53 ENDOCRINE ASPECTS OF THE ROTHMUND-THOMSON SYNDROME.

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Three siblings (15 6/12 to 17 6/12 yrs.) with the Rothmund-Thomson Syndrome showed the following characteristic features: low birth weight for gestation, severe growth failure (present height: 110-113 cm), mental retardation, alopecia, hypoplastic nails, absent sexual development with cryptorchidism in the males, microdontia and anodontia, aphakia, decreased sweating, and congential poikiloderma, Routine studies were normal. Radiographs revealed delayed bone age in the males, complete epiphyseal fusion in the female, and generalized skeletal abnormalities. Endocrine studies revealed normal glucose responses with hyperinsulinemia to oral glucose, I.V. tolbutamide, and arginine. All had normal serum TSH, thyroxine and serum cortisol levels. Serum growth hormone (hGH) responses were variable but each subject showed at least one value over 10 ng/ml to argine (0.5 gm/kg) or insulin (0.10 u/kg) with insulin insensitivity, Serum hGH response to L-DOPA (0.5 gm p.o.) were all less than 6 ng/ml. Basal serum LH, FSH and testosterone were decreased and LH-RH (100 ug S.C.) did not produce a significant rise in serum LH or FSH in any of the subjects. The patients were treated with testosterone 10 mg/day, hGH 15 units/week or estradiol 50 µg/day respectively, for 6 months, with no clinical benefit. These studies suggest normal pituitary function for TSH, ACTH, and hGH, but the absent LH/FSH response to LH-RH with low basal levels suggest diminished pituitary gonadotropin reserve.

54 METABOLIC STUDIES IN CHILDREN WITH CONSTITUTIONAL SHORT STATURE

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We have previously reported on a group of children and adolescents with constitutional short stature (CSS), lean body, retarded skeletal age, and low insulin response to arginine and glucose. It was hypothesized that the low insulin output was the cause of the growth failure. For further clarification the following investigation was performed in some of these children: 1) I.V. Glucagon test. 2) Plasma Glucagon determination during i.v. Arginine, 3) Dietary investigation in the above children and childrer with CSS, lean body, and normal insulin.

The results obtained were as follows: (1) 7 out of 8 children showed a normal insulin peak at 2 minutes during the i.v. Glucagon test (range:53 uU/ml-180 uU/ml). (2) 22 children showed a relatively low glucagon response during i.v. Arginine test (Δ 194±25 Pg/Ml in the patients vs.Δ268±32 Pg/ml in controls). (3) The total caloric intake of the children of group a) was 3021; 55% as carbohydrates. In group b) 2996; 54% as carbohydrates.

The absence of glucose intolerance may be attributed to an intact "rapid" insulin pool in the Beta cell, and a relatively low glucagon response. The low insulin and leanness of body are not related to the caloric intake.

55 ANDROGEN AND ESTROGEN TREATMENT IN TURNER'S SYNDROME.

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The value of androgen treatment and ideal timing of estrogen replacement in Turner's syndrome are uncertain. We have followed 26 girls, aged 6-19 years, for 1-5 years. All received fluoxymesterone, 0.1 mg/kg daily, for 0.7-3.2 years. 14 have been started on estrone, 1.5 mg/day, at 15-18 years. Psychologically, the young girls were quite normal, but after 13 years the puberty and growth of peers caused an intense concern about own lack of development. Progressive isolation from peers, emotional regression and faltering of sexual identity followed. - During androgen treatment the growth accelerated by the mean of 2.2 cm/year (in 13 of 15 > 1 cm/year). Estrogen had no effect on growth rate. Effect on final height was assessed using index of potential height (IPH): the deviation of height, in SD, from mean for bone age (BA). Change in IPH during androgen treatment varied from -2.1 to + 0.9 (mean -0.5). This variation was dependent on initial epiphyseal BA according to TW II RUS (loss at BA< 10, gain at BA> 13), but random according to Greulich-Pyle Atlas. Estrogen caused no change in IPH according to TW II RUS, but a definite decrease of 0 - -2.0 (mean -0.9) according to G-P. Psychologically, the influence of androgen treatment was beneficial, the experience of growing was strong and the sexual identity was strengthened. Estrogen replacement led to gradual normalization of psychological development. We now start these girls on a small dose of both fluoxymesterone and estrogen not later than the last classmates go into puberty.

