† **414** EFFECT OF SHORT TERM SEX STEROID THERAPY ON SOMATOMEDIN-C GENERATION IN GROWTH HORMONE DEFICIENT CHILDREN. José F. Cara, Richard W. Furlanetto, and Charles A. Stanley, Univ. of Pa. School of Medicine, Children's Hospital of Philadelphia, Philadelphia, Pennsylvania.

Sex steroids (SS) are known to stimulate linear growth and increase somatomedin-C (Sm-C) levels in normal children. To determine if SS potentiate the Sm-C response to growth hormone (GH) or if this increase is secondary to SS enhanced GH secretion, we investigated the effects of short term SS therapy on immunoreactive Sm-C levels in GH deficient children. Six males were treated with oxandrolone (0.125 mg/kg/d) and 4 females with ethinyl estradiol (0.25 ug/kg/d) before and during GH therapy (0.1 IU/kg/d). Sm-C levels were determined before starting therapy (basal), three days after beginning SS, three days after combined GH + SS, and three days after GH alone.

	Basal (mean ± SEM)	SS	GH + SS	GH
males (6)	.08 ± .02	.07 ± .02	.31 ± .09	.51 ± .18
females (4)	.03 ± .02	.03 ± .01	.15 ± .07	.20 ± .05
total (10)	.06 ± .01	.05 ± .01	.25 ± .06	.39 ± .11

Using the paired t test, no difference was noted between the basal and SS treatment levels. In all patients, the GH alone and GH + SS concentrations were greater than the basal levels ($p < .01$). The mean Sm-C levels were significantly lower during GH + SS therapy than during therapy with GH alone ($p < .05$). These data suggest that short term SS therapy does not potentiate, and may inhibit, the Sm-C response to GH. We conclude that the increase in Sm-C observed during puberty in response to sex steroids in normal children may be mediated by enhanced GH release.

415 TESTOSTERONE PRODUCTION IN POORLY CONTROLLED ADOLESCENT DIABETIC MALES. S. Castells, M. Noval, and M. Fusi, SUNY, Downstate Med. Ctr., Dept. of Peds., Brooklyn, N.Y.

There are suggestions of an impairment in testosterone synthesis and/or testosterone secretion in diabetic animals and humans. The kinetics of human chorionic gonadotropin-induced steroidogenic response of the human testis was evaluated by administration of hCG to six normal adolescent controls (N) and six insulin-dependent adolescent diabetic males during a period of poor diabetic control (DPC) and repeated three months later after obtaining good control (DGC) by multiple daily insulin injections. HCG was administered in a single injection of 6,000 UI (Pregnyl, Organon Lab) at 9:00 a.m. and bloods were drawn at 0, 1, 2, 4, 6, 12, 24 and 48 hr for plasma testosterone levels, determined by RIA. Hg A/C was $N 5.0 \pm 1.4$, DPC 13.2 ± 1.9 , DGC 7.5 ± 1 ($p < .01$). Plasma testosterone levels mean $\pm$ SE (ng/ml) in DPC was at 0 452 ± 115 ; 1 hr 448 ± 110 ; 2 hr 591 ± 151 ; 4 hr 569 ± 120 ; 6 hr 581 ± 127 ; 8 hr 502 ± 124 ; 12 hr 620 ± 153 ; 24 hr 932 ± 239 and 48 hr 1345 ± 364 . In DGC was at 0 723 ± 87 ; 1 hr 743 ± 39 ; 2 hr 860 ± 51 ; 4 hr 953 ± 137 ; 6 hr 856 ± 142 ; 8 hr 970 ± 127 ; 12 hr 1116 ± 200 ; 24 hr 1566 ± 298 and 48 hr 1896 ± 231 . Plasma testosterone in DGC were not different from N. Juvenile diabetics in poor control had low basal and post hCG plasma testosterone levels than during a period of good diabetic control. This study suggests impaired androgen production in male adolescent diabetics in poor control. Low testosterone production may be related to sexual dysfunction, growth retardation, and atherosclerosis in adolescent diabetics. (Supported by NIH grant RR-318).

● **416** GLYCOSYLATION OF HEART MYOGLOBIN IN DIABETIC RATS. S. Castells, S. Smith, and D. Kirschenbaum, SUNY, Downstate Medical Ctr., Depts. of Peds. and Biochem., Brooklyn, N.Y.

We have reported cardiopathy in juvenile diabetics in poor control which improves with good glycemic control (Ped Res 16: 97A, 1982). Glycosylation of heart myoglobin may play a role in this type of reversible diabetic cardiopathy. Myoglobin is similar to the B-chain of hemoglobin (Hgb) and has a sufficient number of lysine residues and amino terminus to be glycosylated like Hgb. Twelve rats, 2m old, were injected with 60mg/kg streptozotocin by the penial vein and 12 control (C) rats were injected with saline. Glycosuria and hyperglycemia (blood sugar greater than 400mg/dl) were present in the diabetic (D) rats. After 12 wks the rats were killed. Hearts were perfused through coronary arteries with 0.85% NaCl until clear. D had heart wts of 1.11 ± 0.07 gm vs C 0.98 ± 0.18 gm. Hearts were minced in a mortar, leached with 10 times its volume 0.01M potassium phosphate buffer, pH 7.0, with 5mM EDTA and centrifuged at 20,000 g for 10 min. The clear supernatant containing myoglobin was filtered through a 1.6×40 cm column of Sephadex G-100 superfine gel and diluted in 2.1ml fractions with the phosphate buffer. Protein was measured by Lowry and glycosylation by the modified TBA method of Mey et al (Anal. Biochem 118:294, 1981). D rats had 8.26 ± 2.50 (m±SE) OD443 per mg protein and control 2.19 ± 0.32 , $P < .005$. Markedly increased glycosylation of heart myoglobin may change the oxygen affinity and subsequently the contractility of cardiac muscle and contribute to the cardiopathy of juvenile diabetics in poor control.

