

**▲ 488** INSULIN-LIKE GROWTH FACTOR 1 IN THE DEVELOPING RHESUS MONKEY. Dennis M. Styne, Linda M. Falloon and Sean J. Barry, University of California, Davis, Department of Pediatrics and the California Primate Research Center, Davis, CA.

Although the rhesus monkey is an excellent model of human growth hormone physiology, no developmental survey of serum concentrations of the growth hormone dependent somatomedin, insulin-like growth factor 1 (IGF-1), is available. Thus, we studied serum values of IGF-1 collected between birth (NB) and 17 years (17yr) of age in 83 animals in a cross-sectional study and between 3 months (3M) and 4 years (4yr) of age in 6 animals in a longitudinal study. RIA incorporated antibody to IGF-1 (provided by the NHPP), synthetic IGF-1 (provided by Dr. C.H. Li) as radioligand, and pooled rhesus monkey serum as standard. All sera were extracted with acid-ethanol to eliminate the effects of binding proteins. Results from the cross-sectional study were (values in U/ml):

Age	NB	3-4W	10M	2Yr	3½-4Yr	7-13Yr	14-17Yr
Mean	.15	.18	.71	1.2	2.2	1.3	.76
SEM	.02	.03	.15	.18	.26	.17	.16

Pubertal animals of 2-4 years had significantly higher values than younger or older animals ( $P < .001$ ). There was a correlation of bodyweight with IGF-1 values in the males ( $R^2 = .717$ ,  $p < .0005$ ). This trend was confirmed in the longitudinal study. In conclusion, the rhesus monkey, like the human being, has higher IGF-1 values during the pubertal period, and should afford a useful model of IGF-1 regulation in human development.

**▲ 489** REGULATION OF mRNA FOR INSULIN-LIKE GROWTH FACTOR II (IGF-II) IN THE FETAL TESTIS. Raimo Voutilainen and Walter L. Miller, Department of Pediatrics, University of California, San Francisco.

Steroid hormone synthesis and accumulation of mRNAs for the cholesterol side-chain cleavage enzyme (P450<sub>scc</sub>) and IGF-II occur in parallel in human granulosa cells stimulated with chorionic gonadotropin (hCG), follicle-stimulating (FSH) or cyclic AMP (cAMP), in fetal adrenal cells stimulated with adrenocorticotropin (ACTH) or cAMP, or placental cells stimulated with cAMP (R.V. and W.L.M., Proc. Natl. Acad. Sci. USA, in press). However, the regulation of IGF-II in the testis is unknown. We detected IGF-II mRNA in Northern blots of RNA from fetal adrenal, placenta, liver, kidney, muscle and testis, but not ovary. In testes of 25 fetuses from 13 to 26 weeks gestation, the abundance of IGF-II mRNA closely followed the pattern shown for P450<sub>scc</sub> mRNA (R.V. and W.L.M., J. Clin. Endocrinol. Metab. 63:1145), with a peak at 14-15 weeks and diminishing thereafter. In 20 week gestation total testicular cells cultured with serum, 100 ng/ml hCG elicited no change in amounts of mRNAs for P450<sub>scc</sub>, P450<sub>c17</sub> (17 $\alpha$ -hydroxylase/17,20 lyase) or IGF-II, while 1 mM cAMP increased P450<sub>scc</sub> and P450<sub>c17</sub> mRNAs 10-fold, but did not change IGF-II mRNA. 100 ng/dl hCG increases P450<sub>scc</sub> and IGF-II mRNAs in cultured granulosa cells, and 1 mM cAMP induces accumulation of both mRNAs in fetal adrenal placenta and granulosa cells. Thus, in contradistinction to IGF-II mRNA in other steroidogenic tissues, fetal adrenal cells or placenta, fetal testicular IGF-II mRNA does not respond to factors stimulating steroid hormone synthesis, despite similar age-dependent regulation during gestation.

**490** SALT LOSS AND MINERALOCORTICOID RESISTANCE IN AN INFANT: A VARIANT OF PSEUDOHYPOALDOSTERONISM. Philip A. Walravens, Ronald W. Gotlin, Paul V. Fennessey, L. Mark Harrison, University of Colorado Hlth. Sci. Ctr., Dept. of Ped., Denver, Colorado

Gas Chromatography/Mass Spectrometry (GC/MS) analysis of urinary steroid derivatives has extended our understanding of a variety of metabolic disease states. GC/MS was used to evaluate a suspected case of adrenal hyperplasia. A 4 week-old male presented with failure to thrive, absence of excessive virilization, hyponatremia (Na 120 mmol/L) and hyperkalemic metabolic acidosis. Serum 17-OHP and urinary 17-ketosteroids and pregnanetriol were normal. Treatment with IV saline and IM DOCA resulted in improvement, but  $\alpha$ -fluorocortisone alone was ineffective and NaCl supplements at doses of 8mmol/kg/day were needed. Plasma aldosterone was 840 pmol/L (27 ng/dL); PRA was 125ng/ml/hr after 5 months of treatment. An older brother with salt losing in infancy had responded to sodium and  $\alpha$ -fluorocortisone and was considered to be an 18 hydroxylase complex deficiency. GC analysis confirmed the normalcy of glucocorticoid and androgen pathways as well as an abnormal elevation of THB. In addition, there was a marked elevation of THA (TH corticosterol), confirmed by MS, which has not been previously reported. In contrast with other cases of pseudohypoaldosteronism and abnormalities in aldosterone biosynthesis, the present combination of features suggests problems in both aldosterone synthesis and tubular insensitivity to mineralocorticoids. The latter may possibly result from competitive inhibition by THA.

