451 IMPAIRED PUBERTAL MATURATION IN BOYS FOLLOWING SUCCESSFUL THERAPY FOR TESTICULAR RELAPSE IN ALL. Lawrence S. Frankel, Robert N. Marshall, Deborah K. Coody, Clara S. Holleyman, & H. Grant Taylor, U.T. M.D.Anderson Hospital and Tumor Institute, Dept. of Pediatrics, Houston, Tx.

Four boys demonstrated variable delays in pubertal development following testicular irradiation(XRT) for biopsy proven testicular relapse(TR).The initial diagnosis of ALL was made by marrow aspirate and patients(pts) followed standard treatment (Rx) protocols. In 3 pts, the testis was the only site of relapse; the 4th had a concurrent CNS relapse. All pts are off Rx from 1 to 30 mos, having completed 2 additional yrs of systemic Rx and 2400-2500 Rads XRT to both testicles.Three pts have elevated leutenizing hormone (LH) and follicle stimulating hormone (FSH) reflecting testicular damage. Endocrine evaluations are as follows:

Age @ Dx	Age @ TR	Present Age	Serum LH/FSH (0-15/0-20)	Serum Testos (300-1000)	Bone Age	Ht%
2.5	5.2	13.8	26/44		12.5	<3
4.3	7.6	12.1	6/14	<8	10.5	<5
6.9	9.3	13.8	68/149	240	15.5	15
12.5	14.6	16.6	27/66	477	15.5	15

CONCLUSIONS:1) After successful Rx for TR in ALL, hormonal response must be monitored throughout puberty.2)Supplementation with exogenous testosterone is likely to be needed in all cases.3)Pts with TR after onset of puberty may have the best chance for normal growth and sexual maturation.4)While sufficient Leydig cell function may be present to initiate pubertal development and increase testosterone above prepubertal levels, there does not appear to be adequate testosterone to complete virilization.

● 452 SOMATOMEDIN-C STIMULATES GLYCOGEN SYNTHESIS IN FETAL RAT HEPATOCYTES. Michael Freemark, A. Joseph D'Ercole and Stuart Handwerger, Duke University Medical Center and The University of North Carolina, Departments of Pediatrics, Durham and Chapel Hill, NC

The role of somatomedin-C/IGF-I (Sm-C) in the regulation of fetal metabolism is poorly understood. Since Sm-C has insulin-like effects on tissues of postnatal animals, we have compared the effects of highly purified Sm-C and insulin on glycogen metabolism in cultured hepatocytes from 20 day old fetal rats. Sm-C (50-750 ng/ml, 6.5-100 nM) stimulated dose-dependent increases in ^{14}C-glucose incorporation into glycogen (14.4-72.9%, $p<0.001$) and total cell glycogen content (10.6-34.3%, $p<0.01$). Maximal stimulation of glycogen synthesis by Sm-C occurred at 2-4 hrs of incubation. Insulin (10 nM-10 uM) also stimulated ^{14}C-glucose incorporation but its potency was only one tenth that of Sm-C. The time course of stimulation of glucose incorporation by insulin was identical to that of Sm-C, the dose-response curves of the two hormones were parallel, and the maximal effects of insulin were not enhanced by simultaneous exposure of cells to Sm-C. These findings suggest that Sm-C and insulin stimulate glycogenesis in fetal liver through similar or identical mechanisms. Since the potency of Sm-C was greater than 10 times that of insulin, the glycogenic action of insulin in fetal liver may be mediated through binding to a hepatic receptor which also binds Sm-C. In addition to its mitogenic effects on fetal tissues, Sm-C may have direct anabolic effects on fetal carbohydrate metabolism. Supported by NIH HD07447 and HD06301.

● 453 EFFECT OF GROWTH HORMONE ON EPIDERMAL GROWTH FACTOR EXCRETION. J. Paul Frindik, Stephen F. Kemp, M. Joycelyn Elders. University of Arkansas for Medical Sciences, Department of Pediatrics, Little Rock, Arkansas.

Epidermal growth factor (EGF) is a growth promoting factor known to accelerate proliferation and to stimulate growth in multiple tissues, but no disease state associated with a deficiency, excess, or changing pattern of EGF excretion has been identified. To study the influence of growth hormone (GH) deficiency and GH administration on EGF excretion, we measured urinary EGF in normal children and GH deficient children prior to GH therapy, after 4 days of GH (0.08 U/kg BID) and after 2, 6, and 12 months of therapy (0.08 U/kg TIW). Data are shown below:

URINARY EGF EXCRETION

Normal	No.	µg/gr/cr	µg/M²/24 hr.
Ages 2-5	10	41.2±3.2	38.2±5.2
6-12	10	35.6±7.3	32.9±5.9
GH Def.			
Before	10	21.4±4.2	19.8±4.8
4 days	10	24.1±4.2	22.6±6.1
2 months	8	47.3±4.1	44.2±5.6
6 months	6	43.1±5.3	39.9±5.3
12 months	5	42.0±5.9	39.1±5.7

We conclude that GH deficient children have lower EGF excretion as compared to normals prior to treatment and that it increases after treatment. This effect is not immediate, but after 2 months EGF excretion was higher in children on GH than in controls, suggesting that growth hormone influences EGF excretion.

