● 458 FAMILIAL RESISTANCE TO THYROID HORMONE PRESENTING AS NEONATAL THYROTOXICOSIS. Anjali Malkani, Danilo Escoto, Allen W. Root, Barry B. Bercu. Univ. of South Florida College of Med., All Children's Hospital, Dept. of Pediatrics, St. Petersburg, FL 33731

Familial resistance to thyroid hormone is characterized by elevated thyroid hormones and non-suppressed TSH in euthyroid individuals. We present a unique occurrence of an infant with neonatal hyperthyroidism and resistance to thyroid hormone in a family with 3 generations of resistance to thyroid hormone. He was born at 35 weeks gestation to a consanguinous relationship (first cousins), birth weight 1480 g, length 46 cm. He had fetal and neonatal (200 beats/min) tachycardia and exophthalmos. At 3 weeks of age the following was obtained: T4 50.7 ug/dL, T_3RIA 1349 ng/dL, T_3RU 45.9%, rT_3 618 ng/dL, TSH 389 uIU/mL, free T4 25.7 ng/dL, free T3 5385 pg/dL, TBG 2.3 ng/dL, TBII 18 (nl<14), TSIg 167% (nl<130%), 4h ^{123}I uptake 87% and 24h 50%, moderately enlarged gland on scan, negative thyroid antibodies. TRH increased the TSH from 317 to 413 at 30 min. Patient's father, paternal aunt and paternal grandmother have well documented resistance to thyroid hormone. One month postpartum the mother had the following: T4 19 ug/dL, T_3RIA 298 ng/dL, free T4 4.5 ng/dL, free T3 698 pg/dL, TSH 1.0 uIU/mL, TBG 2.8 ng/dL (nl 1.6-3.6), negative TBII and TSIg, nl TSH response to TRH. Maternal grandfather also had elevated thyroid indices (T4 15.2 ug/dL, T_3RIA 229 ng/dL), nonsuppressed TSH 2.2 uIU/mL, and normal TRH stimulated TSH. We postulate that this neonate is a homozygote for this gene defect. We hypothesize that this infant's hyperthyroxinemia resulting in thyrotoxicosis may be expressed due to genetic inherited factors from both parents.

● 459 GROWTH HORMONE (GH) INJECTIONS DIRECTLY INTO AN EPIPHYSEAL PLATE (EP) FAIL TO STIMULATE LINEAR GROWTH IN THE RHESUS MONKEY (RM). Saul Malozowski, Manuela Caruso-Nicoletti, Song G. Ren, Robert Udelsman, Lynn Loriaux, Fernando Cassorla. DEB, NICHHD, NIH, Bethesda, MD 20892.

Whether or not GH can stimulate growth directly at the EP remains an important unanswered question. Several investigators have shown that the local administration of GH into the EP of hypophysectomized rats leads to linear growth. If this were true in primates, it could serve as a theoretical basis for selective bone remodeling. We studied this question in six prepubertal gonadectomized RM. Lower leg (LL) growth velocity (LLG) was assessed using a modified Valk measuring device. Baseline LL measurements were performed weekly on both legs for 14 weeks. The EP was then identified by fluoroscopy and GH was injected 3 times a week for one week into one leg while saline was injected into the other. GH was given in a dose of .4 and .8 units per injection. Each RM served as his own control. The investigators were blinded to the injection schedule. Testosterone enanthate, as a single intramuscular dose of 2 mg/kg, was given to 3 RM as a positive control for LLG. The results of these studies, expresed as percent growth change over baseline, are presented below

TOTAL DOSE	EXPERIMENTAL GROUP	CONTROL GROUP
GH 1.2 U	66%	187%
GH 2.4 U	59%	166%
T 2mg/kg	285%	85%

It is clear from these data that in our primate model GH administered directly into the EP failed to accelerate LLG.

460 UNEXPLAINED HYPOGLYCEMIA IN BECKWITH-WIEDEMANN SYNDROME WITH BLUNTED GROWTH HORMONE RESPONSE. Ben R. Mandac, M. Shohat and Alan H. Klein, UCLA School of Medicine, Cedars-Sinai Medical Center, Dept. of Pediatrics, Los Angeles.

We report a 34 week female infant, birth weight=3.7 Kg, length=49.5 cm with macroglossia, microcephaly, diastasis recti, pulmonic stenosis, visceromegaly, abnormal ear crease and multiple other problems including increased direct bilirubin and liver function tests. Severe hypoglycemia developed when weaned from parenteral nutrition at 6 weeks of age. Initial studies revealed growth hormone (GH)=7.7 ng/ml, cortisol (C)=9.7 mcg/ml, insulin (I)=2.1 mcU/ml when blood glucose (BG)= 21 mg/dl. Euglycemia was maintained by continuous gastric feeding. Subsequent fasting showed GH=1.1,I <2.5, C=19.4, IGF I <0.6 U/ml, IGF II=532 ng/ml,C-peptide=1.1 ng/ml when BG=35. IV glucagon increased BG to 52. Therapy with GH (1 U IM QD) did not ameliorate hypoglycemia. Repeat glucagon stimulation on GH therapy demonstrated maximum I= 10 mcU/ml 1 minute after infusion and maximum GH= 3.7. Liver biopsy was negative for glycogen storage disease. Brain MRI and chromosomes were normal. Hyperbilirubinemia resolved during GH therapy. One week post GH therapy an arginine infusion test revealed:

TIME	0min	30min	60min	90min	120min
Insuli	3.1	5.2	4.1	4.5	4.9
GH	5.5	5.2	7.9	5.7	6.6

The reason for the hypoglycemia is unclear. Hyperinsulinemia or abnormal IGF I and II were not demonstrated. GH therapy was unsuccessful. Factors other than insulin, growth hormone and the known IGF's appear to play an important part in the macrosomia and hypoglycemia seen in this infant.

