● **480** HYPOTHYROIDISM BLUNTS THE GROWTH HORMONE (GH) RELEASING EFFECT OF HUMAN PANCREATIC GROWTH HORMONE-RELEASING FACTOR (hpGRF) IN THE ADULT MALE RAT. Jennifer L. Root, Gregory E. Duckett, Margaret Sweetland, Jack A. Strzelecki and Allen W. Root. University of South Florida College of Medicine, Department of Pediatrics, All Children's Hospital, St.Petersburg, Florida

The 44 amino acid peptide hpGRF (Bachem) was administered to 300 gram male control or hypothyroid rats under pentobarbital anesthesia. In euthyroid animals (T4=5.0±1.9(SD) ug/dl), intravenous bolus injection of 1.0 ug of hpGRF (N=4) increased serum concentrations of rat GH from 157±95 to a peak of 1871±1458 ng/ml ($p<0.01$ vs base) within 5-10 minutes. At a dosage of 10 ug (N=5) hpGRF increased rGH levels in control animals from 213±95 to a peak of 3123±923 ng/ml ($p<0.01$ vs base) in 5-15 minutes. In rats rendered hypothyroid by the ingestion of 0.05% propylthiouracil in drinking water for 21 days (T4-0.6±0.1 ug/dl, $p<0.01$ vs control) 1.0 ug of hpGRF (N=8) increased rGH concentrations from 39±24 to a peak of 79±37 ng/ml ($p<0.01$ vs base) in 5-30 minutes, while 10 ug of hpGRF (N=7) increased rGH values from 42±26 to a peak of 99±47 ng/ml ($p<0.01$ vs base) in 5 to 15 minutes. Basl and post hpGRF rGH concentrations were significantly ($p<0.01$) higher in control than in hypothyroid animals. We conclude that primary hypothyroidism blunts the GH-releasing effect of hpGRF in male rats in vivo.

481 **THE EFFECT OF HYPOGLYCEMIC CONVULSIONS ON COGNITIVE DEVELOPMENT IN YOUNG DIABETICS.** **Joanne F. Rovet, Robert M. Ehrlich, Marla S. Gore, Departments of Pediatrics and Psychology, The Hospital for Sick Children, University of Toronto, Toronto.**

Twenty-seven children with early onset (<3 years) diabetes (EOD), 24 with late onset (>4 years) diabetes (LOD), and 30 sibling controls were compared in their performance on tests of intellectual functioning and school achievement. The results revealed that EOD subjects, primarily EOD girls, scored significantly ($p<.05$) lower on tests of visuo-spatial but not verbal ability. There were more EOD girls having difficulty at school and receiving special education (38.5%) than were children in the other groups (11.2%). Examination of the diabetic control factors showed that EOD had more hypoglycemic convulsions than LOD ($p<.05$) and that this was higher for girls than boys. HBA_1 levels at the time of cognitive testing were also higher for females (11.7%) than males (10.5%, $p<.05$) and girls were more likely than boys to have had ketoacidosis after the onset of IDDM (32% vs 12%, $p<.05$). A regression analysis indicated that hypoglycemic convulsions before the age of three was a significant predictor of spatial task performance, stronger than parental IQ.

Conclusions. **Hypoglycemic convulsions under age 3 affects cognitive development in diabetics. Girls appear particularly susceptible. These findings are important when setting levels of metabolic control for young diabetics.**

482 RADIATION INDUCED PITUITARY FAILURE IN CHILDREN WITH MEDULLOBLASTOMA. Abdollah Sadeghi-Nejad and Olumbunmi Abayomi. Departments of Pediatrics and Therapeutic Radiology, Tufts University School of Medicine, New England Medical Center, Boston.

Medulloblastoma is a relatively common intracranial tumor in children. We report the retrospective analysis of the treatment results in 20 patients (11 males and 9 females, age range 2-19 years) with medulloblastoma who were referred consecutively to our Department of Therapeutic Radiology between 1969 and 1977. At surgery 17 patients had tumor grossly confined to the cerebellum, three had extension to the spine. Sixteen of 17 patients had greater than 90 per cent resection of the tumor. The three with spinal extension only had incisional biopsy. All received 3,600 rads to the whole brain, an additional 2,600 rads to the posterior fossa and 3,000 rads to the spinal column.

Eight females and 3 males (55%) were alive 5-12 years after diagnosis. Ten of the 11 survivors were short or had diminished growth rate. Six ot the 7 tested had growth hormone deficiency. Adrenal response to insulin-induced hypoglycemia was normal in 5 of the six patients tested. All three post-pubertal girls had amenorrhea; one also had galactorrhea and ACTH deficiency. Seven patients had normal thyroid function tests; four were not tested. Posterior pituitary function was intact in all.

Children with medulloblastoma are frequently followed only by radiotherapists. Endocrine gland failure is a common, but often undetected, late sequallae of therapy in these patients. We emphasize that early recognition and therapy can contribute significantly to the well being of these children.

483 PREVALENCE OF GROWTH HORMONE DEFICIENCY IN CHILDREN WITH CLEFT LIP/PALATE (CLP). Abdollah Sadeghi-Nejad, Julia Lockwood, and Hermine M. Pashayan. Department of Pediatrics, Tufts University School of Medicine, New England Medical Center, Boston.

