492 KIDNEY TISSUE SOMATOMEDIN-C INCREASE AFTER NEPHRECTOMY IS INDEPENDENT OF GROWTH HORMONE. Alan D. Stiles, A.J.D'Ercole and Barry T. Smith, Harvard Medical School, Boston and University of North Carolina, Chapel Hill; Departments of Pediatrics.

Somatomedin-C (SmC) is a peptide mitogen whose serum and tissue levels are considered to be growth hormone dependent. We previously reported that tissue SmC is significantly elevated in regenerating kidneys after contralateral nephrectomy. In the present study, we measured SmC tissue levels in the surgically removed left kidney of 12 wk old hypophysectomized rats and in the remaining kidney 5 days later. Similar measurements were made on kidneys from hypophysectomized rats following sham surgery.

Kidney Tissue SmC (units/gm±SD)

Nephrectomy (n=6)
right kidney 1.58 ± 0.23*
left kidney 0.86 ± 0.15 *p<.0001

Sham (n=6)
right kidney 0.85 ± 0.31
left kidney 0.88 ± 0.43

Serum concentrations (nephrectomy: 1.17±0.17 units/ml; sham: 1.09±0.21 units/ml) were no different. Injection of ¹²⁵I-SmC into nephrectomized and sham operated animals showed no difference in right kidney uptake 5 days after surgery.

Thus, SmC is increased in regenerating kidney tissue even in the absence of growth hormone. Since there was no change in renal uptake of labelled SmC, the changes observed do not reflect renal clearance. (Supported by NIH grant HL-25907)

493 CUSHING'S SYNDROME AND HIRSUTISM DUE TO A MALIGNANT OVARIAN TUMOR. E. Stoner, S. Pang, A. Berkley, SE Oberfield, LS Levine, MI New, New York Hospital-Cornell Medical Center, New York, 10021

Ovarian tissue is classically devoid of 11 β -hydroxylase and 21-hydroxylase activity. We report a 19-year-old female who presented with Cushing's syndrome, hirsutism and secondary amenorrhea and was found to have a metastatic ovarian tumor autonomously producing cortisol (F). ACTH levels were within the normal range. Peripheral levels of Δ 4-androstenedione (Δ 4-A) were markedly elevated. The tumor was only minimally responsive to ACTH and neither glucocorticoid nor androgen levels were suppressible with dexamethasone. This suggests that F production in the ovarian tissue was not under ACTH control. Upon removal of the tumor, androgen levels fell to within the normal range and serum F returned to a normal circadian pattern. Excess facial hair vanished and menses resumed within one month of tumor removal. Pathology was consistent with lipid cell tumor of the ovary, but adrenocortical carcinoma arising in an ovarian-adrenal rest tumor could not be ruled out. The patient was therefore begun on monthly courses of chemotherapy with adriamycin, cis-platinum, and opODD therapy. The hormonal results are tabulated below.

	F (µg/dl)	Δ 4-A (ng/dl)	T (ng/dl)	DHEA (ng/dl)	ACTH (pg/ml)
baseline	30	550	39	185	30.7 a.m. 30.2 p.m.
post-Cortrosyn	43	770	56	258	
Dexamethasone					
2 mg/d x 2 d	40	653	52	160	
8 mg/d x 2 d	40	757	62	301	
post-op					
8 a.m.	13.1	134	undetectable	309	42.3
4 p.m.	4.9	78	undetectable	100	28.8

We therefore report a metastatic ovarian tumor resulting in Cushing's syndrome with autonomous cortisol secretion.

494 McCUNE ALBRIGHT SYNDROME - EVIDENCE OF AUTONOMOUS ENDOCRINE FUNCTION. Dinesh Talwar, Indu Agarwal, John J. Iaccone, Michael J. Bourgeois, Surendra K. Varma, Texas Tech University Health Sciences Center, Department of Pediatrics, Lubbock, Texas.

The origin of sexual precocity in McCune Albright Syndrome is still in question, whether hypothalamic or ovarian in origin. We studied a 5 year old girl who presented with breast enlargement, episodes of menstrual bleeding, pubic and axillary hair and right sided facial prominence. She had radiological evidence of polyostotic fibrous dysplasia and ultrasound evidence of ovarian cysts. A Neuroendocrine workup was done which demonstrated low basal levels of LH and FSH and failure to respond to GnRH, but her Serum Estradiol levels on two occasions were elevated (52 pg/ml and 18 pg/ml).

		GnRH Stimulation Test					
Mins	0	15	30	45	60	75	90
FSH	<1	<1	2	2	3	3	4 mIU/ml
LH	<3	<3	5	7	4	6	7 mIU/ml

Thyroid functions were normal and TRH Stimulation Test showed a normal TSH and Prolactin response. Somatomedin-C by RIA was 2.7 U/ml (Normal 0.8-2.4). Serum Cortisol was normal. Wedge resection of the ovaries was done after which her Estradiol fell to 9 pg/ml and there has been regression in her breast size, no further menstrual bleeding and no evidence of progression of sexual precocity during short term follow up. Our studies and follow up indicate that the sexual precocity in McCune Albright Syndrome is ovarian in origin. Long term follow up is continuing.

