●434 GROWTH HORMONE (GH) DEFICIENCY ASSOCIATED WITH CRANIAL RADIATION IN ACUTE LYMPHOCYTIC LEUKEMIA (ALL)

Gertrude Costin,.Univ. So. Calif., Sch. of Med., Childrens Hosp. of L.A., Dept. of Ped., Los Angeles.

Thirteen longterm survivors of ALL, 8 males and 5 females, 9-17 yrs of age, treated with chemotherapy and cranio-spinal radiation (1800-2500 rads) were evaluated for GH deficiency. Patients (pts) were separated based on their stimulated GH levels (SGH) into group 1, SGH > 10 ng/ml and group 2, SGH < 10 ng/ml. All pts in group 1 and 8 pts in group 2 were pubertal. Anthropometric and laboratory data are indicated in Table.

	Group 1 (n=5)	Group 2 (n=8)	P value
Age (yr)	13.7 ± 0.6	12.8 ± 0.7	NS
Growth rate cm/yr	3.6 ± 0.5	4.4 ± 0.3	NS
Height (SDS)	-1.8 ± 0.2	-1.5 ± 0.4	NS
Midparental ht.	169.3 ± 3.4	170.4 ± 2.1	NS
SGH (ng/ml)	16.8 ± 4.5	5.9 ± 1.0	<0.025
24-hr GHC (ng/ml)	3.2 ± 0.3 (n=3)	1.7 ± 0.1 (n=6)	<0.0005
Sleep GH peak	21.2 ± 7.0 (n=3)	7.1 ± 1.4 (n=6)	<0.025
SmC (U/ml)	1.3 ± 0.3	0.8 ± 0.2	NS

GHC=GH concentration; SDS=standard deviation score, ht.=height
The 24-hr GHC correlated significantly with sleep GH peak, SGH and gonadal steroid level but not with Sm C, growth velocity, total rads or age at time of radiation.
CONCLUSIONS: 1. Complete or partial GH deficiency occurred in 60% of pts treated with cranial radiation, 2. Puberty associated growth spurt masked the decline in growth velocity due to GH deficiency, and 3. The severity of growth retardation did not correlate with GH reserve suggesting that spinal radiation had a significant deleterious effect on stature.

435 UNILATERAL MACRONODULAR ADRENAL HYPERPLASIA: A RARE CAUSE OF PRIMARY HYPERALDOSTERONISM.

Gertrude Costin, Carl Grushkin. Univ. So. Calif. Sch. of Med.,Childrens Hosp. of L.A., Dept. of Ped., Los Angeles, CA

An 11 yr old white male with severe hypertension (150-170/100-120), hypokalemia (2.6-2.9 mEq/L) and suppressed plasma renin (PRA)(<20 ng/dl/hr) was studied. Initial random serum and urine aldosterone (Aldo) were 19 ug/dl and 11 ng/dl. Antihypertensive therapy and potassium supplementation were begun. Results of dexamethasone (Dex) suppression, ACTH stimulation and adrenal vein sampling are indicated in Table.

	SERUM					24HR URINE
	ALDO	18-OHB	B	DOC	F	PRA	ALDO
	ng/dl				ug/dl	ng/dl/hr	ng/dl
BASAL	94	286	1,107	18	15.6	<20	27
DEX 96 HR	40	177	218	6	1.6	68	28
ACTH 8 HR	27	199	1,360	56	20.9	<20	204
LT ADRENAL	3100	10,010	13,000	1024	87.0		
RT ADRENAL	141	635	17,400	1176	196.0		

B, corticosterone; DOC, Deoxycorticosterone; F, Cortisol.
The partial suppression of Aldo by Dex and stimulation by ACTH suggested hyperplasia; however, the paradoxical decline in Aldo with upright posture suggested a tumor. Adrenal venography indicated an enlarged left adrenal not confirmed by computed tomography. Because spironolactone failed to correct hypertension, a left adrenalectomy was performed which revealed macronodular hyperplasia. After surgery, hypertension improved along with normalization of biochemical and hormonal abnormalities. Adrenal vein sampling was the most useful test in determining the etiology of hyperaldosteronism.

