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DISCREPANCY BETWEEN THE RESULTS OF THYROID ECHOGRAPHY (TE) AND THYROID SCINTIGRAPHY (TS) IN CONGENITAL HYPOTHYROIDISM (CH).

It has been proposed that TE could replace TS in the detection of thyroid tissue for the diagnosis of CH suspected by neonatal screening. However, only limited experience is presently available on TE in normal and CH infants. Therefore 1) we determined the echographic characteristics of the thyroid gland in normal newborns; 2) we compared the results obtained by TS and TE in CH infants. We studied 48 normal newborns aged 5±3 days, and 9 infants with CH detected in the neonatal period and aged respectively 11, 14, 18, 19 days, 3, 4 months and 1, 8, 9 years. TE was performed in all infants but TS only in the CH infants. Results :1) Normals: the mean (±SD) thyroid volume (V of one lobe : length x Breadth x Deepth x ½)was 801±354 mm3. As compared to the neck musculature, the thyroid appeared hypo-(13 %), slightly hyper-(79 %) or strongly hyperechogenic (8 %). 2) CH infants : 99mTc TS displayed no uptake in 4 cases (agenesis) and a low uptake at the base of the tong in 5 cases (ectopia). In contrast, TE unquestionably revealed in all cases a small, bilobate and strongly hyperechogenic tissue located in the normal position of the thyroid with a mean volume of 512±95, irrespectively of age and sex. Conclusion : in 9 cases of CH with thyroid agenesis or ectopia, TE systematically detected structures in the normal position of the thyroid, though different in size and echogenicity as compared to the normal gland. This tissue could represent the ultimobranchial bodies. Therefore, TE cannot replace TS for the diagnosis of CH.

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BEHAVIOR OF T3, T4, TSH AND ACID LIPASE(AL) ACTIVITY IN THYROIDECTOMIZED RATS TREATED WITH T3 AND T4.

Studies have shown a differential sensitivity of various biological systems to T3 and T4; it has therefore been questioned whether TSH supppression truly reflects euthyroidism at the periphery. To explore this differential sensitivity, the acute effects of graded doses of T3 and T4 on TSH suppression and hepatic AL activity were determined in hypothyroid rats.

TSH suppression(>90%) and maximal AL activity occurred by 24h with 2-daily injections of 0.4µg T3/100gbw; 2.0µg T4/100gbw was needed to achieve the same degree of TSH suppression by 24h and maximal AL activation by 48h. TSH was suppressed and AL activity was increased to a greater extent in T4-injected animals when T4-derived T3 reached serum levels comparable to those reached with T3 injection. T4 doses resulting in either mild chemical hyper- or hypo-thyroidism caused T3 levels to remain in the physiologic range. These data (a)are consistent with the ability of the pituitary(and liver) to increase nuclear/plasma T3 ratio by intracellular T4 deiodination, (b)suggest autoregulation of T4 to T3 deiodination to maintain euthyroidism with respect to the more active T3 and (c)imply that the most reliable indicator of euthyroidism is suppressed TSH with normal circulating T3.

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MOLECULAR FORMS OF THE INSULIN-LIKE GROWTH FACTOR (IGF) BINDING PROTEINS (BP) : REGULATION BY GH.

IGFs are synthesized especially by the liver, and circulate in the blood bound to specific, high-affinity binding proteins. After SDS-PAGE of serum followed by transfer onto nitrocellulose, incubation with labelled IGF and autoradiography, five molecular forms of BP with MWs of 42, 39, 34, 30 and 24K have been identified. In normal serum the 42 and 39K BPs predominate and constitute the binding units of the "large complex". In acromegalic serum, the 42 and 39K BPs strongly enhance and the 24K BP less so, whereas the 34K BP is barely detectable. With treatment, clinical remission is accompanied by a return to normal of IGF levels and the electrophoretic profile of the BPs. In hypopituitary serum, the 42 and 39K BPs significantly diminish and the 34K BP strongly enhances. With GH therapy, the normal doses restoring growth induce an increase in the levels of the IGFs and 42 and 39K BPs and a reduction of the 34K BP, although normalization is not complete. In the foetus, whose growth is not under GH control, the BP profile between 19 - 37 weeks of gestation is stable, with particularly depressed levels of the 42 and 39K BPs and a predominant 34K BP. The 34K BP is also the major in cerebrospinal fluid. From our results we infer that 1) the 42 and 39K BPs are regulated by GH, their abundance being related to IGF levels 2) the 34K BP may be negatively controlled by GH 3) western blot analysis of the BPs may constitute a complementary index in the surveillance of acromegaly and hypopituitarism.

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SOMATOMEDIN-C (Sm-C/IGF-1) SYNERGISES WITH FIBROBLAST GROWTH FACTOR (FGF) ON SERTOLI CELLS (SC) MULTIPLICATION AND DIFFERENTIATION.

