428 HLA-DR PHENOTYPES IN CHILDREN WITH AUTOIMMUNE THYROIDITIS (AIT). Maria Buithieu, William J. Riley and Noel K. Maclaren. University of Florida, Depts. of Pediatrics and Pathology, Gainesville, FL.

Previous studies in AIT looking for an association with the immune response genes in the HLA region have had conflicting findings. We studied 41 patients (33 females and 8 males) who had presented before the age of 21 with + thyroid microsomal antibodies (TMA), goiter and/or hypothyroidism without other endocrine disorders. The mean age of onset was similar in both sexes (11.72 vs 11.40 yrs respectively). Goiter was present at onset in 75%. All were studied for TMA by indirect immunofluorescence and for HLA-DR phenotypes. TMA were present in 64.1%. There was an increase in the frequency of HLA-DR3 (NS) and 4 ($p \approx 0.05$) and decrease of HLA-DR2 (NS) in the patients with AIT compared to 467 controls (C). The relative risk with HLA-DR 3 was 1.80 and, with HLA-DR 4, 1.99. The preventive fraction for HLA-DR 2 was 0.15. The frequency of DR phenotypes was similar between goitrous and non-goitrous AIT. Previous studies and our study in these families suggested that the genetic predisposition to AIT was not linked to the HLA region. The association to certain HLA-DR alleles suggests that these HLA-DR genes enhance the clinical expression of AIT at an early age. On the other hand, these patients with the HLA-DR 3 and/or 4 may represent a subgroup at higher risk for developing other endocrine autoimmune diseases associated with HLA-DR 3 or 4.

DR	C	AIT
1	20.6%	19.5%
2	28.9	17.1
3	22.1	34.1
4	30.2	46.3
5	20.8	17.0
6	22.9	26.8
7	26.8	21.9
8	7.3	4.9
9	0.6	0.0
10	1.9	12.2

▲429 INSULIN-LIKE GROWTH FACTOR-I (IGF-I) POTENTIATES LH-INDUCED STIMULATION OF ANDROGEN SYNTHESIS BY RAT OVARIAN THECA-INTERSTITIAL (TI) CELLS. Jose' F. Cara and Robert L. Rosenfield. Spon. by L. Levitsky. Pritzker Sch. Med., U. Chicago, Dept. Ped., Chicago.

We tested the hypothesis that IGF-I plays a role in ovarian TI cell cytodifferentiation.

Dispersed TI cells obtained from 21 day old hypox Sprague Dawley rats were cultured in serum-free medium in the absence and presence of increasing concentrations of LH, IGF-I or a combination of these hormones. The culture medium was changed every 48 hours and the androsterone (andro) concentration in the culture supernates, determined by RIA, was used as an index of TI cell differentiation.

In the absence of LH or IGF-I, TI cells produced less than 0.1 ng/ml of andro. In the presence of 0.1, 10, and 50 ng/ml of LH, andro synthesis increased progressively to peak levels of 0.4, 0.85 and 1.35 ng/ml, respectively. IGF-I alone did not increase andro synthesis above control values. However, 1, 10 and 100 ng/ml of IGF-I potentiated the andro response induced by 10 ng/ml of LH to peak levels of 32±11, 220±115, and 435±65 ng/ml (mean±SEM), respectively. Peak andro levels were obtained between 48 and 96 hours of culture. Andro synthesis subsequently decreased, probably because of substrate depletion.

These results suggest that IGF-I plays a role in LH-induced differentiation of normal ovarian TI cells.

●430 HUMAN GROWTH HORMONE ADMINISTRATION INCREASES PLASMA OSTEOLCALCIN CONCENTRATIONS IN GROWTH HORMONE DEFICIENCY. Salvador Castells, Kenneth Rebong, Fenella Greig, Seiichi Yasumura, Sam Smith. SUNY Health Science Center at Brooklyn, N.Y., Depts. of Pediatrics and Physiology.

We investigated plasma osteocalcin levels before and during treatment with human growth hormone (GH) in 4 patients (pts.) with GH deficiency. GH deficiency was defined by increase in serum GH<10 ng/dl after stimulation with Insulin and L-Dopa and/or 24 hr. integrated GH<3.2 ng/dl. All 4 pts. had low bone density measured by radiographic photodensitometry as compared to normals for age and sex. All 4 pts. were treated with a new GH produced by recombinant DNA and chemically identical to human GH at the dose of 0.1 mg/Kg every other day for 6 months. Plasma osteocalcin was determined by RIA.

		Osteocalcin (ng/ml) (mean±SD)			
		Before	During HG treatment		
			1 wk	4 wk	8 wk
Normal	(21)	24.4±12.5			
Pts.	(4)	13.0±6.8	94.2±34.9	121.3±9.1	74.5±13.8
p<			.003	.001	.001

These data show that patients with GH deficiency have low bone density and low plasma osteocalcin levels. Treatment with GH increases bone density and plasma levels of osteocalcin. The GH induced increased in circulating osteocalcin suggests stimulation of new bone formation and mineralization by GH.

