469 SERUM PROLACTIN IS ELEVATED IN CHILDREN WITH CONGENITAL GROWTH HORMONE DEFICIENCY ASSOCIATED WITH PERINATAL COMPLICATIONS. J. Michael McMillin, M.C.Matustic, T. Aceto, Jr., & D. R. Brown; USD School of Medicine, Sioux Falls; St. Louis U, Glennon Children's Hospital, St. Louis; and Minneapolis Children's Medical Center, Minneapolis.

Children with idiopathic congenital growth hormone deficiency (ICGHD) frequently have a history of significant perinatal complications. We have investigated the hypothesis that children with perinatal complications represent a discreet etiologic subset of children with ICGHD characterized by abnormalities of prolactin secretion. Thirty-two children with newly diagnosed ICGHD were studied by measuring the prolactin response to TRH. Fifteen normal children were studied as controls. Children were classified as ICGHD on the basis of documented growth hormone deficiency, growth records compatible with a congenital onset and absence of findings suggesting an acquired or definable lesion. Sixteen of the ICGHD children had a history of significant complications during the perinatal period. Mean baseline prolactin in this group was 22.0 ± 4.2 ng/ml (Mean ± SEM). This was significantly greater than the baseline prolactin in children with ICGHD and normal perinatal histories (11.4 ± 1.7 ng/ml) and normal children (8.7 ± 1.6 ng/ml, $p < .03$, Student's t-test). There was no significant difference in peak prolactin concentration 15 minutes after TRH injection in the three groups (51.7 ± 7.3, 52.1 ± 7.8 and 45.8 ± 4.7 ng/ml, $p > .05$). We conclude that hypothalamic compromise associated with perinatal complications is the etiology of growth hormone deficiency in a subset of children with ICGHD. Vigorous follow-up of at-risk children is recommended.

† 470 THYROTROPIN RELEASING HORMONE (TRH) ADMINISTRATION TO PREGNANT WOMEN STIMULATES FETAL T_3 PRODUCTION. F. Moya, P. Mena, E. Paiva, A. Foradori, F. Heusser, P. Michand, I. Gross. Yale Univ Sch of Med, Dept Ped, New Haven CT and Hospital Sotero Del Rio, Depts Ped, Nuclear Med, Endoc, Santiago, Chile.

Thyroid hormones enhance fetal lung maturation; this effect is synergistic with that of glucocorticoids. Their potential clinical usefulness for the prevention of RDS is limited by poor transplacental passage. TRH has been reported to cross the placenta and to stimulate the fetal pituitary-thyroid axis. In order to evaluate its effectiveness pregnant women at term were injected with either saline (n=3), TRH (Thypinone, Abbot) 400 µg (n=4), or TRH 600 µg (n=3), 2 h prior to elective cesarean section. Serum levels of TSH, T_3 and prolactin were determined by RIA in mothers and neonates. Administration of 400 µg TRH resulted in a 275% increase in maternal TSH levels and a 22% and 75% increase in T_3 and prolactin levels, resp. 600 µg of TRH produced a 309% increase in maternal TSH, but no further increase in T_3 or prolactin. The cord blood levels in the babies were as follows:

	TSH	T_3	Prolactin
Controls:	3.2 µunits/ml	66 ng/dl	219 ng/ml
TRH, 400 µg:	25 µunits/ml	149 ng/dl	309 ng/ml

All neonates exhibited the normal postnatal surge in T_3 and prolactin levels. No side effects were noted in the mothers or infants. Maternal administration of TRH results in a large increase in fetal T_3 levels. TRH could potentially be used to accelerate fetal lung maturation in humans.

471 DIFFERENTIAL MEASUREMENT OF VITAMIN D_2 AND D_3 METABOLITES: ASSESSMENT OF COMPLIANCE WITH VITAMIN D_2 THERAPY. Francis Mimouni, Victoria A Neumann, Reginald C Tsang and Bruce W Hollis. University of Cincinnati and Case Western University.

An adolescent boy with pseudohypoparathyroidism was treated with massive doses of vitamin D_2 (D_2) and oral calcium for 8 years. At age 13 he had a convulsive episode due to severe hypocalcemia (serum calcium 5.8mg/dl). Serum 25-OH vitamin D (25-OHD) concentration was high, (40ng/ml) but much lower than his "usual" therapeutic levels which varied between 300 and 600ng/ml. The patient and his parents denied any lack of compliance. Manufacturing error was excluded by measuring D_2 concentration in the D_2 preparation taken, and malabsorption of lipid-soluble nutrients was ruled out by normal serum levels of vitamin A, E, and carotene. Differential analysis of D_2, D_3, 25-OH D_2 and 25-OH D_3 showed: a normal serum concentration of D_3 and of 25-OH D_3 while D_2 and 25-OH D_2 concentrations were slightly above the normal range. Normal 25-OH D_2 levels indicated a normal hepatic 25-hydroxylation; on the other hand, a low 25-OH D_3 serum concentration was expected in this patient receiving massive doses of D_2, due to preferential binding of D_3 to serum D-binding-protein, which allows more "free" D_2 to be available for 25-hydroxylation. Non-compliance with treatment was demonstrated, and the patient admitted not having taken his medication for a month. Differential analysis of D metabolites allowed direct assessement of compliance with vitamin D_2 therapy in this patient.

472 ESTROGEN AT LOW DOSES RAPIDLY AUGMENTS GROWTH HORMONE (GH) RELEASE INDEPENDENTLY OF SOMATOMEDIN-C (SM-C). George Wm. Moll, Jr. & Robert L. Rosenfield, Univ. of Chicago,Wyler Children's Hosp.,Depts. of Ped.& Med., Chicago,Il.

