● 464

NEUROENDOCRINE CHANGES WITH D His GnRH ANALOGUE (D-His-A) T.M. Mendes, C.M. Foster, N.J. Hopwood, I.Z. Beitins, R.P. Kelch, University of Michigan, Department of Pediatrics, Ann Arbor, Michigan.

To correlate neuroendocrine changes with clinical response, 4 girls (4-7 yrs) and 1 boy age 6 with central precocious puberty were treated with D-His-A subcutaneously. D-His-A was given at a dose of 4 µg/kg/day for 4 mos; then, the dose was increased to 8 µg/kg/day. The children were serially studied at 0, 3, and 6 mos. Blood was analyzed for GH, LH, FSH q 20 min (1800-0600). GnRH (2.5 µg/kg IV) tests and response to D-His-A (usual treatment dose sc) were followed. Gonadal steroids fell to prepubertal range in the first 3 mos. Results of mean growth velocity (GV), GH, Somatomedin C, LH and FSH, GnRH and D-His-A Tests are shown:

	Pretherapy	3 mos.	6 mos.	
GV (annualized)	9.4	10.4	8.9	cm/yr
GH (mean)	6.4	4.2	4.5	ng/ml
Somatomedin C	323	210	163	ng/ml
LH (mean)	7.1	5.3	2.6	mIU/ml
FSH (mean)	7.6	2.5	1.4	mIU/ml
GnRH (Δ max LH)	63	1.2	0.7	mIU/ml
D-His-A (Δ max LH)	-	5.5	1.5	mIU/ml

Bone age advanced 6 mos/6 mos therapy. We conclude D-His-A at 4 µg/kg/day for 3 mos did not decrease growth velocities despite decreases in mean overnight GH, Somatomedin C and gonadal steroids. Mean overnight LH and FSH values showed stepwise decrease with higher doses of D-His-A. We suggest that children with D-His-A need a minimum of 8 µg/kg/day and that D-His-A response should be used to evaluate therapy rather than GnRH tests.

● 465

ACTH RECEPTOR DEFECT IN ADRENOLEUKODYSTROPHY (ALD). Walter J. Meyer, III, Eric M. Smith, Gail E. Richards, Nancy G. Greger, Patrick G. Brosnan, Bruce S. Keenan, University of Texas Medical Branch, Depts. of Psychiatry and Pediatrics, Galveston, Texas.

ACTH insensitivity is a cardinal feature of ALD, but the mechanism is unknown. We studied a 10 year old hyperpigmented boy with glucocorticoid insufficiency of 8 years duration and a history of two generalized tonic clonic seizures associated with febrile episodes with normal blood glucose. His neurological exam was normal, EEG showed non-specific slowing with normal auditory evoked responses, and Magnetic Resonance Imaging showed areas of increased signal intensity in the cerebral peduncles and the internal capsule. ALD was documented by increased plasma very long chain fatty acids, i.e., C26/C22 = 0.055 (control = 0.01 ± 0.01); C26= 1.572 µg/ml (control = 0.33 ± 0.18 µg/ml). Basal ACTH was elevated at 1840 pg/ml (normal = <100 pg/ml). Cortisol was 7.0 µg/dl with no response to exogenous ACTH. Basal and stimulated renin and aldosterone were normal. The child's leukocytes had no detectable ACTH binding sites in a radioligand binding study. In contrast, normal mononuclear leukocytes possess high and low affinity receptors for ACTH that appear identical to the prototype adrenal receptors. These studies suggest that the adrenal failure associated with ALD is secondary to an ACTH receptor defect. Whether the ACTH receptor defect is primary or secondary to the long chain lipid abnormality is under investigation.

466

ISOLATED GROWTH HORMONE DEFICIENCY IN ASSOCIATION WITH HUMAN IMMUNODEFICIENCY VIRUS (HIV) INFECTION. John D. Miller and John A. Zaia, City of Hope National Medical Center, Division of Pediatrics, Duarte, CA 91010.