**491** SPECIAL EDUCATIONAL NEEDS IN CHILDREN WITH ADVANCED SEXUAL DEVELOPMENT. Bruce E. Wilson and Peggy McCordle. (Spon. by Itzhak Brook) Walter Reed Army Med Ctr, Dept of Peds, Washington, DC; and USUHS, Dept of Peds, Bethesda, MD.

We examined a total of 37 children referred to the Pediatric Endocrine Clinic with either congenital adrenal hyperplasia (CAH) or idiopathic precocious puberty (IPP), utilizing educational history and selected objective testing instruments. Of the 15 patients with CAH, 6 (40%) had special educational needs. 5 of these were functioning below the normal range, and 1 was in an advanced program. Of the 24 patients referred with IPP, 11 (46%) were in remedial placements. 6 of this group had sufficiently severe cognitive deficits that they were felt to represent neurogenic, rather than idiopathic, precocity. The percentage of children in each group requiring special educational consideration is much higher than in the general population (approximately 12%). This data is in contrast to previously published studies which documented elevated mean IQ scores in both CAH and IPP. Data on the educational and socio-economic background of those patients are not described. However, there were no discernible differences in socio-economic class, or level of parental education between the various groupings in our series. While conflicting, both the previous reports and our series argue that all children in whom either CAH or IPP are entertained as a diagnosis should receive full cognitive and educational assessment.

**● 492** ABNORMAL SLEEP EEG IN IDIOPATHIC SHORT STATURE. Richard HK Wu, Yolaine St. Louis, Michael J. Thorpy, Scott Bredbart, and Paul Saenger. Albert Einstein Coll. Med., Montefiore Hosp. Med. Ctr., Dept. Peds., Sleep Wake Center, Bronx, New York.

Polysomnographic recordings were obtained in six patients with idiopathic short stature (ISS), aged 4-10/12 to 16-1/2 yrs and seven patients with growth hormone deficiency (GHD) aged 6-3/12 to 10-5/12 yrs. ISS patients had GH levels  $\geq 10$  ng/ml and GHD patients had GH levels  $\leq 7$  ng/ml during provocative testing. Both groups had growth velocities below the 50th percentile and all patients were euthyroid. The results of the polysomnographic recordings (mean  $\pm$  SD) are shown below for ISS, GHD and normals aged 6-13 yrs.

	PERCENT OF TOTAL SLEEP IN STAGES				
	REM	1	2	3	4
ISS	20.3 $\pm$ 2.6	6.9 $\pm$ 5.1	45.7 $\pm$ 9.0	10.3 $\pm$ 3.2	16.4 $\pm$ 6.0
GHD	19.5 $\pm$ 6.0	9.7 $\pm$ 5.8	41.0 $\pm$ 7.9	10.0 $\pm$ 2.0	19.7 $\pm$ 7.3
Normal	28.3 $\pm$ 4.2	2.3 $\pm$ 1.1	47.9 $\pm$ 4.4	3.4 $\pm$ 1.2	17.7 $\pm$ 3.8

ISS and GHD patients had identical percentages of stages of 1-4 and REM sleep. Both groups had significantly less REM and more stage 1 and 3 sleep (%) than normals. ISS patients had qualitatively, poorer sleep with an average of 66.7 minutes of wake-time during the sleep period as compared with  $<10$  min. in GHD and normals. There was no correlation between wake-time and mean GH concentrations or secretory rates, although some ISS patients had very low mean GH range (2.0-9.5 ng/ml). Conclusions: Sleep architecture is abnormal in ISS and is indistinguishable from that seen in GHD. Coupled with low mean GH seen in some ISS patients, these abnormalities may be the cause(s) for the growth retardation in ISS.

**493** ACUTE EFFECT OF AUTHENTIC (METHIONINE-FREE) HUMAN GROWTH HORMONE (AhGH). Zvi Zadik\*, Malka Chen\*, A. Avinoam Kowarski\*\*, Amnon Gonenne\*\*\*, \*Kaplan Hospital, Rehovot; \*\*University of Maryland School of Medicine, Baltimore, MD; \*\*\*Bio-Technology General, Rehovot, Israel.

AhGH 0.1 mg/kg (Bio-Technology General-Israel, Ltd.) was administered subcutaneously to 8 healthy volunteers (27 to 47 yrs) every other day for one week (3 doses). The GH blood level reached a peak 5.7 $\pm$ 1.8 hrs after the first injection of AhGH (mean  $\pm$  1SD). The peak GH level was 64.3 $\pm$ 11.4 ng/ml.

IGF-1 plasma concentration increased from 0.55 $\pm$ 0.19 U/ml to 1.08 $\pm$ 0.17 after 24-hours and to 2.18 $\pm$ 0.31 U/ml 24-hours after the third AhGH administration.

Morning blood samples obtained prior to the first AhGH injection, and following the third injection, revealed significant difference ( $P < 0.05$ ) in the following parameters: urea-decreased from 27 $\pm$ 6.8 to 22.3 $\pm$ 8.1 mg/dl; glucose-increased from 90 $\pm$ 15 to 106 $\pm$ 14.7 mg/dl and cholesterol-decreased from 209 $\pm$ 60 to 117 $\pm$ 41 mg/dl. There were no significant effects on the blood count and differential, blood chemistry, or urinalysis.