456 PROLACTIN RESPONSES TO THYROTROPIN RELEASING HORMONE IN DISORDERS OF SEXUAL DEVELOPMENT. Thomas Moshang, Jr., Barry Marx, Peter Snyder, University of Pa. School of Medicine, The Children's Hospital of Philadelphia, Department of Pediatrics, Philadelphia.

Spitz et al recently suggested that adult men with hypothalamic hypogonadism (HH) can be distinguished from children with constitutional delay of growth and development (CD) by the significantly lower prolactin (Prl) responses to thyrotropin releasing hormone (TRH) in the HH patients. These investigators attributed the diminished Prl responses to the absence of estradiol. The latter hypothesis was tested by evaluating Prl responses to TRH in Turner Syndrome patients. Prl responses to TRH in other disorders of sexual development were also evaluated and compared to the Prl responses in normal children and adolescents.

	Basal Prl(ng/ml) mean ± SEM	Peak Prl(ng/ml) Mean ± SEM	Statistical Significance
Normals	12.6 ± 3.9	52 ± 8.09	NS
CD	7.6 ± 2.04	44.6 ± 7.3	NS
Turner Syn.	20.4 ± 6.7	99.8 ± 17.0	$p<0.025$
HH	14.9 ± 1.61	31.2 ± 8.5	$p<0.05$
Prec.Puberty	11.6 ± 2.69	90.2 ± 8.5	$p<0.001$

Our findings indicate that although patients with HH tested during adolescence have significantly lower Prl responses to TRH, the overlap of values between patients and normal children was considerable and, on an individual basis, not nearly as distinguishable as the data reported for adult men. The exaggerated Prl responses to TRH in Turner Syndrome and in precocious puberty suggest that the pituitary lactotrophs may be sensitized by GnRH rather than estradiol.

457 PULSATILE GROWTH HORMONE SECRETION IS INCREASED DURING FAILURE OF CATCH-UP GROWTH. H. David Mosier, Regina A. Jansons, and Cynthia B. Good, University of California, Irvine, Department of Pediatrics, Irvine, California.

The role of growth hormone (GH) in catch-up growth is unknown. However, pulsatile secretion of GH is increased in rats undergoing catch-up growth after fasting. We now report the pattern of GH secretion in a rat model characterized by failure of catch-up growth. Male Long-Evans rats were injected with cortisone acetate s.c. (n=7) 5 mg/d for 4 d or the same volume of saline for controls (N=7) from 40 d of age. During recovery, the rats resumed a normal rate of growth without catch-up growth acceleration. During 17 to 31 d of recovery plasma was sampled at 15 min. intervals from a 21 h lights-on period. The rats were chronically cannulated and isolated from environmental disturbance. There were 10 sampling periods with repeats in 2 control and 3 treated rats at intervals of 5 days or greater. The cortisone rats showed normal cycles of pulsatile GH release but they had an increased number of GH peaks above 100 ng/ml ($p<0.005$), above 200 ng/ml ($p<0.005$), above 500 ng/ml ($p<0.01$) and above 100 ng/ml ($p<0.05$). The area under the GH concentration curve of the treated rats was greater than that of the controls, 94.5±13.7 (mean ± SE) area units vs 54.5±5.3 ($p<0.01$). Regression analysis showed lack of dependence of area under the curve on age in both groups. We conclude 1) that increased GH secretion persisted in spite of failure of catch-up growth and 2) that the control GH release is linked to a mechanism which senses the discrepancy between actual body size and a reference point in the organism (set-point) for normal size for age.

458 FAMILIAL PERSISTENT THYROID STIMULATING HORMONE ELEVATION. Michael L. Netzloff. Michigan State University College of Human Medicine, Department of Pediatrics/Human Development, East Lansing, MI.

Three affected members of a family with persistent TSH elevation, ages 2 1/12, 3 3/12 and 5 9/12 years were assessed at 9:00 a.m. for other pituitary tropic hormones and for their response to thyrotropin releasing hormone (TRH). The two younger brothers had been off thyroid medication for over one year, and their older sister had never received thyroid. TRH was given IV at 7 mcg/kg, and TSH measured at times 0 and +30 and +60 minutes. Growth hormone, ACTH, LH and FSH were also measured at time 0 and prolactins measured following TRH.

Patient Age Years	GH ng/ml	ACTH pg/ml	FSH mIu/ml	LH	Prolactin ng/ml	TSH/TRH µIU/ml Time 0	30	60
2 1/12	11	33	2.5	16	49	55	180	162
3 3/12	8.3	20	2.5	13	–	71	255	268
5 9/12	1.3	26	2.5	11	35	25	115	52

The baseline TSH's and responses to TRH suggest primary hypothyroidism, but the T-4's are all normal; e.g. 8.4, 9.6 and 8.4 µg/dl (free T-4 = 1.2 ng/dl), and bone ages and height ages are normal. In addition, all three children studied have elevated LH's, which do not appear functional, since none have signs of precocious puberty. The TSH elevation in this family may be functional: A 23 year old affected member of the pedigree recently had a thyroid follicular adenoma removed. Because chronic TSH stimulation may result in thyroid carcinoma, all affected persons have been placed on exogenous thyroid medication.

