69 THE CLINICAL SIGNIFICANCE OF THYROID STIMULATION-BLOCKING IMMUNOGLOBULINS.

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Immunoglobulin G (IgG) fractions from three mothers with primary myxedema, who delivered neonates, 6 patients with goitrous Hashimoto's disease and one adolescent girl with primary myxedema were tested for their ability to alter TSH stimulation of cAMP production in porcine thyroid follicles of suspension culture and the binding of TSH to its receptor in Smith's assay. The results suggested the presence of at least two types of IgG: 1) one inhibits TSH-stimulated cAMP responses and TSH binding to its receptors; 2) the other inhibits TSH-stimulated cAMP responses but does not inhibit TSH binding to its receptors. The former was detected in all three mothers and the thyroid stimulation-blocking activity of the IgG was most significant in the mother of transient neonatal hypothyroidism. The latter was detected in 5 patients with goitrous thyroiditis. The accumulation of cAMP by 1 mU/ml TSH decreased with increasing quantities of both IgGs (the dose range 1-15 mg/ml). The present study suggests that one of the IgGs which inhibits TSH-stimulated cAMP responses may be responsible for thyroid dysfunction in primary myxedema and also for transient neonatal hypothyroidism. However, the clinical significance of another blocking IgG which does not inhibit TSH binding to its receptors should be clarified.

70 Familial Congenital Hypothyroidism Secondary to Transplacental Thyroid Inhibitory Autoantibodies -

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Each of three children in a family was found to be hypothyroid at birth as part of the neonatal hypothyroid screening program. Their mother had developed Graves disease at age 8 years but became hypothyroid at age 25 - 3 years before the 1st child. Serum obtained 6 years after the 1st child was born, inhibited TSH binding to human thyroid cell membranes in vitro. At birth each child was found to have increased TSH concentration. In retrospect thyroid microsomal autoantibodies were present at 1:6400 at 2 months of age in first boy and at 1:6400 at 3 days of age in third child. The oldest two children have been followed 3 months off thyroxine therapy and continue to have normal thyroid function (T4, unbound T4, T3 and TSH).

In patients with congenital hypothyroidism in whom the mother has autoimmune thyroiditis or there is a family history of thyroiditis, the possibility of a transient condition secondary to transplacental immunoglobulins should be sought.

71 INCIDENCE OF THYROID ANTIBODIES IN NEWBORNS WITH PERMANENT CONGENITAL HYPOTHYROIDISM

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The influence of maternal autoimmune thyroid disease and placental transfer of antithyroid antibodies has been discussed as one cause of congenital hypothyroidism. In order to evaluate this hypothesis thyroid microsomal antibodies(anti-M), thyroglobulin antibodies (anti-T) and TSH-receptor antibodies(anti-TSH-R) were determined in serum samples of 36 newborns with confirmed permanent hypothyroidism.

TSH receptor antibodies were found to benegative in all newborns. In four patients anti-M and in two of these also anti-T were detected. These results and the thyroid scan findings are listed in the table

Patient	anti-M	anti-T	anti-TSH-R	THYROID SCAN
1	1:100	1:80	neg.	orthotopic
2	1:100	1:80	neg.	orthotopic
3	1:100	neg.	neg.	orthotopic
4	1:25.000	neg.	neg.	Athyreosis

The mother of patient 4 with a high anti-M titer also had a significant anti-M titer of 1:400.000, while anti-T were absent. Thyroid function tests in the mother were normal and she was clinically euthyroid. Thyroid antibodies in the child decreased during the first six months of life and remained undetectable since then. 123 J Thyroid Scan at two years of age revealed the absence of any thyroid tissue.

The incidence of thyroid antibodies in our children with congenital hypothyroidism detected by TSH-screening is 11%. The absence of thyroid tissue was found only in the patient with high antibody titers suggesting a causal relationship between fetal thyroid growth and maternal antithyroid antibodies.