454 EXTRAUTERINE ONTOGENETIC DEVELOPMENT OF ADRENOCORTICAL FUNCTION IN THE HUMAN PREMATURE. Ronald W. Gotlin, Adrian W. Pike, David B. Christie, Jared L. Klein, Deborah L. Evans, and Paul V. Fennessey. Univ. of Colo. Schl. of Medicine, Dept. of Pediatrics, Denver, Colorado, 80262.

While clinical signs suggestive of adrenal glucocorticoid and mineralocorticoid insufficiency are common in the human premature, previous biochemical estimations of newborn adrenal function employing a variety of biochemical methods have reported normal to high blood and urine concentrations of adrenal corticosteroids. Our studies were designed to examine longitudinally biochemical indices of adrenal function in premature and term infants between 30 and 42 weeks of gestational age. Urinary profiles from twenty-four hour urine samples collected in 4 hour aliquotes at weekly intervals were enzymatically hydrolyzed, derivatized to form methyloxime-trimethylsilyl ethers and analyzed by gas chromotography and mass spectrometry-selected ion capture. Severely ill infants were not studied but subjects were not otherwise excluded on the basis of clinical presentation or course. Clinical course including light-darkness (eye patching) and treatment were monitored.

The urinary steroid profiles from premature infants of 30-37 weeks gestational age do not reflect a continuous transition from the fetal 16 hydroxy 5-ene pattern to the 17 hydroxy-4-ene pattern of the mature adrenal. The results indicate that adrenal glucocorticoid and mineralocorticoid insufficiency may be a common finding in premature infants and may result in characteristic clinical features requiring replacement therapy. (Supported in part by NIH Grants RR01152 and RR69).

● 455 KETOCONAZOLE TREATMENT IN BOYS WITH PRECOCIOUS PUBERTY. F.John Holland,Leona Fishman,John D.Bailey (Spon. by S.W.Kooh) University of Toronto and Hospital for Sick Children, Toronto, Canada.

Three boys with familial gonadotropin-independent precocious puberty (Rosenthal et al,JCEM 57:571,1983)were treated with LHRH analog for periods of 1-4 mos,without clinical or biochemical response.The effects of the antifungal drug ketoconazole were studied in these boys prompted by the observation that this agent may interfere with testosterone biosynthesis.With 200mg/12 h P.O. there was an immediate significant fall in serum testosterone(T) from a pre-Rx level of 7.0±1.6 nM/L (mean±SEM)to 1.3±1.1 (N<1.5), with a reciprocal rise in 17-OHP from 2.3±1.5 to 7.2±1.1 nM/L. DHAS and androstenedione levels were unchanged. The T response to hCG remained intact.Major improvement in behavior,linear growth & skeletal maturation were sustained for the duration of treatment.

Pat	Age	Pre Rx			Duration Rx	Post Rx		
	(yrs)	BA	Ht vel*	ΔBA/ΔCA	(mos)	BA	Ht vel*	ΔBA/ΔCA
1	4.2	8	17	1.9	9	9	4.8	∿1
2	5.3	8	11	1.51	5	-	6	-
3	4.0	9.5	17	2.25	5	10	4.8	∿1

The cortisol response to ACTH$^{1-24}$ was significantly blunted after 5 days of Rx,but returned to normal after 1 mo with normal diurnal rhythm.Hepatic abnormalities were not observed in up to 9 mos of treatment.We conclude that ketoconazole may provide effective long-term control of precocious puberty in males through C 17-20 lyase inhibition,and speculate that this drug may play an important therapeutic role in other conditions of androgen excess. *cm/yr

456 PREMATURE ADRENARCHE: CLINICAL AND DIAGNOSTIC FEATURES. PB Kaplowitz and JL Cockrell* (intr. by HM Maurer), Dept. of Pediatrics, Childrens Medical Center, Medical College of Virginia, Richmond.

Premature adrenarche (PA), or isolated development of pubic hair before age 8, is common in the Richmond area. We have compared the clinical findings, family history and serum concentrations of dehydroepiandrosterone sulfate (DHEA-S), in 21 new cases of PA seen in the past 2 yrs and in 17 control children. Since 17/21 of the PA patients were black females, black girls between 3 and 8 yrs were used as controls. The height age was on the average 7.5 mo greater than the chronological age in the PA patients, but was also greater (by 8.1 mo) in the control group. Twenty of 21 patients, but none of the controls, had a history of an adult-type axillary odor, which in 8 cases preceded the growth of hair by more than 3 months. There was a positive family history for PA in only 3 of 21 children with PA, and in 1 of 17 controls. The average age of maternal menarche was not significantly different for the PA and the control groups. Serum DHEA-S (Nichols Institute, Los Angeles, CA) was significantly higher in the PA children at all ages. For children < 6 yrs, PA= 49 ± 29 µg/dl (range 10 to 92) and control = 11 ± 8 µg/dl (range < 5 to 26), $p < .001$; for children 6-8 yrs, PA = 52 ± 23 µg/dl (range 19 to 110) and controls = 20 ± 16 µg/dl (range <5 to 62), $p < .001$. We conclude that (1) the presence of axillary odor is a useful clinical marker for PA, (2) serum DHEA-S is useful in confirming the clinical impression of moderately increased adrenal androgen secretion in these children, and (3) familial factors probably do not play a major role in the etiology of PA.