SEXUAL PRECOCITY SECONDARY TO OPTIC NEUROFIBROMATOSIS FOLLOWED BY 2° AMENORRHEA AND LOSS OF GH AND TSH WITH NORMAL ACTH AND TONIC FSH AND LH SECRETION. Amelia V. Agustin, Thomas P. Foley, Jr., and Frederic M. Kenny, Univ. of Pgh. Sch. of Med., Children's Hosp. of Pgh., Dept. of Ped., Pgh., Pa.

Sexual precocity at age 5 years was treated at age 6 years by radiation of an optic neurofibroma. Rapid pre-treatment growth rate and normal GH response to arginine-insulin provocation (ATT-ITT) were followed (post radiation) by decelerating growth rate with failure of GH response to ATT, ITT and during sleep. T4 fell to 1.6 µg% but TRH induced TSH release indicating hypothalamic deficiency and this was treated with L-T4 replacement. ACTH was normal (metyrapone test). FSH (390 ng% LER 907) and LH (96 ng%) were normal adult. Menarche at age 9 years was followed by amenorrhea. The data suggested selective hypothalamic damage. Therefore, estradiol 15 ng/kg/d was given IM x 5 days. FSH and LH were incompletely suppressed and both showed rebound after, but no "surge" during estrogen administration. Control → during estrogen → post control values respectively were FSH 310 - 340; 190 - 224; 213 - 242 and LH 80 - 90; 43 - 74; 89 - 140 ng% LER 907.

Conclusion: The data are consistent with the hypothesis that in this patient there was preservation of the "tonic" gonadotrophin releasing center with tumor and/or radiation damage to the "cyclic" center; anatomically the latter may be situated near the growth hormone and TRH releasing centers in the hypothalamus.

THE GLUCAGON INFUSION TEST (GIT): GROWTH HORMONE SECRETION IN SHORT STATURE AND IN ABNORMAL ANTERIOR PITUITARY FUNCTION. Theodore W. AvRuskin, Shiu-C. Tang, and Christina S. Juan (Intr. by S. Castells). New York Univ. Sch. Med., The Brookdale Hosp. Med. Ctr., Dept. of Ped., Brooklyn, New York.

Prior studies have shown that IM, SC, and IV bolus glucagon (GL) consistently and significantly increased serum immunoreactive growth hormone (IRGH) in normal children, but less so in patients with pituitary disorders. To evaluate alterations in peaks and times of responses, GL was administered as 30 min infusion. Twenty-three children with genetic short stature, ages 3-15 yrs., 4 patients with acromegaly, and 2 hypopituitary children had GIT (0.03 mg/kg-max. 1 mg) and sera obtained for 180 mins. for blood sugar (BS), insulin (IRI), and IRGH determinations by RIA. Twelve other short statured children received IM GL.

IVGIT produced significant BS, IRI, and IRGH increments in all, excepting those with hypopituitarism and acromegaly. BS rose from 86±2 mg/100 ml(M±SE), to 150±7 mg/100 ml($p<0.001$) at 38±4 mins. IRI rose from 11±2 to 102±11 µU/ml at 32±1 mins. ($p<0.001$). Baseline IRGH was 3.1±0.9 ng/ml, peak value was 14.9 ±1.7 ng/ml($p<0.001$), at 115±10 mins. IM tests showed BS responses from 72±4 mg/100 ml to 145±7 mg/100 ml($p<0.001$), IRI from 9±1 to 28±7 µU/ml at 30 mins.($p<0.001$), and IRGH from 1.4±0.2 ng/ml to 7.4±1.1 ng/ml at 72±9 mins.($p<0.001$). Hypopituitary patients had no IRGH response; acromegalic subjects had persistently elevated IRGH. GIT is as effective as SC, IM, or IV tests, producing similar magnitudes and times of GH response.

A NEW RADIORECEPTOR ASSAY FOR MEASUREMENT OF NATURAL AND SYNTHETIC GLUCOCORTICOIDS. Philip L. Ballard and John D. Baxter (Intr. by W.H. Tooley), Cardiovas. Res. Inst. NHLI Sp. Ctr. of Res. Pulm and Metabolic Res. Unit, Depts. of Ped., Med and Biochem., Univ. Calif., San Francisco, California.

Common assays for determining plasma cortisol detect natural but not synthetic glucocorticoids. We have developed a radioreceptor assay that measures the glucocorticoid activity of both natural and synthetic steroids. Ethanol extracts of 0.05 ml of plasma are tested for their ability to inhibit ^{3}H-dexamethasone binding to glucocorticoid receptors from cultured hepatoma cells using a charcoal absorption technique. Competition relative to cortisol (100) is: dexamethasone 945, 9α-fluorocortisol 573, corticosterone 370, triamcinolone acetonide 405, prednisolone 232, 11-deoxycorticosterone 45, aldosterone 57, 11-deoxycortisol 23, progesterone 12, cortisone 2. The assay accurately measures cortisol at 0.5 µg/100 ml or dexamethasone at 0.05 µg/100 ml. Glucocorticoid values generally correlate with plasma cortisol levels determined by the fluorometric and transcortin binding assays. This supports the idea that cortisol is ordinarily the major source of glucocorticoid activity in man. The assay detects the expected increase in glucocorticoid activity in plasma of patients receiving synthetic steroids and has been useful in diagnosing factitious Cushing's syndrome. Thus, the radioreceptor assay is a simple test either for determination of the level of any synthetic glucocorticoid or for evaluation of adrenal function.