436 GROWTH HORMONE SECRETORY PATTERNS IN NORMAL STATURED SUBJECTS.

Gertrude Costin, Francine Kaufman, Jo Anne Brasel, Univ. So. Calif., Childrens Hosp. of L.A. Los Angeles and Harbor UCLA Med. Ctr., Torrance, CA.

To determine whether a correlation exists between height and the quantity of growth hormone (GH) secreted during physiologic conditions, we measured 24-hr GH concentration(GHC)in 29 non-obese, normal statured subjects, 16 males, 13 females, 7-18 yrs. Results (mean ± SE) are indicated in Table.

	PREPUBERTAL (n=16)	PUBERTAL (n=13)	P-value
HEIGHT (SDS)*	-0.1 ± 0.2	+0.1 ± 0.2	NS
24-HR GHC(ng/ml)	3.3 ± 0.3	4.4 ± 0.5	< 0.05
GHC WAKEFUL HRS	2.0 ± 0.2	3.8 ± 0.5	< 0.005
GHC SLEEP HRS	6.0 ± 0.7	5.7 ± 0.7	NS
SLEEP PEAK GH	18.7 ± 3.6	17.7 ± 1.8	NS
NO PULSES>5ng/ml	2.8 ± 0.4	4.9 ± 0.3	< 0.0005
SMC U/ml	0.9 ± 0.1	1.9 ± 0.1	< 0.0005

SDS*, standard deviation score
The data indicates that in normal statured subjects, 1) 24-hr GHC ranges from 2.1 to 6.2ng/ml, which overlaps with values reported in hypopituitarism, 2) GHC during sleep is significantly greater than during wakeful hrs and correlates well with 24-hr GHC (p<.01) 3) The puberty associated increase in 24-hr GHC results from an increase in GHC during wakeful hrs, 4) GHC does not correlate with height(SDS), age, SmC or midparental height, but correlates inversely with weight(SDS) and bone age in pubertal subjects only and 5) SmC correlates with age, bone age and sexual stage (p<.01). IN CONCLUSION: In normally growing subjects, stature does not appear to be determined by the amount of GH or SmC, but by genetic influences, including perhaps responsiveness to growth factors. Further, GH deficiency cannot be diagnosed solely by 24-hr GHC.

▲437 SOMATOMEDIN-C/INSULIN-LIKE GROWTH FACTORS I (Sm-C/IGF-I) AND IGF-II mRNAs DURING LUNG DEVELOPMENT IN THE RAT.

Marsha L. Davenport, A.Joseph D'Ercole, Jane C. Azizkhan and P. Kay Lund . University of North Carolina at Chapel Hill, Departments of Pediatrics and Physiology, Chapel Hill.

Sm-C/IGF-I and IGF-II are peptide mitogens that are synthesized in multiple organs and are implicated in regulation of organ growth. To investigate the ontogeny of their synthesis during lung development, Northern and dot blot hybridizations were performed on poly(A+)RNAs from lungs of fetal rats at 16, 17, 19, and 21 days gestation and postnatally at 0, 1, 2, 3-4, 6-7, 10, 14, 21, 28 and >50 days. A ^{32}P-labelled rat Sm-C/IGF-I genomic fragment, a mouse Sm-C/IGF-I cDNA, and a human IGF-II cDNA were used as probes. These analyses revealed that the abundance of total Sm-C/IGF-I mRNA is 1.5 to 2.5-fold higher in lungs of fetal than postnatal animals and that multiple Sm-C/IGF-I mRNA species of estimated sizes 7.5, 4.7, 1.7 and 1.2 kb are observed at every age examined. For IGF-II, a high abundance of total hybridizing mRNA is found in fetal lung; it rapidly declines in the first week after birth to a plateau that is 20-fold less than in the fetus. Multiple lung IGF-II mRNAs of 4.7, 3.9, 2.2, 1.75 and 1.2 kb are observed. In the fetal and immediate postnatal periods, the 4.7 and 3.9 kb mRNAs are predominant. By one week postnatally, the 2.2kb mRNA is increased in relative abundance and the 1.2 kb mRNA is not detected. These data suggest synthesis of Sm-C/IGF-I and IGF-II throughout lung organogenesis. The abundance of mRNA for each peptide is developmentally regulated, and for IGF-II the developmental stage may determine the mRNA species expressed.

