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Pituitary-gonadal function in children treated for acute lymphoblastic leukaemia (ALL).

Twenty-four children (12 males) age 8.5 to 19.2 yr. were studied following LHRH stimulation, and HCG stimulation in boys. Additional tests of germ cell and corpus luteal function were perfomed in post-pubertal boys and girls respectively. Standard anti-leukaemic therapy had been discontinued for a median period of 3.1 yr. in 17 children at the study time. In most instances, prepubertal children showed appropriate LH and FSH responses and in boys, appropriate testosterone increments. Post-pubertal boys had normal Leydig cell function, but evidence of germ cell damage based on seminal analysis. Post-menarchal girls had regular menses and the use of salivary progesterone profiles throughout complete menstrual cycles indicated normal ovulation in some girls. Increasing time in remission from ALL may show recovery of endocrine dysfunction and this can be monitored in post-menarchal girls with ease, utilizing the simple and non-invasive technique of home salivary progesterone profiling.

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Growth Response to GH therapy in Children with Radiation-Induced GH deficiency.

Six children who received cranial irradiation for brain tumours which did not directly involve the hypothalamic-pituitary axis, were studied. The radiation dose received by the hypothalamic-pituitary axis ranged from 3000-4750 rads (over 3 weeks).Pituitary function was assessed between 2 and 10 years after DXT and impaired GH responses to insulin hypoglycaemia and Bovril stimulation tests were seen in all subjects. The remainder of pituitary function was essentially normal. The bone age was retarded in 5 of the 6 subjects and the initial standing height SDS varied between -1.7 and -3.3. During the pre-treatment year the children, all of whom were prepubertal, grew between 2.0 and 5.1 cm.Subsequently all received 5 units GH 3 times weekly for 1 year.The growth rate of each child was at least 2 cm. greater during the treatment year (range 6.0 to 10.1cm.) than the pre-treatment year.In 5 of the 6 the improved growth rate could be totally ascribed to GH therapy. In the sixth there was significant pubertal maturation during the treatment year and only in this subject did the bone age advance at a significantly greater rate than the chronological age.We conclude that radiation-induced GH deficiency is one of several important factors in the aetiology of short stature complicating the treatment of brain tumours in childhood. If such a child is clinically well,shows a poor growth rate and biochemical evidence of GH deficiency,then a 1 year trial of GH is justified.

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Pituitary receptor sites for LHRH: their relationship to regulation of gonadotropins secretion in male rats.

Pituitary plasma membranes contain high affinity, low capacity binding sites for LHRH, that are likely to represent specific receptor sites for this hypothalamic hormone. The use of a highly potent analog of LHRH, DesGly^{10}[DTrp^{6},(N-Et)Pro^{9}]LHRH as radioiodinated tracer allows a specific and sensitive measurement of these receptor sites (Biochem. Biophys. Res. Comm. 90:1249,1979). Castration of male rats produced a rapid and sustained increase of pituitary LHRH receptor content (LHRH-R) which parallelled the well-established augmentation of LH and FSH secretions and decrease of hypothalamic content of LHRH. Treatment during 7 days with either testosterone or estradiol allowed to fully restore, in a dose-dependent manner, normal levels of plasma gonadotropins, pituitary LHRH-R and hypothalamic LHRH content in acutely castrated (2 days) but not in chronically castrated (>28 days) rats. In the latter group, only plasma gonadotropins were normalized by sex steroid treatment. It is concluded that the rapid feedback action of sex steroids for the control of gonadotropins secretion is exercised mainly at the pituitary level rather than the hypothalamic level in chronically castrated rats.

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FSH binding and action on rat Sertoli cells depends on the stages of spermatogenesis.

The number of available peptide hormone receptors is believed to be of importance for the sensitivity of a target cell to hormonal stimulation. Receptor concentration can vary, depending on e.g. the degree of hormonal stimulation. This may serve as a local regulator of cell activity.

The binding of FSH was studied in homogenates of rat seminiferous tubules that were in different stages of the spermatogenetic wave. After dissection, the tubules were homogenized and incubated at 25°C for 16 h with varying concentrations of ^{125}I-hFSH. The number of receptors was quantitated by Scatchard analysis. Although the seminiferous tubules were exposed to the same hormonal milieu, there was a significant variation in FSH binding, depending on the stage of spermatogenesis. Binding was maximal in stage XIII-I (4.3×10^{-15} mol/200 mm tubules), minimal in stages VII-VIII (2.0×10^{-15}). The pattern of FSH binding did not correlate with the FSH stimulated secretion of cAMP or with the secretion of the Sertoli cell specific androgen binding protein (ABP). The results show that FSH binding to Sertoli cells is dependent on the functional state of the cell, or on the nature of the neighboring cells.

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Comparison of two androgen receptor assays using skin and cultured fibroblasts.

A specific receptor for 5 ∝-dihydrotestosterone (DHT) has been demonstrated in cytoplasmic extracts of human foreskin and by whole cell binding studies in fibroblasts cultured from the same skin samples. The receptor is of high-affinity, low capacity and sediments in the 4-5 S region on sucrose density gradients. Application of these methods has shown specific DHT receptors in the homogenized clitoris and fibroblasts of a CAH patient, and in two patients with male pseudohermaphroditism due to 17-ketosteroid reductase deficiency and dicentric Y chromosome anomaly, respectively. The practical use of these two methods is compared, particularly with the intention of facilitating the early investigation of disorders of sexual differentiation in infants and children.

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Location of melatonin receptors.

We attempted to locate melatonin receptors in different organs of rats. Experiments with plasma membranes and cytosol from rat liver revealed binding activity in both cell fractions. In both cases maximal binding was achieved after 3 hours at 20°C and after 6 hours at 4°C. Both binding sites had an optimum pH at 7.5 and were inhibited by trypsin. Plasma membrane receptors seem to be more Ca^{++} dependent than cytosol binding sites. Dissociation constants were $8 \cdot 10^{-9}$M for membrane receptors and $6 \cdot 10^{-8}$M for cytosol binding sites. Receptor concentration of liver, lung, spleen and heart cytosol varied between 50-200 fmoles/mg protein; that of testes, kidney and eyes was 2-3 times as high; that of pituitary gland, hypothalamus, epididymis and adrenals was 6-8 times as high. Melatonin receptor concentrations of plasma membranes from liver and testes were about 10 fold lower than in the cytosol fraction whereas spleen and lung membranes showed no melatonin binding activity. The search of melatonin in different organs of normal rats or animals treated with melatonin have shown significant concentration or accumulation in organs which showed also high concentrations of melatonin binding sites: eyes, brain, testes, epididymis, adrenals and kidney. These organs with the exception of kidney are known to be presumably targets for melatonin action.