 children, diagnosed by neonatal CH screening during the first two years of life. All of them were clinically euthyroid in our multidisciplinary follow-up program(normal growth rate, absence of hypo/hyperthyroidism symptoms, normal neuropsychological development). Clinical evaluation and hormonal profiles (fT3,fT4,T3,T4,TSH) were assessed every three months. We found a significant correlation between total hormones, fT4,lT4 dosage and TSH levels. TSH levels were well above the normal range during the first year of life,varying widely between and within patients;fT3 concentrations were not correlated with TSH levels and were well in the normal range during the study. The correlation between lT4-TSH, fT4-TSH and lT4-fT4 shows that increasing the dose of lT4 decreases TSH levels according to an elevated threshold for TSH inhibition by an increase in fT4 levels but TSH does not fall in the normal range at the recommended therapeutic dose. This increase in fT4 and decrease in TSH does not seem to affect the thyroid status, since fT3 does not change for individual compensatory mechanism in fT4/fT3 conversion in the usual therapeutic range; increase of lT4 to completely inhibit TSH probably renders patients hyperthyroid.FT3 seems to be the best index for therapy.

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Growth and maturational responses to thyroid hormones.

Although congenital hypothyroidism(CH) affects linear-growth (LG), bone-maturation(BM) and brain development little data exists concerning the time needed to reverse these parameters. This study investigates LG, BM and head circumference(HC)growth (indirect index of brain growth) in infants with CH at time of diagnosis and after replacement therapy. 47 infants were studied (31-ectopia;8-agenesis;8-goiter). Follow-up was only in patients growing along a costant growth channel at least 9 months(n=21).

Results: a) Delay in BM at diagnosis depends on serum levels of T4(r=+.84)and age at diagnosis(r=-.83). b) 12±2mos after therapy BM shows normal progression with respect to elapsed time with no evidence of "catch-up". c) LG is markedly impaired by the time of diagnosis(27±10days) but shows immediate "catch-up" converting into a normal velocity after 8±2mos. d) HC is not affected in the untreated CH infantin the first 2 months of life regardless of the serum T4 concentration but is markedly decreased after this time only in infants with athyreosis.

Conclusion: The 3 parameters studied respond differently to presence or absence of T4 suggesting that different thresholds may exist for various thyroid-dependent functions.

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Free T4 in plasma. Usefulness for monitoring thyroid replacement therapy.

The one-step RIA of free thyroxine (FT4) using a gamma-coated kit (Travenol) was used in this study. In 341 normal controls age 1 day to 18 years, it showed a transient rise at 2-3 days, then a slow decrease until age 4 years ($p<.001$) and a slight increase at 4-10 years, with a mean level of 18.0±3.5µM. Among 21 untreated hypothyroid infants age 15-22 days, FT4 was undetectable in those with athyreosis, while in cases with dysgenetic thyroid it was variable, correlated to the width of the gland ($r=.77$, $p<.01$). In 44 hypothyroid patients treated with l-T4, a highly significant positive correlation was found after the 1st month of treatment between plasma FT4 and the daily l-T4 dose ($r= .46, p<.01$), and a negative one between FT4 and plasma TSH ($r= -.59$, $p<.001$). It is concluded that measurement of FT4 offers a valuable means for control of diagnosis and treatment in congenital hypothyroidism, especially useful for avoiding both under-and overtreatment. Its correlations suggest that it is the most reliable of hormonal measurements in the follow-up of hypothyroid children.