438 ABSENCE OF ULTRADIAN RHYTHM OR DIURNAL VARIATION IN CIRCULATING SOMATOMEDIN-C (Sm-C) IN RATS.

Kim C. Donaghue, Thomas M. Badger, William J. Millard, and William E. Russell (Spon: Lewis B. Holmes), Harvard Medical School, Mass. Gen. Hosp., Children's (KCD,WER), Gynecology (TMB), & Neurology (WJM) Services, Boston.

We studied the variation in plasma Sm-C in unrestrained, cannulated rats. Six rats were sampled every 15 min for 6 hr, and 5 rats were sampled every 2 hr for 36 hr. Plasma was assayed for Sm-C (RIA) before and after acid-ethanol extraction (AE), and for growth hormone (GH). AE increased the immunoreactivity of Sm-C in heparinized rat plasma and in freshly-collected serum 3-fold. AE had no effect on serum stored at -20^0 C. >4 wks, which had comparable potency to AE serum and AE plasma. In rats sampled every 15 min, GH showed high amplitude, light entrained pulses every 3.3 ± 0.15 (SEM) hr. By visual inspection, there were no pulses of Sm-C. We further analyzed the data with 2 computer algorithms designed to detect hormone pulses. Of the 5 Sm-C pulses identified by both programs in unextracted plasma, only 1 was also identified in the corresponding AE plasma. When both pulse detection methods were applied to the data from both unextracted and AE plasma from all 6 rats, no pulses were identified in 10 of the 24 series of measurements. In 19 identical dilutions of a single serum sample, one program identified 2 "pulses," and the other, none. In rats sampled every 2 hr for 36 hr, there was no episodic fluctuation of Sm-C. Thus, there is little evidence for episodic release of Sm-C into blood, either as pulsations entrained to light or to feeding cycles. Sm-C measurements made on single blood samples from normal animals reliably reflect Sm-C concentrations over the course of 24 hr.

439 ADRENAL VEIN ALDOSTERONE LEVELS MAY DIFFERENTIATE ADENOMA FROM UNILATERAL HYPERPLASIA IN PRIMARY HYPERALDOSTERONISM.

Margaret K. Downey, Maria I. New, The New York Hospital-Cornell Medical Center, Department of Pediatrics, New York NY 10021.

Primary hyperaldosteronism (PHA) is a rare cause of low-renin hypertension in childhood. Only rarely in children does PHA result from an adrenal adenoma (APA), in which cases the hypertension is cured by adrenalectomy. Most often in children, the syndrome arises from idiopathic bilateral hyperplasia, which is not amenable to surgery. In a case of unilateral adrenal hyperplasia (uIHA) in a child (Oberfield et al. 1984 Hypertension 6:75), all data indicated an adrenal adenoma, including imaging, adrenal vein sampling and supine/upright aldosterone (aldo) response. Three years post-adrenalectomy, the contralateral adrenal was functioning normally and the patient was normotensive, a situation similar to uIHA seen in adults (Ganguly et al. 1980 JCEM 51:1190). We reviewed our experience with PHA associated with APA vs. uIHA (see table) in order to determine whether PHA secondary to these two causes in children could be distinguished.

Adrenal vein aldo (ng/dl)	APA (15y/M)	uIHA (10y/M)
ipsilateral	14,733	5,795
contralateral	15.4	107
low IVC	11.4	89
peripheral	21.0	62

Our patient with an adenoma (APA), similar to others (Ganguly et al. 1980 Pediatrics 65:605) had complete aldo suppression in the contralateral adrenal, whereas patients with uIHA maintained normal aldo in the contralateral adrenal.
Conclusion: Abnormally elevated unilateral adrenal vein aldosterone, when concurrent with normal adrenal vein aldosterone contralaterally, should strongly suggest unilateral hyperplasia rather than adenoma.