The prevalence of growth hormone (GH) deficiency in the general population is about one in 3,000-4,000 or one per cent in children who are below the third percentile for height. Rudman et al reported a prevalence of 32% in short children with CLP (J Pediatrics 93:378, 1978). The criterion used was an average peak concentration of GH. Since this reported prevalence is strikingly high, we examined the records of 373 children who were on the active files of our CLP Clinic.

Of these, 40 patients with overt CLP (21 CL&CP, 18 CP, 1 CL) were at or below the 5th percentile for height. In this group of 40, 12 had multiple congenital anomalies or clearly defined syndromes. Fourteen had familial short stature and were growing at a normal rate for height. Of the remaining 14 children (8 boys, 6 girls, mean age 6.2 years) two were lost to follow up and two refused endocrine evaluation. None of the remaining 10 had growth hormone deficiency.

Using the standard criteria of impaired growth rate and lack of response to arginine-insulin provocative test (peak less than 5 ng/ml) we were unable to document that a single patient in this group had GH deficiency. Clearly our findings are discordant with those reported by Rudman et al. A possible reason may be that different criteria were used for diagnosing GH deficiency.

† **484** EFFECT OF HYPOTHYROIDISM (HP) AND HYPERTHYROIDISM (HT) ON ^{125}I-EPIDERMAL GROWTH FACTOR(EGF) SPECIFIC BINDING(S.B.) TO NEWBORN(NB) LUNG(L) AND BRAIN (B) PLASMA MEMBRANE(PM) F.Sadiq, S.Devaskar, V.Chechani, S.Harris and U.Devaskar (Spon. W.J.Keenan) Dept. of Peds., St. Louis University School of Medicine, St. Louis, Missouri

Receptor mediated role of EGF in fetal/neonatal L development and stimulating multiplication of B glial cells is well established. T_4 enhances L maturation and CNS myelination. EGF receptor and T_4 interactions were explored by examining the effect of HP and HT on S.B. of ^{125}I-EGF to NB (<24 hours) rabbit LPM and BPM. NB were made HP by administering .05% PTU in drinking water at 24d of pregnancy. HT was achieved by administering 100ug/kg (I.M.) of T_4 to the doe on 29th and 30th d. of gestation. LPM and BPM were isolated and characterized by protein % recovery, DNA and 5'-nucleotidase assay. S.B. of ^{125}I-EGF to LPM or BPM was assessed at 37°C, pH 7.45 after 75' of incubation. (ANOVA, *$p<.01$)

	Free T_4 (ng/dl)	mg prot. gm. B.	% S.B. .2mg BPM Prot.	mg.prot. gm. L.	% S.B. .1mg LPM prot.
HP (n=5)	$\bar{X}$±*<.08 SEM	55±5	*.625±.07	48±7	2.01±0.5
Control (n=4)	.34±.05	57±7	1.06±.013	44±4	2.24±.28
HT (n=3)	*1.86±.20	64±1	*1.71±.04	37±2	2.26±.13

From these preliminary results we suggest that T_4 status of the 1d. NB may influence the development of B but not L EGF R.

485 EFFECTS OF NALOXONE AND CLONIDINE ON GONADOTROPIN SECRETION IN EARLY PUBERTAL BOYS. S.E. Sauder, R.P. Kelch, N.J. Hopwood, I.Z. Beitins, and J.C. Marshall, Univ. of Michigan, Dept. of Ped. and Int. Med., Ann Arbor, MI.

To investigate mechanisms of neuroendocrine regulation of gonadotropin secretion during puberty, we studied 3 early pubertal boys with delayed adolescence (range: CA 13 7/12 - 17 2/12; BA 11 6/12 - 13 6/12 yrs) by: 1) antagonism of endogenous opiates (naloxone); and 2) α-adrenergic stimulation (clonidine). From 2000h to 0800h on two consecutive study days, blood was obtained every 20 min for plasma LH (mIU/ml) while patients A and B received i.v. infusions of saline or naloxone (1 mg/m^2/hr). On Day 3, testosterone (T) enanthate (A=75 mg/m^2, B=50 mg/m^2) was administered i.m. The protocol was repeated 1 week later when $\bar{x}$ plasma T was 9.9 and 8.8 ng/ml in A & B, respectively. Results are shown below (A/B, $\bar{x}$ ± SE).

	$\bar{x}$ LH	# pulses	$\bar{x}$ pulse amp
saline	7.4 ± 0.5/5.2 ± 0.4	7/8	4.2 ± 0.6/3.0 ± 0.6
naloxone	6.1 ± 0.3/5.9 ± 0.4	8/10	2.6 ± 0.5/2.6 ± 0.4
saline $\bar{p}$ T	2.0 ± 0.1/0.9 ± 0.1	2/3	1.0 ± 0.1/0.9 ± 0.1
naloxone $\bar{p}$ T	2.5 ± 0.1/0.9 ± 0.1	5/1	1.2 ± 0.2/0.8

In patient C, plasma gonadotropins were measured q20 min for 36h before and 24h after clonidine, 0.15 mg p.o. A significant increase ($p<.01$) in mean LH was first apparent 5h after clonidine and persisted for at least 19h (LH $\bar{x}$ ± SE: control day/night 1.7 ± 0.1/5.1 ± 0.2; clonidine day/night 3.3 ± 0.2/6.3 ± 0.3). These studies suggest the following: 1) endogenous opiates do not influence nocturnal LH secretion in early pubertal boys before or after short term exposure to adult male range concentrations of T and 2) increasing α-adrenergic tone may be important for augmentation of LH secretion during puberty.