We have characterized Sm-C secretion and regulation by immature porcine SC cultured (ESPE 86). The present study evaluates the autocrine action of Sm-C on SC. The presence of IGF type I receptors on SC was identified by binding ($Kd=10^{-9}$M) and cross-linking. No detectable insulin receptor was found. FGF and Sm-C stimulate SC DNA synthesis with observed ED50 of 2.0 and 7.5 ng/ml respectively. Synergistic effect of FGF+Sm-C was found at saturating concentration of both factors. SC multiplication was increased compared to controls by Sm-C, FGF, Sm-C+FGF by a factor of 1.65, 2.05 and 3.2 respectively. When SC function was studied, FSH receptor number was increased by 1.65, 2.05 and 3.2 respectively. When SC function was studied, FSH receptor number was increased by 1.6 by FGF alone with no effect per se nor synergistic of Sm-C. FSH stimulated cAMP secretion by SC was enhanced by FGF (140%), FGF+Sm-C (195%), but not Sm-C alone. When Plasminogen Activator secretion by SC was measured, a 3.0 and 22 time increase in basal secretion was observed with FGF and FGF+Insulin respectively compared with controls ; furthermore, in the presence of FGF and FGF+Insulin, additional 3.3 and 1.24 respective increment factors were observed after FSH stimulation. All the insulin effects were observed at 5 µg/ml and are likely to be mediated through IGF type I receptors. Conclusions : These data demonstrate that Sm-C/IGF-I secreted by SC may have an autocrine effect expressed by the stimulation of SC multiplication and by the synergistic effect with FGF on SC function. These effects of Sm-C on SC, combined to its paracrine effects on Leydig cells (ESPE 86) emphasize the complex but key actions of Sm-C on testicular function and its maturation.

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RAT C6 GLIAL CELLS EXPRESS INSULIN-LIKE GROWTH FACTOR (IGF) RECEPTORS AND SYNTHESIZE AND SECRETE IGF-I.

The IGFs have been proposed to play a role in growth and maintenance of cells in the central nervous system (CNS). In the present study we use the C6 rat glial cell line as a model system to study the role of IGFs in the CNS. Competitive binding and affinity crosslinking experiments using ^{125}I-IGF-I and -II demonstrated type I and type II IGF receptors on C6 cells; insulin receptors were not detected. [^{3}H]-thymidine incorporation into C6 cell DNA was stimulated equally well by serum from normal and hypox (IGF-deficient) rats. Furthermore, exogenous IGFs did not stimulate DNA synthesis further when added to hypox rat serum. These results suggested that C6 cells might synthesize an IGF-like peptide. Therefore,serum-free conditioned medium from C6 cultures was gel filtered on a Sephadex G-75 column in 1M acetic acid. IGF-I and -II were measured using specific radioimmunoassays, IGF binding proteins determined using a charcoal-separation assay. IGF-I and IGF carrier protein, but not IGF-II were detected. Northern blot hybridization of C6 mRNA confirmed the presence of IGF-I mRNA and the absence of IGF-II mRNA. The level of IGF-I was 0.4-4 ng/ml based on a human IGF-I standard. The IGF-I like material inhibited ^{125}I-IGF-I binding to the type I receptor of chick embryo fibroblasts and stimulated [^{3}H]-thymidine incorporation into fibroblast DNA. We conclude that C6 glial cells possess IGF receptors, and synthesize and secrete IGF-I that is receptor-active and bioactive. We propose that IGF-I may serve as an autocrine growth stimulus in C6 glial cell cultures.

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GONADOTROPIN MEDIATED REGULATION OF mRNAs FOR INSULIN LIKE GROWTH FACTOR II (IGF-II) AND MÜLLERIAN-INHIBITORY FACTOR (MIF) IN HUMAN OVARIAN GRANULOSA CELLS.

IGFs are produced in many tissues suggesting they function in a paracrine or autocrine fashion. We studied the expression of IGF-I and II genes in cultured human granulosa cells (from in vitro fertilization patients) using Northern and dot blot analysis. IGF-I mRNA was barely detectable in these cells and it was not increased by gonadotropins. IGF-II mRNA was abundant in granulosa cells and it was further increased by FSH, hCG and cAMP in a dose dependent fashion ($p<0.001$ for all). Prolactin, growth hormone, human chorionic somatomammotropin, progesterone, estradiol and dexamethasone had no effect on IGF-I or II mRNA. MIF is the glycoprotein responsible for Müllerian duct regression in male fetuses. Small amounts of MIF are synthesized in granulosa cells, where its function is unknown. We used a synthetic oligonucleotide probe based on the sequence of the human MIF gene (Cell 45: 685) to study the hormonal regulation of MIF gene expression. The abundance of MIF mRNA in unstimulated granulosa cells was only 1-4 % of the average fetal testicular MIF mRNA amount. However, FSH, hCG and cAMP treatments increased MIF mRNA accumulation in a dose dependent fashion up to 1.4, 4.3 and 8.0 fold, respectively. The stimulatory effect of gonadotropins on IGF-II and MIF mRNAs suggests that IGF-II and MIF have some local growth regulating functions in human ovaries.