459 ABSENCE OF NEUROPSYCHOLOGIC PROBLEMS IN HYPOTHYROID CHILDREN DIAGNOSED BY NEONATAL SCREENING-New England Congenital Hypothyroidism Collaborative We have reported that hypothyroid children diagnosed by neonatal screening have normal Stanford-Binet IQs at ages three to five years. Reports in the literature indicate that hypothyroid children even,with normal IQs, have neuropsycholoqic handicaps and do poorly in school. Because of this, several of our patients have been assigned to "slow learner" classes on entering schoolsolely on the basis of their known hypothyroidism despite their normal IQs. To counteract this bias and obviate the danger of low expectations by teachers, we are reporting preliminary results of WISC-R examinations and the Halstead-Reitan battery of neuropsychologic tests at 6 years of age and of standard achievement tests taken at the end of the first grade in school in our patients and control subjects. The mean WISCscores of 30 hypothyroid patients did not differ from that of the 40 euthyroid sibling controls ($109^{+}15$ vs. $108^{+}14$). There were also no significant differences between scores of the patients and controls on the neuropsychologic tests and school achievement tests. The percentage of scores that deviated by more than two standard deviations from the control mean of individual test items was less than the expected 2.3% for both patients and controls. The number os such deviant results correlated inversely with IQ in both patients and control subjects. Thus, we have been unable to document neuropsychologic deficits or school problems in hypothyroid children with normal IQs. We, therefore, urge that such children be treated similarly to the general population of students.

●460 **PITFALLS OF PRENATAL DIAGNOSIS OF 21-HYDROXYLASE DEFICIENCY CONGENITAL ADRENAL HYPERPLASIA (CAH).** S Pang, M Loo, MS Pollack, B Dupont, O Green, G Clayton, MI New. New York Hosp-Cornell Med Ctr, Memorial Sloan-Kettering Cancer Ctr, New York, NY 10021; Children's Mem Hosp, Chicago, IL 60614; Baylor Univ Col Med, Houston, TX

Hormonal measurements and HLA genotyping, of amniotic fluid at midgestation correctly predicted the postnatal dx of CAH in 26 of 29 fetuses at risk for CAH. Of these 26, 6 were predicted to have classical 21-hydroxylase deficiency (21-OH def) based on elevated amniotic fluid 17-hydroxyprogesterone (17-P) and Δ4-androstenedione (A). These 6 fetuses and their index cases were ultimately proven to have salt-wasting classical 21-OH def. Of 3 HLA typed, genotype was identical to the index case. Normal amniotic fluid 17-P and A in the remaining 20 predicted fetuses unaffected with classical CAH, and these patients have been clinically asymptomatic to date or biochemically proven not to be affected with classical or nonclassical CAH. Of the 20 fetuses, 6 were HLA genotyped and predicted to be homozygous unaffected or heterozygous. However, in 3 of the 29 fetuses, prenatal diagnosis was incorrect. In one, the fetus was predicted to have CAH based on HLA identity to the index case. However, amniotic fluid 17-P and A were normal and the fetus was normal. The index case of this family did not have CAH but was a normal child. Thus, amniotic fluid hormone levels accurately predicted a normal fetus while HLA genotyping was not relevant in prenatal dx because the index case was unaffected. The second fetus was predicted to be a carrier on the basis of HLA genotyping and normal amniotic fluid 17-P and A. However, during infancy the female infant was shown to have nonclassical CAH and to be HLA identical to the index case. The index case in this family, presumed to have classical CAH, was later diagnosed to have nonclassical CAH. Thus, in nonclassical CAH, hormonal measurement of 17-P and A is not useful in prenatal dx; only correct HLA genotyping of the fetus is valuable. In the third case, the fetus was predicted to be a heterozygote by HLA genotyping and to be unaffected by hormonal measurement. Postnatally, at age 2 7/12 yrs, the male child was shown to have non-salt-losing classical CAH and was shown to be HLA identical to his brother (index case) who also has non-salt-losing CAH. CONCLUSION: These data demonstrate that in salt-losing classical CAH, prenatal dx of the homozygous affected fetus is reliable by the measurement of amniotic fluid 17-P and A. In nonclassical or non-salt-losing classical CAH, amniotic fluid 17-P and A are in the normal range, thus prenatal dx is not possible by hormonal evaluation. Both hormonal and HLA studies of fetal amniotic fluid, as well as correct dx of the specific form of 21-OH def and HLA studies of the index case, are essential in diagnosing the specific form of 21-OH def CAH in the fetus.

461 GROWTH HORMONE RELEASING FACTOR GENE STRUCTURE IN GROWTH HORMONE DEFICIENCY. John S. Parks, Laura C. Sexton, Edwin F. Slott, Jr., Richard L. Mallonee and John A. Phillips, III. Emory University, Department of Pediatrics, Atlanta and Johns Hopkins University, Department of Pediatrics, Baltimore.

We have used a cDNA probe for human pancreas growth hormone releasing factor (GRF) to characterize GRF genes in DNA from normals and children with autosomal recesssive isolated growth hormone deficiency (IGHD) IB or multiple pituitary hormone deficiency (MPHD). Pvu II, which recognizes sites in the middle of both GRF cDNA sequences, generated 4 hybridizing fragments of similar intensity with lengths of 8.5, 4.5, 3.2 and 2.7 kb. The patterns produced by Pvu II in combination with 7 other enzymes were also inconsistent with a single GRF gene less than 6 kb in length and suggested 2 or more non-allelic GRF genes per haploid genome. In a search for genetic linkage markers, we digested DNA specimens representing 17 to 104 sets of normal chromosomes with 15 endonucleases which collectively screen for variation in a minimum of 280 base pairs. No variation in GRF fragment length or number was detected. Affected individuals in 5 pedigrees with IGHD IB and 3 pedigrees with MPHD did not show gross abnormalities of GRF gene fragments. We conclude that deletion of GRF genes is not a common genetic mechanism in these familial disorders. Identification of polymorphic variation in or near the GRF genes will be needed to determine whether these forms of GH deficiency are due to subtle alterations in GRF genes.