I. Thyroid and Parathyroid

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EVALUATION OF "PAIRED TSH ASSAY" AS A SCREENING TEST FOR DETECTING CONGENITAL HYPOTHYROIDISM.

K.Miyai[1], H.Mizuta[1], K.Ichihara[1], N.Amino[1], K.Nishi[1], T.Fujie[1], K.Nakatani[1], O.Nose[2], T.Harada[2], T.Oura[2], T.Tsuruhara[2], K.Matsukura[4] and M.Kawashima[5]. Central Laboratory for Clinical Investigation[1], Department of Pediatrics, Osaka University Hospital[2], Osaka City Children's Hospital[3], Kankyo-Hoken-Kyokai[4] and Osaka Kessei Laboratories[5]. Osaka.

A new paired TSH assay method was developed and evaluated for mass screening of congentital hypothyroidism. I a first assay, equal parts of the extracts of dried blood spots on filter paper (9mm diameter) from two infants 4-7 days old are combined and assayed for TSH by a sensitive two step double antibody radioimmunoassay. If the value obtained is over the cut off point (4 percentile in the latest system C), the remaining extracts are assayed separately for TSH in a second assay to identify the abnormal sample with over 4 percentile. Theoretical analysis by computer and a model experiment indicate that congenital hypothyroidism with high TSH over 3 S.D. can be clearly differentiated from normal babies. From November 1975 to March 1978, a total of 113,890 babies from a general population were screened, 102 subjects (1/1,100, 1/544 in C) were recalled, 15 cases (1/7,600, 4/4,150 in C) with congenital hypothyroidism and 8 cases with "transient infantile hyperthyrotropinemia" were found. The method is valuable to save labor and expense.

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THYROXIN AS A PRIMARY INDEX IN MASS SCREENING PROGRAM FOR NEONATAL HYPOTHYROIDISM.

K.Satoh, T.Saito, Y.Yajima and F.Takeya. The Tokyo Metropolitan Institute of Medical Science. Tokyo.

In order to evaluate the significance of thyroxin(T_4) in dried blood spot for the mass screening of neonatal hypothyroidism, the T_4 in filter paper disc was assayed as the following 3 kinds of RIA kits. Concept-4 system (A:Micromedic)assays T_4 in dried blood 3mm disc using antibody coated tube in automatic machine. In Thyroscreen kit (B: Abbot) 6mm disc was used and B/F separation was done by polyethylenglycol method. In Gamma Coat (C:Travenol) 6mm disc was used in antibody coated tube. The sensitivity of Concept-4 was 1.0 µg/dl. The coefficient of variance of between assay ranged; A:6.5 to 8.1%, B:10.1 to 16.7% and C: 16.2 to 17.4%, respectively. The maximum number of samples assayed by each of kits were ; A:600, B:282 and C:400 (samples per day by oneself). Considering these values main screening procedures were performed using Concept-4 system. After assaying T_4 in all samples, 18 % of the disc samples which showed low T_4 level were assayed for TSH. Using this system 2 cases of primary hypothyroidism, 2 cases of trasient hypothyroidism and 6 cases of TBG deficiency were found out of 35054 samples. T_4 in dried blood spot may be useful: (1) to concentrate the doubtful grop out of all samples, (2) to confirm the case after TSH screeing or (3) to check the appropriatense of T_4 treatment in hypothyroid patient.

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A RADIOIMMUNOASSAY FOR MEASUREMENT OF 3,3'-L-DIIODOTHYRONINE AND ITS CLINICAL APPLICATION.

T.Nogimori and T.Mitsuma. 4th Department of Internal Medicine Aichi Medical University. Aichi.

A sensitive, specific and reproducible radioimmunoassay for measurement of 3,3'-L-diiodothyronine(T2) in unextracted human serum is described. The binding antiserum was prepared by immunization of rabbits with T2-bovine serum albumin conjugate. The antiserum did not crossreacted significantly with various thytoid hormone derivatives. Assay sensitivity was considered to be 0.5ng /dl by statistical criteria. The mean recovery was 101%. Intraassay reproducibility averaged and interassay variation were 4.0% and 6.0% respectively. 8-anilino-1-naphthalene sulfonic acid(200ug/tube) was used to inhibit binding of T2 to serum protein. The mean(Mean±SD) serum T2 concentration was 6.3 ±3.3 ng/dl in normal subjects, 31±18 ng/dl in hyperthyroidism, 3.2±2.5 ng/dl in hypothyroidism. T2 levels in serum were decreased to normal range in patients with hyperthyroidism during antithyroid drug treatment. T2 levels in serum were increased to normal range in patients with hypothyroidism during thyroxine treatment. T2 levels were low in myocardial infarction, gastric cancer, acute hepatitis and anorexia nervosa. The changes in serum T2 levels before and after hemodialysis in patients with renal failure did not showed the same trend. These data suggest that this assay system renders attractive for clinical determination of T2.

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RADIOIMMUNOASSAY OF URINARY IMMUNO-REACTIVE TRIIODOTHYRONINE(T-3) AND THYROXINE(T-4).

Shiro Noguchi, K.Kato, Y.Ueno, Noguchi Thyroid Clinic and Hospital, Beppu

The measurement of thyroid hormones and their metabolites in urine might be useful in the study of thyroid hormone metabolism. A radioimmunoassay method for urinary T-3 and T-4 was developed. Portions of urine were mixed with thyroid-hormone-free serum, specific antibody and labelled T-3 or T-4, and incubated for 2 hours at room temperature, then PEG was added for separating free from bound hormone. The recovery rates of T-3 and T-4 were 101% and 94% respectively. Hematuria had no effect to the measurement but proteinuria gave slightly higher values in 2 of 16 nephropathy patients without thyroid disease. The average urinary T-3 in normal subjects and Graves disease were 1.0 +0.2µg/day and 4.3±1.8µg/day respectively. In normal subjects T-3/creatinine ratio was strikingly consistent in each individual and no circadian variation was found. In Graves disease, the ratio can vary widely up to 5 folds without rythmic pattern. Urinary T-4/creatinine ratio had poor correlation with serum total T-4;r=0.46. In 4 of 34 patients with untreated hyperthyroidism, urinary T-4 was undetectable. 24-hour urinary T-3/serum T-3 ratio was less than 800ml in normal subjects, contrasting to more than 900ml in Graves disease; indicating a higher clearance rate of T-3 in hyperthyroidism.