35 PROLACTIN ACTIVITY BEFORE AND AFTER LH-RH- IN PRECOCIOUS PUBERTY.

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During the 1st month of life basal plasma gonadotropins are higher than in the following 4 years (1). In female newborns episodic LH-secretion can be assumed. In this study suitability of LH-RH-testing in precocious puberty in early childhood was investigated. We studied 14 girls, aged 5 mths till 13 years, under suspicion of disturbed puberty or with stated diagnosis. The 2 oldest girls were on cyproterone acetate (CPA) therapy. They could be studied twice using different doses of CPA. Results: Reduced sensitivity up to 4 years was found on testing with 25 ug LH-RH i.v. at different basal gonadotropin levels. In the youngest girls we found highest values for prolactin before and during LH-RH (541U/ml). The 2 oldest girls on CPA therapy showed low basal levels for their age, modest stimulation of LH and FSH (LH_{bas} 53, $_{max}$ 214ng/ml; FSH_{bas}191, $_{max}$3o4 ng/ml) and no change of prolactin. The younger untreated girls showed greatest sensitivity (LH_{bas}21, $_{max}$ 196 ng/ml; FSH_{bas} 17o, $_{max}$ 867 ng/ml). Our results suggest that it is advisable to include prolactin determinations in LH-RH-tests. Success of therapy seems to depend on inhibition of gonadotropin as well as prolactin release. Involution of the precociously enhanced activity of the gonadostat probably will take place along with low prolactin activity.

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36 GLUCOSE INDUCED INSULIN RELEASE FROM HUMAN FETAL ISLETS IN TISSUE CULTURE.

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Pancreatic islets prepared from hysterotomy specimens of 12-2o weeks gestational age by collagenase dissection were grown in tissue culture for lo days. Islets were cultured in medium containing 4 or 18 mM glucose for lo days or in 4mM glucose for 5 days and 18mM glucose for 5 dys. The effects of chronic exposure to a high extracellular glucose concentration on ß-cell development were measured functionally by estimating the rate of insulin release into the medium (ng/islet/24h) and by light and electron microscopy.

Islets grown in 18mM glucose for lo days released significantly more insulin from days 6 to lo than those grown in 4mM glucose and electron microscopy revealed degranulation of the ß cells. Islets grown in 18mM glucose from days 6 to lo showed ß cell degranulation but no significant change in the rate of insulin release. We conclude that chronic exposure to a high extracellular glucose concentration can induce insulin secretion from human fetal ß cells of 12-2o weeks gestation.

37 LACK OF EFFECT OF HYPERGLYCEMIA ON APOMORPHINE INDUCED GROWTH HORMONE RELEASE IN NORMAL MAN.

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Experimental and clinical studies have demonstrated that hypothalamic monoaminergic neurons are involved in the regulation of growth hormone (GH) secretion, but the roles of the specific monoamines and the exact site within the central nervous system at which the monoamines act to regulate GH secretion are, however, still unclear. Apomorphine, in contrast to L-dopa, is considered to stimulate dopamine receptors without affecting noradrenaline receptors or the content of serotonin in the brain. It has been shown that hyperglycemia suppresses L-dopa induced GH release and there is evidence for a glucoreceptor mechanism in the hypothalamus. Studies were performed in male volunteers to investigate GH release following the s.c. injection of apomorphine (o.75 mg) and the influence of hyperglycemia on this response. Both under normoglycemia and hyperglycemia all subjects responded to apomorphine with a marked increase in plasma GH with a maximum after 3o-6o min. The results support the view that GH release in man can be influenced through a dopaminergic mechanism. The finding that the plasma GH rise after apomorphine is not suppressible by glucose indicates that apomorphine activates dopaminergic receptors localized distally in the hypothalamus or in the anterior pituitary. Apomorphine in low dosage may be used clinically to test the capacity of the pituitary to release GH in man.

