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Plasma immunoreactive TRH (IR-TRH) in normal and anencephalic neonates and their mothers.

To further investigate neonatal thyroid function IR-TRH was studied by RIA after plasma chacoal extraction. TSH and IR-TRH were measured in paired maternal cord samples and in 40 min and 24 h old neonates.

	Mother	Cord	40 min	24 h
n =	11	11	11	6
TRH pg/ml ± SD	12.4 ± 7.5	50.3 ± 19.2	48.4 ± 13.7	42.7 ± 24.1
TSH µU/ml ± SD	8.2 ± 6.0	12.6 ± 7.2	120.2 ± 47	13.9 ± 3.8

IR-TRH was higher in cord than in maternal plasma ($p<0.001$) and remained constant during the first 24h of life. No correlation with TSH was observed. IR-TRH was undetectable in 3 to 6 months old normal infants. In 2 anencephalics, cord IR-TRH was 15 and 8 pg/ml and no acute variation of TSH was observed during the first 2 h of life.

In conclusion : High plasma IR-TRH was observed in human neonates at birth. Low values in anencephalic babies is in favour of the hypothalamic origin of this material.

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Analysis of heritable variation in the human growth hormone(HGH)/human placental lactogen(HPL) gene cluster.

Cellular DNA from 30 normal and 19 hypopituitary subjects was studied to determine whether heritable HGH deficiency is due to alteration in the HGH/HPL gene cluster on human chromosome 17. Subjects included 5 with multiple pituitary hormone deficiency, 3 with bioinactive HGH, 8 with isolated HGH deficiency without affected siblings and 2 pairs of siblings with autosomal recessive isolated HGH deficiency. DNA fragments containing HGH and HPL-related gene sequences were detected by Southern blot hybridization to a ^{32}P-labeled HPL cDNA probe. HGH and HPL genes exist in multiple, non-allelic forms. They are not resolved in Eco RI digests but can be distinguished in Bam HI and Bgl II digests. We have detected 3 variant polymorphic Bgl II restriction patterns which are traceable through pedigrees and can be used to test for physical linkage of HGH deficiency to HGH/HPL gene cluster variation. All HGH/HPL restriction patterns found in hypopituitary individuals were also found in normals. Thus, there were no instances in which HGH deficiency could be attributed to deletion of an HGH gene. Also, discordance for Bgl II restriction patterns in 2 siblings with autosomal recessive HGH deficiency provided evidence against HGH gene mutation as the cause of the disease.

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Ontogenesis of somatogenic and lactogenic liver receptors in male and female rats.

To study the regulation of the liver somatogenic (GH) and lactogenic (PRL) receptors during development, their number and affinity were determined at weekly intervals in male and female rats; the results were correlated with growth velocity and the hormonal changes induced by puberty. The GH and PRL binding sites of liver homogenates were analyzed using ^{125}I-bovine and ^{125}I-ovine PRL. In the males, the PRL receptors were present at day 21 (2.0±0.5 pmoles/liver; mean±1 S.E.; n=5), reached a peak at day 35 (9±2; n=5), then decreased to be undetectable at day 63. In the females, their evolution was similar until day 35; thereafter, a four-fold increase occurred, a plateau being reached at day 49 (52±8; n=5). The number of GH receptors exhibited a progressive increase in males (day 21: 9±1; n=5; day 120: 47±9, n=5) and females (day 21: 5±1, n=5; day 120: 73±10, n=5). At the time of pubertal growth spurt the mean number of GH receptors was equal to 50% of the adult values. The affinity (Ka) of GH and PRL receptors showed no significant change with age and sex (bGH: $0.61\pm0.03\times10^9$ M^{-1}; oPRL: $0.93\pm0.06\times10^9$ M^{-1}; n=60). These data suggest that in the male, the pubertal rise of testosterone inhibits the PRL receptors, while in the female the surge of estradiol induces a sharp increase of these receptors. The GH receptors do not appear to be regulated by gonadal steroïds.