461 USEFULNESS OF LH, FSH, AND TESTOSTERONE DETERMINATIONS AT 2 TO 10 WEEKS OF AGE (THE WINDOW PERIOD) IN MALE PSEUDOHERMAPHRODITISM. Scott H. Mandel, Cheryl E. Hanna, Stephen H. LaFranchi. Oregon Health Sciences University, Department of Pediatrics, Portland, Oregon.

To assess whether LH, FSH, and testosterone (T) values are helpful in the differential diagnosis of male pseudohermaphroditism, we evaluated 22 patients in the window period (2-10 weeks of age) and compared results with those obtained by karyotype, genitogram, and hCG stimulation. While 3 patients with panhypopituitarism had low LH ($\bar{X}$ = 3 mIU/ml) and low T ($\bar{X}$ = 11 ng/dl), one had a high FSH (52 mIU/ml). Two patients with Prader Willi had normal gonadotrophins and high T (509, 610 ng/dl). Two patients with mixed gonadal dysgenesis (XO/XY) and 3 patients with XY gonadal dysgenesis with müllerian remnants had normal to high-normal LH ($\bar{X}$ = 19 mIU/ml) and low-normal T ($\bar{X}$ = 158 ± 32 ng/dl); FSH was high-normal to high ($\bar{X}$ = 15 mIU/ml). Values in a patient with "vanishing testes" were FSH 212 mIU/ml, LH 167 mIU/ml, and T <30 ng/dl. A patient with Leydig cell hypoplasia had low T (22 ng/dl), normal FSH (2.9 mIU/ml), but low LH (3 mIU/ml). Two patients with high gonadotrophins and normal testosterone and dihydrotestosterone are awaiting tests of androgen receptor function. In 6 patients who were judged idiopathic, no helpful gonadotrophin pattern was found. Two patients are still being evaluated. In conclusion, we found window period LH, FSH, and testosterone values useful and generally consistent with results obtained by other diagnostic tests.

● 462 **SOMATOSTATIN (SS) SECRETORY RHYTHM IN GROWTH HORMONE RELEASING HORMONE (GHRH)-DEFICIENT CHILDREN.** P Martha Jr., R Blizzard, S Pezzoli, M Thorner, A Rogol, Univ of VA School of Med, Depts Pediatrics and Internal Medicine, Charlottesville, VA.

Nocturnal GH secretory patterns in response to GHRH (1 ug/kg/3h SC) were studied in 6 GHRH-deficient children. Four received GHRH therapy for at least 6 mo and were studied repeatedly. Two received GHRH every 3h for 24h before and then during testing. During 19 study periods GH rose significantly in response to 66 of 72 GHRH doses (92%) as determined by a regional threshold pulse analysis program. The amplitude varied with time in all subjects during the study periods without relationship to duration of therapy. In the four with multiple studies one GH pulse predominated and occurred at a constant time of day in each individual. Peak GH levels (ng/ml) for one patient are shown (times are of GHRH doses).

Mos. Rx	2000h	2300h	0200h	0500h
2	3.4	6.4	12.0	19.3
4	9.5	6.7	13.8	20.9
7	5.7	2.9	3.1	11.6
9	4.4	6.2	2.8	20.8

The time of greatest response was 0500h in three of the four. No child had a pretreatment dominant pulse at the same time as the one during GHRH therapy. The persistent variability in GH response to multiple equal GHRH doses suggests a SS secretory rhythm. The temporal consistency of maximal GH release to GHRH might reflect that individual's nadir of nocturnal SS secretion. These data suggest that treatment of some GHRH deficient children with a sustained release form of GHRH will result in pulsatile GH secretion.

● 463 **TREATMENT WITH ATENOLOL INCREASES THE GROWTH HORMONE (GH) RESPONSE TO EXOGENOUS GH RELEASING HORMONE (GHRH) BUT FAILS TO AUGMENT ENDOGENOUS GH SECRETION IN NON-GH DEFICIENT SHORT BOYS.** Paul Martha Jr., Robert Blizzard, Susan Pezzoli, Michael Thorner, Alan Rogol - Univ of VA School of Medicine, Depts of Peds and Internal Medicine, Charlottesville, VA

Selective beta-adrenergic blockade (BAB) with atenolol (A) increases the GH response to iv GHRH in normal men as previously reported from this laboratory. This study was designed to determine (1) if A would enhance GH release in GHRH-deficient patients receiving GHRH therapy and (2) if A would increase GH secretion in boys with constitutional delay of growth (CDG). Two children with idiopathic GHRH deficiency were studied from 2000 to 0800h prior to and while receiving long term GHRH subcutaneously every 3h. Blood was withdrawn every 20 min for GH determination. This test was repeated on the following day both before and while receiving GHRH except A, 25 mg, was given orally at 1030 and 1600h. GH secretion was increased by A before (1948 to 3124 and 718 to 1157 ng/ml min) and during (1460 to 3628 and 1363 to 6386 ng/ml min) GHRH therapy. Six healthy boys ages 7 to 15 y with CDG had BAB with A. Each had a significant increase in the peak GH release to GHRH (55.2 ± 13.5 vs 87.7 ± 19.0 ng/ml, $p<0.01$) and in the area under the GH vs time curve (3916 ± 701 vs 5624 ± 986 ng/ml min, $p<0.01$) following A. However, BAB with A failed to enhance the endogenous (12h nocturnal) GH secretion (5597 ± 637 vs 4168 ± 475 ng/ml min, $p=0.125$) suggesting that A may not be appropriate to promote growth in boys with CDG in contrast to those with GHRH deficiency.