431 FAILURE OF CLONIDINE TO IMPROVE THE GROWTH HORMONE RESPONSE TO L-DOPA ADMINISTRATION. Mariano Castro-Magaña, Moris Angulo, Billy Fuentes, Atilio Cañas and Amanda Sharp. (Spon. by P. J. Collipp). Nassau Cty Med Ctr, SUNY, Stony Brook Health Sci Ctr, Dept of Peds., E. Meadow, NY 11554.

We have previously shown that oral administration of clonidine (C) during one year period increases plasma somatomedin C (SM-C) levels, growth velocity and growth hormone (GH) response to C in prepubertal short children. We have now studied the effect of chronic administration of C on SM-C level and GH response to L-Dopa (DA) administration in three short children (aged 13.8 ± 1.8 yrs) with blunted GH response to DA administration but normal GH response to insulin-induced hypoglycemia and C.

C was administered orally in a single dose (0.15 mg/m^2/body surface area) daily at night during a 3-month period. The GH response to DA (250 mg) administration was determined before and one week after the treatment with C was terminated.

	GH Response to DA Administration			SM-C (U/nl)
Time(Min)	0	60	90	
Before C (GH ng/ml ± SD)	1.5 ± 0.6	4.4 ± 2.4	2.8 ± 1.4	0.62 ± 0.18
After C (GH ng/ml ± SD)	1.7 ± 0.4	5.1 ± 1.8	2.2 ± 1.7	1.8 ± 0.32
"P" Value	NS	NS	NS	0.001

Our results suggest that the increase in SM-C levels seen after long term administration is not mediated by Dopaminergic pathway.

432 THE ROLE OF CARBOHYDRATE IN THE ASSOCIATION OF HCG SUBUNITS. Christopher C. Chang*, David C. H. Yang, Judith H. Brown and Hao Chia Chen. (Spon. by Gertrude Costin). Children's Hospital of Los Angeles, CA, Georgetown University Department of Chemistry, Washington, DC and NICHD, Bethesda, MD.

The significant fluorescence enhancement of 1-anilinonaphthyl-8-sulfonate when bound to an intact hCG, but not to its individual subunits provides a sensitive and effective method to monitor the dissociation-association of the hCG subunits. In an attempt to study the role of carbohydrate in the association of the subunits, deglycosylated hCG subunits were prepared by treatment with anhydrous HF-anisole then by incubation of hCG with 6M guanidine-HCl and separation by a gel permeation HPLC in 0.1 M NH_4OAc-HOAc, pH 4.0. The subunits of deglycosylated hCG reassociated ten-fold faster than those of unmodified subunits. Studies on the reassociation of modified and unmodified subunits revealed that the deglycosylated α-subunit reassociated with either intact or deglycosylated β-subunit at a rate significantly faster than the intact α-subunit with intact or deglycosylated β-subunit. These results have demonstrated that carbohydrate moieties in the α-subunit dominate the reassociation behavior of hCG. Since hCG is implicated in precocious puberty, the elucidation of the functional properties of the two subunits of hCG and a potent antagonist like its deglycosylated derivative may offer promising alternatives in the treatment of this disorder.

▲433 EPIDERMAL GROWTH FACTOR ACUTELY REDUCES SOMATOMEDIN-C/INSULIN-LIKE GROWTH FACTOR-I IN THE NEONATAL RAT. S.D. Chernausek, H.T. Hensgen, S.B. Hoath (Spons. by Mark A. Sperling). Department of Pediatrics, Children's Hospital Medical Center, Cincinnati.

Epidermal growth factor (EGF) administration to very young animals causes growth retardation as well as precocious tooth eruption and eyelid opening. We previously demonstrated that EGF's ability to retard growth in the rat is confined to the first 2 weeks of life and is more pronounced in the immediate postnatal period (days 1-3). To investigate a possible mechanism through which EGF might alter somatic growth, we measured circulating concentrations of immunoreactive somatomedin-C/insulin-like growth factor-I (Sm-C) 4 hours after a single injection of EGF. Rats (aged 1, 8, and 15 days) were given 500 ng/g bw EGF and the Sm-C concentration measured after high pressure liquid chromatography of acidified sera.

Sm-C/IGF-I (U/ml ± SD) After EGF Treatment

Age	1D	8D	15D
EGF	< 0.40*	0.58 ± 0.17*	0.93 ± 0.23
Control	0.70 ± 0.17	0.82 ± 0.12	1.10 ± 0.34

*$p < 0.05$ compared to controls n = 5 for each group

The results show that exogenous EGF acutely reduces circulating Sm-C levels at the ages where it also exerts its growth attenuating effect (days 1 and 8) but not at 15 days of age, when the rat is insensitive to the growth-retarding property of EGF. These results are consistent with the hypothesis that EGF, at this stage of development, promotes differentiation at the expense of growth by altering production or secretion of Sm-C.