417 RESPONSE TO THERAPY IN CHILDREN WITH LOW INTEGRATED CONCENTRATION OF GROWTH HORMONE. Stuart A. Chalew, Salvatore Raiti, and A. Avinoam Kowarski, University of Maryland School of Medicine, Department of Pediatrics, Baltimore.

We have previously demonstrated that the response of GH to pharmacologic stimulation does not always correspond to the actual integrated concentration of GH (ICGH) (JCEM 48:811, 1979). Spiliotis et al have reported that 3 of 7 children who had a normal response to GH provocative tests but a reduced amplitude or frequency of GH pulses, responded to GH therapy (Abstract 528 Endocr. Soc. 1983).

We measured ICGH in 15 growth hormone deficient (GHD) children and in 94 children with growth impairment who exhibited a normal response to GH provocative tests (GHNHR). The ICGH of the 15 GHD children ranged from 0.2 to 2.6 ng/ml. In 75 of the 94 GHNHR children, the ICGH was above 2.6 ng/ml.

The ICGH of the 19 remaining GHNHR children was below 2.6 ng/ml. To date, 6 of these 19 children have been treated with GH for more than 5 months. All 6 responded to GH therapy (2 more than doubled their growth rate, the remaining 4 increased their growth rate by more than 2 cm/yr).

Conclusion: growth impaired patients with low ICGH should be treated with GH even if they exhibit a normal response to provocative tests.

† **418** THE RATIO OF GROWTH HORMONE (GH) BY TANDEM MONOCLONAL ASSAY/POLYCLONAL RIA DOES NOT PREDICT RESPONSE TO GH THERAPY. Stuart A. Chalew, Salvatore Raiti, and A. Avinoam Kowarski, University of Maryland School of Medicine, Department of Pediatrics, Baltimore.

Blethen and Chaslow (JCEM 57:1031, 1983), recently reported that the ratio of GH by Tandem Hybritech monoclonal immunoradiometric assay (Tandem) to standard polyclonal radioimmunoassay (RIA), might predict the outcome of GH therapeutic trials.

We studied the effect of GH therapy on 16 patients whose height was <3rd percentile and bone age delayed >2 SD. Each patient had a normal GH response (≥ 10 ng/ml) to insulin arginine stimulation (assayed by RIA). GH was also assayed by Tandem. Seven patients increased their pretreatment growth rate by >2 cm/yr (R). Nine patients did not respond to GH (NR). Results: (mean $\pm$ 1 SD)

	GROWTH RATE (cm/yr)		TANDEM/RIA	(RANGE)
	Pre-GH	On-GH		
R	3.06 ± 1.14	8.34 ± 2.54	0.40 ± 0.10	(.32-.61)
NR	4.39 ± 1.4	5.13 ± 1.61	0.54 ± 0.21	(.14-.78)

There was no significant difference between the Tandem/RIA ratio of R and NR patients. The ratio did not predict the response to GH therapy.

419 ANDROSTENE SULFATES IN AMNIOTIC FLUID AND CORD BLOOD: A POSSIBLE APPROACH TO PRENATAL DIAGNOSIS OF SMITH-LEMLI-OPTTZY SYNDROME (SLO). Fred Chaslow, Sandra Blethen and Kutay Taysi, Washington University, St. Louis Children's Hospital, Department of Pediatrics, St. Louis, MO.

We have previously shown that during the first month of life there are 4 androstene sulfates present in serum. Two of these have been identified as the sulfates of dehydroepiandrosterone (DHEA) and 16 α -hydroxy-DHEA; the others (II and IV) are unidentified. Of the four, DHEA-sulfate is present in the smallest amounts. We have extended our studies to cord blood and second trimester amniotic fluid. Steroid sulfates were extracted with ethanol-ethyl acetate (1:2) and hydrolyzed with Helix pomatia extract; the 5-androstenes were separated by flash chromatography and detected in a radioimmunoassay in which DHEA and 16 α -hydroxy-DHEA crossreact but pregnenolone and 17-hydroxy-pregnenolone do not. DHEA, 16 α -hydroxy-DHEA and II (an acid-labile material) were found in both cord blood and amniotic fluid; IV was not present in either. When (7 α -³H)DHEA-sulfate was added to cord blood or amniotic fluid, no radiolabel was found in II or 16 α -hydroxy-DHEA. Thus, neither is an artifact of isolation. Compound II may represent the product of an hitherto unidentified pathway. In the first week of life, children with SLO do not have II in their serum. The fact that this material is present in second trimester amniotic fluid from pregnancies with a normal outcome, suggests that it may be possible to diagnose SLO prenatally, if the deficit in II concentration begins early in gestation.