5 A.M. ERMANS[x],A.VAN HUMSKERKE[x],P. KETELBANT-BALASSE[x], P.BOURDOUX[x], and F. DELANGE, Univ.of Brussels,Belgium

Intrathyroidal iodine metabolism in preterm infants and risk of hypothyroidism.

In order to elucidate the mechanisms responsible for the high frequency of transient hypothyroidism observed in premature infants in Belgium, we conducted morphological and biochemical studies of thyroid glands collected immediately after death in 14 premature infants (gestational ages 25-35 weeks) who died less than 12 days after birth and compared the results with those obtained in normal adults and in adults with iodine poor non-toxic colloid goiter. The thyroid glands of the prematures exhibited morphological characteristics of hyperstimulation and their serum levels of TSH at the time of death were markedly elevated (27.1±4.5(SEM) µU/ml). In the prematures and in the adults with colloid goiter as compared to normal adults, the concentrations of intrathyroidal iodine, MIT, DIT, and T_4 were markedly reduced. In the glands of prematures, the MIT/DIT and T_3/T_4 ratios were normal but, as compared to adults with colloid goiter, the concentrations of thyroglobulin and the fraction of organified iodine were markedly reduced. These two factors result in an unsufficient utilization of the available iodine, which partly accounts for the very low iodine content of the thyroids observed in the Belgian prematures (20 to 100 µg v. 10,000 to 20,000 in normal adults). In our country this reduction of the thyroidal pool of iodine could be aggravated by the low dietary supply of iodine and play a decisive role in the development of transient hypothyroidism in prematures.

6 M.E.Klett*,R.Bohnert*,D.Schönberg and L.Wille* Dept. of Ped. Endocrinology, University Children's Hospital, Heidelberg, F.R.G.

Transient hypothyroidism in preterm infants suffering from severe neonatal diseases.

Previous studies of thyroid metabolism in healthy preterm infants have shown significantly lower T4-values if compared with full-term infants. Euthyroidism has been proven by normal concentrations of freeT4 in those infants. Discrepant findings occasionally have been made in preterm infants suffering from severe neonatal diseases. In order to rule out transient hypothyroidism, we investigated TSH,T4,free T4 and T3 in all infants admitted to our intensive care unit. In 30% of the neonates (n=30, 30-37 weeks of gestation) we found a fall of T4 ($\bar{x}$=2,7±1,3 µg/dl), free T4 ($\bar{x}$=0,65±0,22 ng/dl) and T3 (0,64±0,2ng/ml) on the 5th day of life. A control sample, withdrawn on day 10, confirmed the results of transient hypothyroidism. Unexpectedly TSH remained within normal limits ($\bar{x}$=3,2±2,8 µU/ml) on both days. When obtaining the results, a third blood sample was withdrawn, followed by T4-treatment (10 µg/kg b.w.).

Conclusion: Transient hypothyroidism is a common finding in preterm infants suffering from severe neonatal diseases. The pathogenesis is not clear but may be explained by increased thyroxine metabolism and/or by disease-dependent breakdown of thyroid function and its thyrotropin regulation. Early treatment might improve the clinical course of neonatal diseases by ruling out transient hypothyroidism.

7 Comparative kinetics of levothyroxine and total thyroid extracts in newborns selected by the screening for the hypothyroidism. M. PIERSON, E. LORENTZ, A. MORALI, and M.H. MIALHE, Pediatric Department of University of NANCY (France).

1 - Detected as hypothyroid newborns were given either levothyroxine (1 T4) 5 mcg/kg, or bovine thyroid extract (BTE) 1ctg/kg in a single oral dose. With parental approuval, five controls subjects were choosen. TSH, T4, T3, free T4 and TBG were measured in the serum before and 1/2, 1, 1 1/2, 6, 12, 24, and 48 hours after ingestion of the drug. 2 - Before intake of the drug and compaired with controls, TSH was strongly elevated TBG was in the normal range, T3 in the lower limit of the normal and T4 and F. T4 were wery low. 3 - After levothyroxine, T4 reached to a normal value within 30 mn, increased & a maximal peak at 9th hour and decreased slowly until 24 hours remaining in the normal range. T3 concentration increased progressively and remained elevated, TSH demonstrated no changes. 4 - After BTE, serum T4 remained below the normal values for 24 hours, and increased slowly to on optimal concentration reached only at the of the first week of daily therapy.T3 concentration was normal within 1 hour,TSH remained an change. 5 - TSH concentration continued to be very elevated during several months of therapy with BTE, but returned to normal values within two weeks with levothyroxine.These data are discussed with regards of T4/TBG binding, peripheral T4/T3 conversion and suggest that levothyroxine must be prefered as neonatal substitutive therapy.