72 VALUE OF PLASMA THYROGLOBULIN (Tg) MEASUREMENT IN THE DIAGNOSIS AND TREATMENT OF CONGENITAL HYPOTHYROIDISM.

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Plasma Tg measurement was performed in a large group (n=106) of patients with congenital hypothyroidism (CH) in order to better define its role in the diagnosis and the evaluation of treatment. Patients were classified in 3 groups according to thyroid scan (I^{123}). Plasma T4, TSH and Tg were measured prior to therapy. In addition a longitudinal study of plasma Tg was undertaken in a subgroup of 10 patients with measurable Tg treated with LT4. Results were as follow

	Athyreosis (n=15)	Ectopic (n=60)	Eutopic (n=31)
Tg ng/ml ±SD	undetectable (n=10)	112 ± 38	239 ± 231
(range)	in 5 cases =1 to 2.5	(<1 - 665)	(<1 - 665)

Although Tg was undetectable in athyreosis and measurable when some thyroid was present, some discrepancies were observed. In athyreosis 5 patients had measurable Tg and T4 and have probably small thyroid tissue not seen by scintiscan. Tg was not measurable in 1 ectopic case and in 3 patients with goiter. During treatment Tg followed closely TSH with a rapid and parallel decrease of both parameters during the early weeks of therapy. In undertreated patients with elevated TSH, measurement of Tg demonstrate secretion by remnant thyroid tissue even after 12 months of therapy.

In conclusion. Tg is helpfull in the classification of patients with CH. It offers a tool for studying secretion of eutopic or ectopic thyroid glands in treated patients.

73 EUROPEAN COLLABORATIVE STUDY ON MENTAL DEVELOPMENT IN CHILDREN WITH CONGENITAL HYPOTHYROIDISM (C H) DIAGNOSED BY NEONATAL THYROID SCREENING.

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In an effort to obtain, large numbers of data on mental development in children with C H, questionnaires were sent (after previous inquiries) to 28 screening centers in 15 European countries. Thanks to the collaboration of many collegues and psychologists, we have received, so far individual data of 648 children with C H. The data comprises developmental/intelligence quotients (total, subscores) obtained at the ages of 6 months (n=189), 12 m (n=365), 24 m (n=254), 36 m (n=139), 48 m (n=125), 60 m (n=61), 72 m (n=19), and 84 m (n=17). Further data are to be expected during the next weeks.

Developmental/intelligence quotients will be analyzed by the standard deviation score method where applicable, and related to various factors, such as exact diagnosis (athyreosis/ectopic thyroid/others), age at onset of therapy, socio-economic status, pre/peri/postnatal risk factors, and associated findings. Being able to pool a large number of data, this study should yield valid information about the significance of these factors for the mental outcome of children with C H.

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74 DETECTION OF CONGENITAL HYPOPITUITARY HYPOTHYROIDISM: 9.5 YEARS EXPERIENCE IN THE NORTHWEST REGIONAL SCREENING PROGRAM.

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The Northwest Regional Screening Program (NWRSP) uses a primary T_4-secondary TSH approach to screening for hypothyroidism. Samples are obtained at 1 to 5 days of life in all infants with routine second samples by 8 weeks in infants from Oregon. In the past 9.5 years the NWRSP has screened 815,250 infants, detecting 181 with primary hypothyroidism (1:4504) and 6 with hypotituitary hypothyroidism (1:135,875). Filter paper T_4=4.9±1.2 µg/dl, TSH=<25 µU/ml; serum T_4=4.2±2.9 µg/dl (N=4), free T_4=0.5± 0.1 ng/dl (N=2), TSH=4.2±0.5 µU/ml. Nine additional infants with TSH deficiency were not detected by the screening program in the same time period. Five infants were begun on thyroid hormone treatment prior to obtaining the screening sample because of clinical symptoms of hypopituitarism including hypoglycemia, persistent jaundice, microgenitalia, diabetes insipidis, midface hypoplasia, clefting or vision abnormalities. Their serum T_4=4.6 ±1.4 µg/dl (N=4), free T_4=0.3 ng/dl (N=1) TSH=6.4±4.9 µU/ml(N=4) Four infants were not detected despite clinical features of hypopituitarism (in retrospect) and low T_4 and normal TSH on at least one screening sample which was not followed up with a serum sample. Filter paper T_4=5.1±0.6 µg/dl, TSH=<25 µU/ml; serum at diagnosis ($\bar{x}$=2.75 yr) T_4=4.9±0.7 µg/dl (N=3), free T_4 0.6 ng/dl (N=1), TSH 4.7±2.1 µU/ml. Clinical features of hypopituitarism, present in 13 of our 15 infants, may be more helpful than newborn screening T_4-TSH measurements in detecting cases of congenital hypopituitary hypothyroidism. Combining all cases we estimate a frequency of 1:55,000.