56 PHOTOTHERAPY INCREASES PLASMA GROWTH HORMONE CONCENTRATIONS IN NEONATES

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In 22 newborn infants subjected to phototherapy because of neonatal hyperbilirubinaemia, plasma growth hormone (GH) was measured before, during, and after treatment. 105 healthy, full term nursery infants served as control group. GH concentrations in the healthy neonates were 20.4 ± 8.3 (SD) ng per ml on the first, 23.2 ± 7.0 on the 2nd day of life and then slowly declined (14.4 ± 4.7 on the 7th, 8.5 ± 1.7 on the 10th day). Those values, calculated seperately for each day, were taken as 100%. Phototherapy increased GH concentrations to 195 ± 108 %. Before and after irradiation, GH plasma levels were close to those registered in the nursery infants. The differences are statistically highly significant. Constant covering of the eyes, deprivation of the day-night rhythm, or other environmental alterations such as are brought about by incubator care could be at reason for this increase in GH levels.

57 STEROID EXCRETION PATTERNS IN URINE FROM NEONATES WITH CONGENITAL ADRENAL HYPERPLASIA.

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Four neonates (2 boys, 2 girls) with congenital adrenal hyperplasia (CAH) was studied. All of the Children were saltlosers. Two of the children had a sister or brother with CAH. By means of paper and thin layer chromatography the urinary steroids were studied on the 3 to 14 day of life, when signs of adrenal disorder had appeared. Highly increased excretion of 3 beta-hydroxy Δ5 steroids was shown to be present in all 4 patients. Pregnanetriol was less dominant but increased in all the patients, During treatment with cortisone the excretion of the above mentioned steroids returned to normal levels. Repeated studies after 3 months of age showed a typical excretion pattern for 21-hydroxylase deficiency with increased excretion of pregnanetriol and negligible excretion of 3 beta-hydroxy Δ5 steroids.

Our findings confirm the observations that newborn infants with 21-hydroxylase deficiency initially can be misdiagnosed to have a deficiency of the 3 beta-hydroxy-steroid dehydrogenase. The findings also support the theory of the existence of 2 separate 21-hydroxylase systems, one active on pregnenolone and one on 17-alfa-hydroxy-progesterone.

58 THE ADVANTAGE OF INTERMITTENT HGH THERAPY IN PATIENTS WITH ISOLATED AND COMBINED HGH DEFICIENCY.

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Out of 46 patients treated by an intermittent HGH regime, 5 pts. with isol. HGH deficiency (IGHD) and 5 pts. with panhypopituitarism (CGHD) are presented. HGH was administered thrice weekly, 1-3 mg/injection, in courses of 3-14 months duration interspaced by intervals of 2-15 months. The patients received from 3-6 courses over a period of 2 3/12-6 3/12 years. This therapeutic schedule was found to be effective and in contradistinction to the continuous therapeutic schedule there was no progressive decline in growth-velocity. The patients with IGHD were found to respond better than those with CGHD, both in the first course as well as in consecutive courses. When compared to a long-term continuous therapeutic schedule (Table), our regime led to same growth achievement, saving the hormone which is scarce in its availability.

Authors Mode of HGH ℞	No.of Pts	Observation Period Yrs.-Mos/Growth cm		Yrs. Mos. HGH for 10 cm Growth
Present Study(IGHD) Intermittent ℞	5	4:10	33.5	1:5
Prader et al.1972 Continuous ℞	4	3:0	22.9	1:4
Present Study(CGHD) Intermittent ℞	5	4:1	19.8	2:0
Prader et al.1972 Continuous ℞	7	3:0	18.3	1:7