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A monoclonal antibody against anti-müllerian hormone

Anti-müllerian hormone (AMH) has been partially purified from incubation medium of calf fetal testes (Picard and Josso, 1981). It produces müllerian regression in organ culture and contains one major radioactive protein, when testes have been incubated in the presence of tritiated fucose. Identity between AMH and this labelled marker protein has been postulated, and, in consequence, the latter has been used to screen hybridomas for anti-AMH activity. Splenocytes of a BALB/c mouse, injected with partially purified AMH, produced 297 hybridomas after fusion with myeloma cells. Culture medium from 94 was tested, in a double antibody precipitation test, for its capacity to bind the labelled protein contained in partially purified medium. Three IgG hybridomas gave positive results and one was cloned and used to produce ascites in BALB/c mice. Ascites IgG, used as first antibody in a double antibody precipitation test, precipitated the labelled protein and removed anti-müllerian activity from medium containing bioactive AMH. The monoclonal antibody also blocked anti-müllerian activity of calf fetal testicular tissue, indicating that it is directed against the biologically active portion of the AMH molecule. These results prove the identity between AMH and its biochemical marker, and should greatly hasten the isolation and quantitative assay of the hormone.

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Somatomedin in the rhesus monkey fetus

To assess the role of somatomedin in the maturing fetus, a RIA was developed for Multiplication Stimulating Activity (MSA), a major somatomedin. Purified MSA was conjugated to hemocyanin and specific antiserum induced in rabbits. In the RIA there was parallel displacement with unlabelled MSA and acid-extracted human or rhesus monkey serum. There was no cross-reactivity with physiological concentrations of insulin or with the other somatomedins. Immunoreactive MSA(I-MSA) in acromegalic serum extracts was approximately twice that of normal controls, while levels were reduced in growth hormone (GH) deficiency. I-MSA in pooled extracts from sera of 5 adult male monkeys was 84.0 ng/ml. Fetal samples were obtained from rhesus monkeys through catheterized interplacental vessels. At 90 days gestation (term 165 days), I-MSA in 5 fetuses was 70.2 ± 21.0 ng/ml (mean ± SEM), and at 160 days, 172.0 ± 34.3 ng/ml ($P<0.05$). Corresponding GH levels were 50.7 ± 2.0 ng/ml and 24.3 ± 2.3 ng/ml ($P< 0.001$) (reported 61st. End. Soc. 1979, Abst. 601). Because of marked variability, the mean level of I-MSA in day-old neonates was not significantly different from fetal values. The rising levels of I-MSA during the latter half of gestation in these studies suggest that: (1) somatomedins may play an important role in fetal growth; (2) somatomedin may exert feedback inhibition on GH secretion during this period.

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IGF (insulin-like growth factor) levels in cases of idiopathic tall stature.

Serum IGF levels were assayed, after acid extraction, in 26 girls and 32 boys (aged 1 - 22) whose height for their age exceed 3 SD, by a radioligand assay using human IGF (gift from Dr Zapf, Zürich) and a specific binding protein produced by rat liver in culture. Results are expressed in relation to a pool of normal adult serum arbitrarily assigned a value of 1 U/ml. 1) For the 15 children aged 1-10, the mean IGF level was 0.83 ± 0.09 (SEM) U/ml which is significantly higher than that for normal children (0.59 ± 0.05, n = 29) ($p<0.01$). 2) In the 21 10-15 year-old, IGF levels (1.35 ± 0.09) were higher than controls (1.05 ± 0.08, n = 18) ($p< 0.01$). 7 girls and 1 boy had levels (1.52 - 2.46) comparable to those of untreated acromegalics. GH levels 60 min after glucose load (30 g/m^2) were < 5 ng/ml in 11 subjects studied. 3) In the 22 patients over 15, IGF levels (1.09 ± 0.07) were similar to those of normal adults (1.06 ± 0.03 U/ml). 4) In 10 girls under ethinyloestradiol (200-300 µg/day) for a prognosis of a final height exceeding 180 cm, parallel with the decrease in growth, there was a slow but progressive drop in IGF levels (means : 1.49 U/ml after 3 months, 1.08 after 1 year). The abnormally high IGF levels seen with idiopathic tall stature and the drop accompanying oestrogen therapy suggest a direct relation between IGF production and growth rate. The return to normal levels once ossification is complete suggests a regulatory disorder during the growth period.