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Human growth hormone bincing to liver membranes of rats with renal insufficiency.

Binding sites for human growth hormone (hGH) were studied in liver membranes of female rats with chronic renal insufficiency (CRI) associated to marked growth retardation. One month after a subtotal nephrectomy the animals with a plasma creatinine level $\geq$ 3 times that of controls were studied ; their mean statural gain was 56 % that of controls. The specific binding of ^{125}I-hGH to microsomal membranes of rats with CRI was low (62 % that of controls). The number of binding sites rather than the affinity of the binding was affected ; both the lactogenic and the somatotropic sites were decreased as judged on the binding of ^{125}I-oPRL and ^{125}I-bGH. The binding sites of the plasma membranes as well as those of Golgi fractions were reduced. In plasma membranes of rats with CRI the specific binding of glucagon was low and the specific binding of insulin was elevated ; these modifications were associated with a high plasma glucagon level and a decreased insulinemia in rats with CRI. But no modification of the plasma GH and PRL was found ; the hormone level does not appear to regulate the GH binding sites in this system.

The link between the growth defect and the decreased number of GH binding sites in the liver membranes of rats with CRI remains to be established.

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Binding properties of androgen receptors in genital skin fibroblasts of a patient with 5α-reductase deficiency.

Testosterone (T) and dihydrotestosterone (DHT) were found to bind to a specific protein in foreskin fibroblasts of a male pseudohermaphrodite with 5α-reductase deficiency. While maximum number of binding sites (B max) were similar for both androgens, the apparent dissociation constant (K_d) of the androgen receptor for T was greater than for DHT. In competition studies of ^{3}H-T bound to the receptor with unlabeled T or DHT, the inhibitor constant (K_i) for T was two to three fold greater than the K_i for DHT. Also, the dissociation rate constant (k_d) for ^{3}H-T bound to the receptor was greater than for ^{3}H-DHT (t 1/2 for T = 10 h and t 1/2 for DHT = 74.5 h).

These results suggest that T may play a role in the sexual differentiation of patients with 5α-reductase deficiency. Their incomplete masculinization would be explained by the lower affinity and faster turnover rate of the T-receptor complex relative to the DHT-receptor complex.

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Reduced plating efficiency of Turner's syndrome fibroblasts. Evidence for a peripheral resistance to growth factors?

Short stature in Turner's syndrome (TS) has been postulated to be caused by reduced target organ responsiveness to growth factors, although the experimental proof is lacking. Therefore growth properties and cell kinetics of cultured skin fibroblasts from 5 patients with TS (45,XO) were characterized and compared to those of 5 normal fibroblast cultures using 10% fetal calf serum in Eagle's MEM medium as a source of growth factors. Replicate cultures were plated at 2000 cells/cm^2 and grown for 8 days without medium change. Although the final densities reached were lower in TS cultures ($p < 0.05$) the average population doubling times, determined from the increase in cell numbers during exponential growth, revealed no significant difference between the two types of strains (TS = 54 $\pm$ 14 hrs, N = 48 $\pm$ 5 hrs). This discrepancy is demonstrated to be due to a markedly lower ($p < 0.001$) plating efficiency of TS cultures (70 $\pm$ 2.4% versus 81 $\pm$ 2%) calculated from the percentage of cells which adhere to the surface of each culture plate at 6 hrs as compared to the initial number seeded. Reduced plating efficiency of TS cells might reflect an expression of the chromosomal imbalance leading to growth impairment due to factors necessary for optimal cell attachment in vitro. The in vivo significance of this observation remains to be established.

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The investigation of hypothyroid infants identified by a TSH Screening Programme.

10 infants found to have persistant elevation of the serum TSH on a TSH screening programme had extensive investigations of their thyroid function. Serum levels of the TSH, T4, T3, rT3, TBG and Thyroglobulin were measured and a I123 Thyroid scan performed. These findings were then related to the clinical features and the bone age. The activity on the Thyroid scan and bone age correlated with the T4, rT3 and TSH levels but not with the T3 levels which were preferentially maintained. Absent Thyroglobulin may well be useful in the diagnosis of athyrosis. The most frequent scan finding was a sub-lingual ectopic thyroid. In infants with 'compensated' hypothyroidism this may be the only abnormality apart from the raised TSH and this group of infants might account for the high incidence rates found on TSH screening programmes.

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Screening for congenital hypothyroidism - results from a pilot study in Stockholm.

During one year a pilot study was carried out in Stockholm in order to define optimal conditions for routine nationwide screening for congenital hypothyroidism. About 20.000 children were born and all participated in the study. Part of their PKU samples were used, i.e. dried blood on filter paper collected on the fifth day of life. Each sample was analyzed for both T4 and TSH. Children with T4 levels below - 2 SD of the mean and/or TSH levels above 30 mU/l of plasma were recalled for clinical investigation and additional laboratory studies. However, preterm infants were recalled only if the concentration of TSH was increased. A total of 160 newborns (=0.8%) were thus considered to have positive screening results. Among these 6 children were identified with primary hypothyroidism, one with secondary hypothyroidism and 7 with hypo-TBG-emia. Based on the results obtained we suggest that a nationwide screening program for congenital hypothyroidism should be based on the PKU blood sample and TSH analyses. With 50 mU of TSH/l of plasma as the cut off limit the false positive recall rate will be less than 0.1 % and the risk of false negative results will be minimal. The present study was approved by the ethical committee of the Karolinska Institute.

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Neonatal screening for hypothyroïdism by simultaneous determination of T4 and TSH on filter paper.

A simultaneous determination of T4 and TSH has been done on 53.000 new borns since January 1st of 1977 in the Midi-Pyrénées district. 18 cases of hypothyroïdism have been detected, an incidence of 1/2950 new borns. TSH values always were above 80 µU/ml ; T4 values are under m -2σ in 14 cases, normal in 2 cases (8,8 and 9 µg/dl) and between -1 and -2σ in 2 cases. A thyroid scanning with 123 iodine or 99 Tech. has shown the absence of thyroid in 8 cases, an ectopic gland in 8 cases and a thyroid in a normal position in one case. A treatment has been possible before the first month of life in each case. The average D.Q. for the seven oldest new borns (m = 11 months) is 96.

The simultaneous determination of T4 and TSH is a sensitive and specific screening method for hypothyroidism. False-negative are avoided and the number of false-positive results is reduced. All cases of hypothyroidism can be detected (primary hypothyroïdism, hypothalamo-hypopituitary hypothyroïdism, TBG deficiency, etc...). Then, an early and certain diagnosis is made possible (T4 low and TSH increased).