495 PREMATURE ADRENARCHE RESULTING FROM SYMPTOMATIC NON-CLASSICAL CONGENITAL ADRENAL HYPERPLASIA, JW Temack S Pang, MI New, The New York Hospital-Cornell Medical Center, New York, NY 10021

Among 25 patients (19 girls and 6 boys) with premature adrenarche, 8 were diagnosed as having mild, asymptomatic, nonclassical 21-hydroxylase deficiency (21-OH def) based on elevated ACTH stimulated 17-hydroxyprogesterone (17-OHP) and decreased ratio of 17-hydroxypregnenolone (Δ 5-17P)/17-OHP; 2 were suspected of having a partial adrenal 3 β -hydroxysteroid dehydrogenase deficiency (3 β -HSD def) based on high responses of Δ 5-17P to ACTH stimulation and elevated ratio of Δ 5-17P/17-OHP. Elevated morning Δ 5-17P in a 5-year-old girl with 3 β -HSD def revealed diurnal variation. In all 7 patients with suspected genetic steroidogenic defects who received dexamethasone (dex), there was prompt suppression of elevated hormone levels. The remaining 15 patients with premature adrenarche did not have abnormalities in steroidogenesis, although some androgen levels were elevated and suppressed with dex, and those were classified as idiopathic. In conclusion, we propose that premature adrenarche with excessive Δ 5 and Δ 4 steroid production in association with partial steroid enzyme defect is probably due to late-onset, nonclassical congenital adrenal hyperplasia, and this condition is probably more common than has been previously recognized.

	60" post 25U IV bolus ACTH Stimulated (ng/dl)	Δ 5-17P/17-OHP				
	Δ 5-17P	17-OHP	DHEA	Δ 4-A	T	17-OHP
Normal (11)	345±203	302±166	120±164	52±80	19±22	2±2
21-OH def	876±516	4244±1113	565±398	144±77	24±13	.21±.09
3 β HSD def	1699±323	237±98	602±40	86±8	32±33	7.5±1.7
Idiopathic	633±347	262±202	339±144	93±155	11±5	3±1.5

496 UNIMPAIRED 25-HYDROXYLATION OF VITAMIN D IN HEPATIC NECROSIS Marios Theodossiou, May Kung, Donald Fraser Sang Whay Kooh Depts of Physiology & Paediatrics,

Univ of Toronto and Research Institute, Hospital for Sick Children, Toronto, Canada.

To evaluate the metabolism of vitamin D in liver disease, in which 25-hydroxylation may be low, vitamin D deficient rats were divided into control and carbon tetrachloride (CCl₄)-treated groups. Treated rats received a single i.p. injection of CCl₄, 2.0 ml/kg; controls received no CCl₄. Twenty-four h later, the rats received i.v. ³H-vitamin D₃ at doses of 55,550, or 5050 pmol. 24 h later, aliquots of serum and liver were analyzed for ³H-vitamin D₃, ³H-25-OHD₃ and ³H-1,25-(OH)₂D₃ by HPLC. Isolated kidney perfusions were performed to determine whether CCl₄ had an effect on renal metabolism of vitamin D₃. Histology showed massive confluent hepatic necrosis in CCl₄-treated rats. Elevated levels of SGOT, SGPT and total bilirubin, and decreased levels of serum albumin were indicative of severe CCl₄-induced liver damage. Sera of CCl₄-treated rats showed increased ³H-vitamin D₃ and ³H-25-OHD₃ but decreased ³H-1,25-(OH)₂D₃. Livers of CCl₄-treated rats contained more ³H-vitamin D₃ and were heavily infiltrated with fat when compared to control. There was decreased ³H-1,25-(OH)₂D₃ production in kidneys of CCl₄-treated rats. The studies indicate that 25-hydroxylating capacity was not impaired in CCl₄-induced hepatic necrosis in the rat even when tested with supraphysiological doses of vitamin D. Impairment of 1,25-(OH)₂D₃ synthesis was observed. Our results indicate the great reserve capacity of the liver to 25-hydroxylate vitamin D.

497 DEHYDROEPIANDROSTERONE SULFATE (DS) IN NEWBORNS WITH ABNORMAL GROWTH PATTERNS. Jeffrey E. Thompson, David A. Clark, Donald W. Chandler, Gregory Berg, Darrel Mayes, Dept. of Pediatrics, SUNY, Upstate Med. Ctr., Syracuse, NY, and Endocrine Sciences, Tarzana, CA. Spon. M. L. Williams.

To examine the link between DS and fetal growth patterns, DS was measured by RIA following enzymolysis in 178 cord sera of twins, triplets, infants of diabetic mothers (IDM's), LGA newborns of non IDM's, and SGA newborns. Normal levels for AGA preterm and term infants were generated and agreed with previously published data, (29-35 wks. Mean DS 139±59 vs term mean DS 234±89 p <.01). DS did not vary with mode of delivery. AGA premature infants of multiple gestation pregnancies had significantly lower levels in the 35 wk group (74±32 vs 139±59 p<.01), in the 36-37 wk group (119±51 vs 190±60 p<.01) and in the term group (156±36 vs 234±87 p<.01). Furthermore, the sum of the DS in AGA twins was not significantly different than that of the mean values for singletons at matched gestational ages despite twice the adrenal tissue. In 4 of 5 discordant twin pairs the growth retarded twin had a much lower cord DS.

The DS did not differ between term LGA IDM infants (classes A-C) and term non-IDM's (211±53 vs 234±87) although non IDM LGA infants had higher DS (M 295±42 vs 211±53 p<.05). Term SGA infants without major congenital anomalies had lower DS than term AGA infants (125±16 vs 234±87 p<.01).

DS in cord sera closely parallels the abnormal growth of non-IDM LGA or SGA infants and depressed levels precede the fall in the growth rate of multiple gestational births.