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Mechanisms of Sertoli Cell Damage in Experimental Cryptorchidism in the Rat.

In recent years the Sertoli cell has emerged as the director of spermatogenesis. The well known inhibition of spermatogenesis that occurs in cryptorchidism may thus be due to Sertoli cell damage. In experimental cryptorchidism in the rat, Sertoli cell secretion of androgen binding protein (ABP) was found to be markedly impaired. The present study demonstrates that both androgenic hormones and FSH, the only hormones known to be of importance for Sertoli cell function, are available to the cryptorchid seminiferous tubule in abundance. Androgen receptors in the cytoplasm seem to be prosent in equal amounts in testes of hypophysectomized rats, whether they are cryptorchid of not. However, the concentration of FSH receptors in the cryptorchid testis is reduced to very low levels. Thus, peripheral resistance to FSH may be one factor of importance. However, Sertoli cell secretion of ABP is also impaired in vitro at 37^{0} C, even in the absence of hormones, indicating other mechanisms behind the impaired Sertoli cell function at elevated temperatures.

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In vivo interaction of human growth hormone (HGH) with subcellular structures of rat liver.

The interaction of circulating HGH with subcellular structures of female rat liver was studied in the intact animal. Various subcellular fractions including plasma membranes (Biochim. Biophys. Acta 154 : 540, 1968) and Golgi fractions (J. Cell. Biol. 59 : 45, 1973) were prepared from liver homogenates at different time intervals after a single injection of ^{125}I-HGH into a peripheral vein. Labeling of plasma membranes occurred within the first minutes following injection, whereas labeling of Golgi fractions was delayed and reached a maximum by 15 minutes. Labeling of both subcellular structures was inhibited by excess (500 µg) native HGH but was unaffected by insulin. At all times studied virtually no radioactivity was found in the nuclear and mitochondrial-lysozomal fractions. The ^{125}I-HGH eluted from the plasma membranes and from Golgi fractions appeared intact as tested by TCA precipitation and rebinding to rat liver membrane. The results suggest that, following binding to the surface of liver cells, HGH is translocated into Golgi elements under a biologically active form.

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Somatomedin (SM-A) and the carrier proteins: regulation by growth hormone.

SM-A isolated from human plasma is a neutral polypeptide MW 7000, with an anabolic effect in vitro. Determination by specific radioligand assay in serum samples shows a positive correlation to growth hormone status. SM-A is present in serum bound non-covalently to carrier proteins. When sera from normal individuals and acromegalic patients is gel-filtered at neutral pH on Sephadex G-200 SM-A activity is found in the region MW 100,000 (Form I) and 70,000 (Form II). Untreated hypopituitary patients lack the Form I, but apparently this is formed upon GH treatment. The carrier proteins have been purified from plasma by PEG precipitation, ion-exchange chromatography and gel-filtration. Form I differs from Form II both by size and charge and is a glycoprotein. SM-A can be dissociated by acid pH from the carrier protein into the low MW form. A third form of high molecular weight somatomedin, not dissociable in acid is also found in plasma. This corroborates with the findings of Poffenbarger and co-workers.

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Growth of Snell dwarfmice with hGH, insulin and peptide fractions containing SM-activity.

In hypopituitary Snellmice, we studied the effects of hGH, insulin and peptide fractions containing SM-activity(SM-P) and insulin-like activity as measured by radioreceptorassay(RRA), but no L-thyroxine, prolactin, testosterone, insulin and GH, on body length, weight, cartilagemetabolism and serum glucose(SG). Cartilage activity (CA) was estimated by 21 hrs incubation in medium with ^{35}S-sulfate. Treatment for 4 weeks with saline, hGH and SM-P induced an increase(as % of initial value ± SEM) in length of resp.104 ± 1.0, 113.8 ± 1.3 and 109.8 ± 1.3%, and in weight of 114.6 ± 3.3 135.4 ± 5.3, 132.8 ± 1.5%. Insulin, at a dose equal to the insulin-like activity of SM-P in RRA units had no effect on length and weight. After three days of treatment CA is resp.1672 ± 223; 5088 ± 444; 4225 ± 163 dpm/mg dry cartilage; Insulin induced a decrease of SG. SM-P had an equal effect at the same dose level in RRA-units, hGH had no effect.

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Increased concentrations of chorionic somatomammotropin (rCS) serum of hypophysectomized pregnant rats.

Hypophysectomy of rats on the 14th day of pregnancy is not associated with the expected fall of serum somatomedin until after delivery. RCS was measured by radioreceptor assay utilizing membranes prepared from pregnant rabbit mammary gland and [^{125}I] oPRL. As compared to normal pregnant rats we found that serum PRL-RRA (ng/ml) of sera from hypox pregnant rats was higher than that of normal pregnant rats at 16 days 575 ± 83 (n=5) vs 201 ± 70 (n=5) $p<.01$ GH 18 and 20 days (1585 ± 234 (n=5) vs 786 ± 120 (n=3) $p=.05$. Serum GH-RRA measured by pregnant rabbit liver membrane was also higher in hypox than normal pregnant rat. Placental content of rCS was not altered by hypophysectomy. PRL/GH RRA of rCS was about 18.

We conclude that serum somatomammotropin is maintained at higher than normal concentration after hypophysectomy of pregnant rats. We suggest that this peptide maintains somatomedin production in hypox pregnant rats.

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Autoimmune polyendocrinopathy-candidosis syndrome (APECS): Clinical variation, inheritance and HLA association in 40 Finnish patients.

At present age of 8-59 years the manifestation was most variable ranging from life-long mild mucocutaneous affection to 4-fold endocrinopathy. The components are of 3 sorts. 1. Ectodermal dystrophy (nails, enamel, hair, cornea, oral mucosa) proved to be independent of endocrinopathy. 2. Cellular immunodefect appeared as chronic candidosis of oral and vaginal mucosa, nails and skin, and anergy to tuberculin and candida. 3. Autoimmune destruction led to hypoparathyroidism (32 patients), Addison's disease (22), female (6/13) and male (2/8) hypogonadism, pernicious anemia (5), diabetes (3) and hypothyroidism (1). No component was constant. Distribution of ancestors' birth places showed an accumulation at 5 rural areas, indicating involvement of a rare gene. Family pattern fitted to autosomal recessive gene (proportion of affected sibs 0.21-0.27 by different methods) Association was significant with HLA A3 (gene frequency 0.53 in contrast to 0.28 in healthy sibs and general population), but not with chromosome 6. The clinical variation appears to be independent of HLA.