Growth failure has been observed in children with the acquired immunodeficiency syndrome (AIDS), but the growth pattern in asymptomatic HIV-infection or in AIDS-related complex (ARC) is unknown. We report a 6 10/12 year old female with congenital HIV infection and a 2 year history of growth failure. Her father was a member of a major risk group and died of AIDS. The child and her mother are HIV antibody-positive by both ELISA and Western blot assays, but neither have had severe infections nor qualify for the diagnosis of AIDS. Based on her declining T4 cell numbers (current absolute T4 cell number = 33/ul), and persistent splenomegaly, this patient is considered to have ARC. Endocrine evaluation: Her peak growth hormone response to arginine was 1.2 ng/ml and to insulin (glucose = 35 mg/dl) was 2.6 ng/ml; cortisol peak = 27 ug/dl with hypoglycemia; TSH = 5.4 uU/ml; T4 = 10.5 ug/dl; IGF-I = 0.2 u/ml; bone age = 5 6/12 yr; sella and suprasellar areas are normal by MRI scan. Her growth velocity and immune function on methionyl human growth hormone are currently being determined.

The etiology of this child's growth hormone deficiency is presumed to be secondary to congenital HIV infection with late onset of pituitary or hypothalamic failure. Recognition of this syndrome will undoubtedly become importat in the diagnosis and management of pediatric HIV infection.

467

LUPRON TREATMENT OF PRECOCIOUS PUBERTY (CPP) HAS NOT PRODUCED LOSS OF BONE MINERAL. George W. Moll, Jr., Delwood C. Collins and Gordon DePuey (Spon. by John S. Parks). Emory University School of Medicine, Henrietta Egleston Hospital, Departments of Pediatrics, Medicine and Radiology, Atlanta, Georgia.

We tested the hypothesis that GnRH agonist treatment of CPP is associated with loss of bone mineral density (BMD) and content (BMC) after young women treated with GnRH agonists were reported to lose up to 6% BMD in the first treatment year similar to that seen during menopause. We determined lumbar spine (L1-L4) BMD (g/cm^2) and BMC (g) by dual photon absorptiometry and measured growth parameters and blood Ca (mg/dl), alk. phos. (AP,mU/ml) and integrated growth hormone (GH, ng/ml) on CPP patients before and after (3 of our 6 patients to date) six months treatment with the GnRH agonist LUPRON (TAP Pharm., 4-8 ug/kg SC qD). Our patients (3 girls 5-8 yr, 9-10 yr bone age [BA]; 3 boys 3-8 yr, 7-10 yr BA) were Stage 3-4 upon entering the study with informed consent.

	Before LUPRON						After 6 Months LUPRON					
F/M	VorT*	BMD	BMC	Ca	AP	GH	VorT*	BMD	BMC	Ca	AP	GH
F	98	.790	20.0	9.8	310	126	64	.888	26.4	9.3	279	205
F	78	.777	21.0	10.1	264	151	57	.917	26.9	9.0	215	372
M	400	.705	19.2	10.0	213	32	35	.746	18.8	9.8	148	86

*V = Vaginal Index. T = Total Testosterone (ng/dl).

All 6 had similar basal BMD (.724±.05,SEM). Despite reduction of V or T toward prepubertal levels, growth rates and BMC did not decline and GH and BMD increased while Ca and AP decreased.

We conclude that early, partial suppression of CPP with LUPRON is not associated with loss of BMD or BMC. Followup with further suppression of CPP should help to distinguish between variable time courses of end organ responses or therapeutic selectivity.

468

ABORTED PUBERTY:A NEW CLINICAL ENTITY Richard A Noto, Yasmin A Hassan, Maureen Rosati, Mary Ellen Crossan, Vinod LaLa(Spon by Lawrence R Shapiro) New York Medical College, Westchester County Medical Center, Department of Pediatrics, Valhalla, N.Y.