8 P.ROCHICCIOLI, G.DUTAU, B.ROGE, C.ENJAUME, D.GALLEGOS, D.AUGIER, C.H.U. RANGUEIL TOULOUSE FRANCE.

Mental development in congenital hypothyroidism : three years experience of a regional systematic screening program.

The Midi-Pyrenees regional screening program for congenital hypothyroidism, started in 1977, has involved 82.419 new borns and let us to detect 24 hypothyroid children (1/3400). The method utilized is the coupled T4-TSH titration from filter paper collected blood. TSH values were always higher than 80 mU/ml and those of T4 were low in 19 cases but normal in 5. A clinical score was established in comparison with a normal control group. Surface of knee's ossification centers has a significant correlation with T4, clinical score and etiology.

Mental development was tested by the BRUNET-LEZINE score tables at 8 (n=18), 16 (n=12) and 23 months (n=11) and mean development quotient (D.Q) were 97 ± 5 ; 95 ± 8 and 93 ± 9 respectively. At first examen postural and coordination D.Q. were significatly lower than language and sociability scores : 93 against 100,5. Further evolution of postural control, coordination and sociability shows a stabilication of scores but it is not so with language mid falls from 100 ± 10 at 8 months to 84 ± 21 at 23 months.

There was no correlation between D.Q. and the following features : clinical score, etiology, T4 values, bone age, age of start of treatment. In the contrary there was correlation with socio-economic statues. These results show the importance of early treatment in mental outcome of hypothyroid children and the better results obtained in environmental depending fonctions against CNS maturity depending acquisitions.

9 P.H. Heidemann[x], H.-H. Peters[x] and P. Stubbe. Dept. of Pediatrics, University of Göttingen, Federal Republic of Germany.

Transient reduction in TBG, FT_4, T_4 and T_3 during asparaginase therapy in children.

Recently, Garnick et al. (New Engl.J.Med., 1979, 301,252) observed transient thyroxine-binding-globulin (TBG) deficiency in adults during asparaginase therapy. We have studied 6 children with acute lymphoblastic leukemia who were treated with a combination of L-asparaginase, prednisolone, vincristine and daunomycin for inducing remission. Thyroid function was monitored by measuring total thyroxine (T_4), free thyroxine (FT_4), triiodothyronine (T_3), TSH and TBG with specific RIA. Within 3 weeks T_4 fell rapidly from 10.4 ± 1.9 (mean ± SD) to 3.3 ± 2.6/ug/100 ml, FT_4 from 1.7 ± 0.55 to 1.0 ± 0.5 ng/100 ml, T_3 from 1.0 ± 2.7 to 0.26 ± 0.04 ng/ml and TBG from 28.2 ± 1.9 to 9.4 ± 5.2/ug/ml. TSH exhibited only a moderate decrease within normal limits. While on a maintenance therapy (cyclophosphamide, cytosine arabinoside and 6-mercaptopurine) these values became normal within 2 to 3 weeks. In 2 of 5 patients FT_4 was extremely low (< 0.3 and 0.7 ng/100 ml) which is not sufficiently explained by a transient deficiency of TBG. We speculate that some patients might suffer from a special form of transient hypothyroidism during asparaginase therapy caused by acute inhibition of TSH and/or TRH synthesis.

10 R. POMAREDE*, P. CZERNICHOW, J. GONZALES, C. PREVOT, R. RAPPAPORT, J.M. ZUCKER. Pediatric Endocrinology Unit, Hôpital des Enfants Malades, and Pediatric Oncology Unit, Fondation Curie, Paris.

Normal bone maturation in GH and somatomedin (SM) deficient children with pituitary irradiation for retinoblastoma.

Growth hormone deficiency is a frequent consequence of external cranial radiation. Retinoblastoma is a particular situation with radiation (3500 rads) performed before age of 4 yr. 30 prepubertal children were studied with a follow-up of 5-14 yr. In group I, 8 were GH deficient with low SM activity. In group I (GH and SM deficiency) mean bone age (BA) was slightly retarded (BA/CA), but not different from the mean value in group II (normal GH response to arginine-insulin AITT and slightly diminished SM activity).

(m ± Sem)	Age at Rad mth	BA/CA	Standing height SD	AITT GH ng/ml	SM activity U/ml
Group I	22.3	0.88	- 1.8	2.2	0.25
n = 8	± 7	± 0.04	± 0.7	± 0.6	± 0.02
Group II	23.3	0.91	- 0.10	15.3	0.51
n = 22	± 3.5	± 0.01	± 0.3	± 1.1	± 0.05
p	NS	NS	0.05	0.001	0.001

In conclusion, GH and SM deficiency were found in only 26 % of the patients. Bone maturation was normal or slightly delayed (as in the control group II). This could be due to a late appearence of pituitary dysfunction or to a particular still unexplained, situation due to the early age at radiation.