CEREBRAL DWARFISM: HYPOTHALAMIC DYSFUNCTION AND GROWTH RETARDATION. Salvador Castells, Kytja Voeller, Carlos Vinas and Chun Lu. Downstate Med. Ctr., Dept. of Ped., Brooklyn, N.Y.

We have used the term "cerebral dwarfism" to describe the association of CNS dysfunction and growth retardation simulating growth hormone deficiency in four patients (Exc. Med. Int. S., 236:45,71). Ten new cases of brain dysfunction and growth retardation were studied. The neurological abnormalities include mental retardation in all the cases, microcephaly in 6/10, and evidence of cerebral damage manifested in one or more of the following: neurologic examination, dysrhythmia in EEG or cerebral atrophy on pneumoencephalography. History of brain anoxia was found in 5/10. Retarded bone age was present in all the children. In three patients the response in serum IRHGH to insulin and arginine stimulation was blunted (peak <7 ng/ml). In another four only the response to arginine was below normal. There was no increase in serum IRHGH during deep sleep in five patients. Two children that had low plasma cortisols at 8 A.M. failed to respond to metyrapone. The administration of TRF to five produced a normal increase in serum TSH levels. Thus, in cerebral dwarfism there is an abnormality in hypothalamic function, secondary to prenatal or perinatal cerebral anoxia, resulting in a deficiency of HGH and/or ACTH releasing factors. This deficiency explains the retardation in growth and skeletal maturation.

Supported by NIH Grant RR-318

EFFECTS OF ACTINOMYCIN D ON ACTH-INDUCED STEROIDOGENESIS AND RNA SYNTHESIS. Salvador Castells, Nicholas Addo, and Kwaku Kwateng, Dept. of Ped., S.U.N.Y., Downstate Med., Ctr., Brooklyn, N.Y.

A relationship between steroidogenesis and RNA metabolism has been suggested by the increased synthesis of rapidly labelled adrenal RNA at the time of the initiation of the steroidogenic response to ACTH (Endocr. 93:285,73; Steroids 22: 171,73). To further determine the role that RNA synthesis may play during ACTH-induced steroidogenesis, actinomycin D, an inhibitor of DNA-directed RNA synthesis was injected into rats at 10µg/100g body weight. The rats were sacrificed at 24 hrs. later. 25mC of uridine 5-6 H^3 and 3 USP units of ACTH were injected 2 hrs. before death. The control group did not receive actinomycin. The similar increase in plasma corticosterone levels in actinomycin-treated rats and controls indicated that this inhibitor had no effect on the steroidogenic action of ACTH. There were no differences in the incorporation of labelled precursors into the total cytoplasmic RNA and into the different fractions of RNA separated by gel electrophoresis. It appears that early effects of ACTH on steroidogenesis and RNA metabolism are not related to DNA-dependent RNA synthesis.

Supported by National Sciences Foundation grant No. GB-16614

LARON'S DWARFISM: GROWTH AND IMMUNOREACTIVE INSULIN (IRI) FOLLOWING HUMAN GROWTH HORMONE (HGH). Robert D. Clemons*, Gertrude Costin*, and Maurice D. Kogut. Childrens Hosp. of Los Angeles, Dept. Ped., USC Sch. of Med., Los Angeles, CA.

A 13½-year-old prepubertal Mexican boy with features of growth hormone (GH) deficiency had elevated fasting GH (5.7-66 ng/ml). Serum somatomedin (Sm) activity (sulfation factor) was low 0.3 U/ml (normal > 0.3 U/ml) . Sm activity remained low (0.16-0.25 U/ml) during and following HGH, 5 IU daily for 5 days. GH levels increased following insulin-induced hypoglycemia (IH) and L-dopa but not after arginine. Chlorpromazine suppressed fasting GH to <0.8 ng/ml but did not suppress GH release following IH. Dexamethasone did not suppress fasting GH or GH response to IH. Before HGH an oral glucose tolerance test (OGTT) was abnormal with a peak plasma IRI of 21 µU/ml. Plasma testosterone (T) was 85 ng/100 ml. After 3 months of HGH (12 IU/week) the OGTT was normal and peak IRI 37 µU/ml; Sm was 0.22 U/ml and height increase (Δht) 1.9 cm. After 6 months of HGH, peak IRI during OGTT was 74 µU/ml; Sm, 0.19-0.26 U/ml; plasma T, 425 ng/100 ml; and Δht, 3.8 cm. After 8½ months of HGH peak IRI was 69 µU/ml during OGTT; plasma T, 722 ng/100 ml; and total Δht, 6.3 cm.

These data suggest that: a) growth was not mediated by circulating Sm but may have been due in part to insulin and perhaps HGH itself in addition to T; b) HGH had a direct affect on the pancreatic β-cell not mediated by circulating Sm; and c) the hypothalamic GH releasing hormone receptor was partially intact.