Previous studies have shown that gonadotropin response to I/V bolus injection of GnRH differs in prepubertal (PPP) and pubertal patients (PP). In the PPP patients GnRH response is minimal, with the LH/FSH ratio being less than one. In contrast, the PP patient demonstrates a marked response in LH secretion with the LH/FSH ratio being greater than one.

We studied a group of 12 girls, aged 6 to 8 years, designated as Aborted Puberty (AB). They all presented with signs of precocious puberty (breast & pubic hair development) but differed from true precocious puberty in that their early pubertal development spontaneously regressed. These AB patients responded differently to GnRH than expected, as seen in the table below.

Table I Aborted Puberty Patients GnRH Stimulation

Mean Age/Yrs	LH Basal Mean mIU/ml	LH Peak Mean mIU/ml	FSH Basal Mean mIU/ml	FSH Peak Mean mIU/ml	LH/FSH Ratio Mean mIU/ml
7	2.5±1.4	10.9±6.1	3.2±1.6	24.2±13.7	0.33±0.2

They demonstrated a greater rise in both FSH and LH than the PPP patients. In contrast to the PP patients their LH/FSH ratio is less than one.

We submit to have discovered a new variant of normal pubertal development, termed "Aborted Puberty", which is different from all other pubertal states based on its gonadotropin response to GnRH stimulation.

469

ACTH AND ADRENAL STEROID REPONSE TO CORTICOTROPIN RELEASING FACTOR (CRF) STIMULATION IN PATIENTS WITH A GENETIC DEFECT IN ADRENAL STEROIDOGENESIS Songya Pang, Elsie Estrada and Maria I. New, The New York Hosp-Cornell Med Ctr, Dept Ped, NY, NY 10021

To investigate the pathophysiology of hypothalamic-pituitary-adrenal axis in patients (pt) with a mild defect in adrenal steroidogenesis, ACTH and adrenal steroid response (180 min) to ovine CRF (1 ug/kg IV bolus at 1600 hr) in 3 pt with late diagnosis of 11β-hydroxylase (11β-OH) deficiency (def) and in 7 pt with late-onset 21-hydroxylase def (21-OH) or 3β-ol dehydrogenase def (3β-HSD) were compared with the responses in 8 controls. In all pt, levels of adrenal precursor steroids proximal to the particular enzyme block were high following CRF. Basal and CRF-stimulated ACTH & F levels were normal irrespective of enzyme def or magnitude of the rise of the precursor steroid in all pt but 2 (11β-OH def) in whom ACTH response to CRF was high and F response low, with lower precursor steroid response than in the pt with normal ACTH and F. Conclusion: In pt with defects in adrenal steroidogenesis, compensatory ACTH hypersecretion occurs only when F secretion is inadequate. Normal ACTH secretion is seen in pt with normal F secretion despite increased precursor steroids. Mechanism for normal F without excess ACTH remains to be defined.

(mean /range)	ACTH (pg/ml) NL	ACTH (pg/ml) ENZYME DEF nl* ↑		F (ug/dl) NL	F (ug/dl) ENZYME DEF nl* ↓		17-OH (ng/dl) progesterone NL	17-OH (ng/dl) progesterone 21-OH	17-OH (ng/dl) pregnenolone NL	17-OH (ng/dl) pregnenolone 3β-HSD	DOC (ng/dl) NL	DOC (ng/dl) 11β-OH
Basal	21 13-44	20 9-48	33, 90	6	6.7 2-15	0.3, 5-13	60 2.6	284 10-144	92 255-300	170 16-252	10 128-195	338 5-20 38-800
post-CRF	29	29	104,	17	19	0.5,	119	3,300	303	1,430	16	1,188
maximum response	17- 60	14- 53	120	8- 26	14- 22	3.0	28- 269	2,300- 4,395	129- 600	1,021- 1,848	11- 28	176- 2,215

Key:NL, normal; ENZYME DEF: nl*, normal response;↑/↓, high/low response in same pt.