We tested whether low doses of ethinyl estradiol (EE) would stimulate GH independently of SM-C inhibition, after we found EE 50 mcg/m²/d x 2d to augment peak GH responses to L-dopa testing (LDT) while lowering SM (Rich et al, Pediatr.Res. 13:329A,1979).

We first examined the effect of one bedtime dose EE(29±2(SEM) mcg/m²) upon GH reserve in 8 prepubertal short-normal children. L-dopa(0.3 gm/m²) stimulated GH to ≥7 ng/ml inconsistently (6/8) before EE. EE resulted in a significant increase in peak GH response (29±5 ng/ml)($p<.05$) to LDT. EE (10-30mcg/m²) was then given for 2 days prior to repeat LDT in 15 prepubertal children with the following results.

EE (mcg/m²/d)	n	PEAK GH RESPONSE (ng/ml)
Before EE Rx	15	13.9 ± 2.3
12 ± 2	3	13.7 ± 6.7
27 ± 1	12	35.4 ± 3.8 ($p<.01$)

GH responses to LDT were <7 ng/ml in 3/15 prior to EE but were consistently ≥7 ng/ml after EE. Augmentation of the GH response by EE at 27±1 mcg/m²/d was of similar magnitude to that noted with 50 mcg/m²/d EE, but this low-dose EE did not act via lowering SM-C levels (.54±.09 vs .47±.07,n=8).

We conclude that a single bedtime dose of EE as low as 29±2 mcg/m² augments the peak GH response to LDT and enhances the discrimination of L-dopa testing for GH reserve. Our results suggest low-dose estrogen rapidly and directly augments GH release, consistent with its enhancing effect on growth.

† 473 GROWTH HORMONE AND STUNTED GROWTH FOLLOWING HEAD-IRRADIATION. H. David Mosier, Jr., Regina A. Jansons Karl F. Swingle, Charles A. Sondhaus, Lyle C. Dearden and Leslie Halsall. University of California, Irvine, Departments of Pediatrics, Radiological Sciences, and Anatomy.

The role of growth hormone (GH) in stunting following head-irradiation in rodents and humans is unclear. We have reported no response to GH treatment in the stunted head-irradiated rat. Secretion profile of GH and cell size and number in brain, heart, liver, kidney and gastrocnemius muscle (gastroc) were determined in rats X-irradiated with 600 rads to the head only or sham-irradiated at 2 d of age. Blood was sampled for GH RIA from cannulated undisturbed rats at 15 min intervals for 18 h periods (9 h light and 9 h dark) at 47 to 64 d of age. Irradiated rats were significantly stunted in body weight and tail length. At 20-21 d of age they had significantly reduced weight of all organs; decreased brain organ/body ratio ($p<0.0005$) and total DNA ($p<0.0005$); increased DNA/organ in all organs, significant in heart ($p<0.025$) and gastroc ($p<0.025$); decreased protein/DNA in all organs, significant in brain ($p<0.005$), heart ($p<0.01$) and gastroc ($p<0.05$). Irradiated rats had normal rhythm of GH pulses; reduced numbers of GH values from 200 to 499 ng/ml ($p<0.05$) and 500 to 999 ng/ml ($p<0.005$), and reduced area under GH concentration vs time ($p<0.025$). We conclude that GH secretory rhythm is intact in the head-irradiated rat. Cell size and number results exclude neonatal hypopituitarism and/or undernutrition as causes of the growth stunting. Reduced GH secretion may thus only reflect setting of a putative centrally located growth regulator for a smaller body size.

● 474 ACUTE GROWTH HORMONE (GH) ADMINISTRATION: EFFECTS ON SOMATOMEDIN-C (SM-C) AND THE SECRETORY RESPONSE TO GROWTH HORMONE RELEASING FACTOR (GRF) AND CLONIDINE. Jon M. Nakamoto, Joseph Gertner and Myron Genel. Depts. of Peds., Yale School of Med., New Haven and Cornell Med. Coll., New York

Studies in vitro, in animals, and in adults have suggested that SM-C, operating at both CNS and pituitary levels, mediates a feedback inhibition of GH secretion. To test this hypothesis in children we studied 11 short (height < 3rd%) boys, ages 7-14 with delayed bone ages and normal GH responses to standard tests. On successive days 2-hour clonidine (5ug/kg,p.o.) and GRF (0.3ug/kg, i.v.) tests were performed in the fasting state. Daily GH (0.1 U/kg, i.m.) was then given with a repeat clonidine test 20 h after the second dose and a GRF test 20 h after the third. Results are shown below:

Integrated GH (ng/ml/min):	Clonidine	GRF	SM-C(U/ml)
Before GH	582±184	1581±363	0.63±0.14
GH x 2d	362±137*		1.46±0.11*
GH x 3d		487±185*	1.83±0.36*

*Differs from baseline, $p<0.05$

Pre-treatment with GH thus strongly inhibited the GH response to clonidine and GRF, acting at the hypothalamus and pituitary respectively. Although SM-C rose sharply, individual rises did not correlate with suppression of the GH response to clonidine ($r=0.35$;$p=0.3$) or GRF ($r=-.05$). Conclusion: inhibition by GH of its own secretion operates, at least in part, at the pituitary level. While the inhibition may be modulated by SM-C, its extent does not depend directly on plasma SM-C concentrations.