38 FOCAL DYSPLASIA WITH HYPERPLASIA IN CRYPTORCHIDISM:

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We represent the cases of two boys nine years old, with unilaterally cryptorchidism, treated before orchidopexy with chorionic gonadotrophines. The testicular biopsy shows very marked focal lesions not described until now. Both biopsies have two clearly different zones: The first zone shows an important interstitial fibroedema, increased number of Leydig cells, well formed tubules with diminished diameter for the age, absence of spermatogonias, and inmature Sertoli cells hyperplasia. The second zone has an almost complete disappearance of the interstitium, few Leydig cells and fibrosis of the tubular basal membrane. The tubular diameter is at least twice as wide as that of the first zone. In these tubules there are only mature Sertoli cells with absence of spermatogonias, and the lumen of some of them is occupied by an eosinophilic, PAS+material. In our opinion this is a primary focal dysplasia of the testis not described yet. It is probably not influenced by thetreatment with gonadotrophines. Because these tubules show an advanced state of maturation, it seems that their growth is independent of that of the rest of the testis. The specimen biopsy in cryptorchidism must be large enough to discard this type of focal lesion.

39 STUDIES IN VITRO OF TESTICULAR 17 OH STEROID DEHYDROGENASE IN TESTICULAR 17-KETOREDUCTASE DEFECT (CASE I) AND IN THE COMPLETE FORM OF TESTICULAR FEMINIZATION (CASE II).

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3 paired substrates, ^{14}C-testosterone (T)-^{3}H Δ^4-Androstenedione (Δ^4); ^{14}C-Estradiol (E_2)-^{3}H Estrone (E_1) and ^{14}C-Δ^5-Androstenediol (Δ^5)-^{3}H Dehydroepiandrosterone (D) were used for incubating homogenates at various times (15', 3o', 6o' and 12o'). Metabolites analysis was achieved by reverse isotopic dilution, several chromatographic steps and recrystallization to constant $^{14}C/^{3}H$ ratio. In case II, testicular metabolism was rapid and very active as ^{3}H-Δ^4 was almost entirely converted to ^{3}H-T at 15'. Oxidation of ^{14}C-T was neglectable even at 2 h. With the 2 other paired substrates, reduction was greatly favored but a certain degree of oxidation was observed. In case I, minimal $\Delta \rightarrow$ T reduction (9% at 2 h) and T $\rightarrow \Delta$ oxidation (5.5% at 2 h) were obtained. At 1 h and 2 h $E_1 \dashrightarrow E_2$ reduction was less limitated (19%; 3o.7%) while oxidation $E_2 \dashrightarrow E_1$ was only 6.2 and 7.4%; marked D $\rightarrow \Delta^4$ formation (22%, 45%) contrasted with low D $\rightarrow \Delta^5$ reduction (9; 7%). $\Delta^5 \rightarrow$ D and $\Delta^5 \rightarrow$ T were equal until 1 h but $\Delta^5 \rightarrow$ T increased at 2 h (38%). Thus, since in case I T $\rightleftarrows \Delta^4$ were both very limited, while $E_1 \rightarrow E_2$ impaired reduction was more active than $E_2 \rightarrow E_1$ oxidation, since in D $\rightarrow \Delta^5$ metabolism oxidation exceeded reduction, it is suggested that 17 OH steroid dehydrogenase enzyme or kinetics differ for the 3 paired substrates.

40 GROWTH FAILURE FROM SYMPTOMLESS COELIAC DISEASE.

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Among subjects investigated for growth failure we have seen ten, who had no subjective gastrointestinal symptoms, but who were demonstrated to have coeli ac disease. They were 4-19 years of age, and 2-7 S.D. below the height expected for their age and parental heights. In five cases, a history was obtained of a period of diarrhoea in infancy. Five had had an anaemia refractory to iron therapy. Eight had some protuberance of the abdomen. The bone age was markedly lagging in all, by 3-7 years. No consistent chemical abnormality was found: blood hemoglobin and folate, serum iron and TIBC, and fecal fat excretion were abnormal in only 4-5 of the subjects, and all these parameters were normal in two. Three had a subnormal growth hormone response to insulin-arginine test, one of them repeatedly. The diagnosis was based on the demonstration of a flat jejunal mucosa by peroral biopsy. In five, the diagnosis has been confirmed by a significant acceleration of growth after institution of a glutein-free diet. We presently include jejunal biopsy in the routine evaluation for abnormally short stature.