337

INTERACTION OF GROWTH HORMONE AND GASTRIC INHIBITORY POLYPEPTIDE IN HYPOPITUITARY PATIENTS: Carolyn A. Romshe, Samuel Cataland, Ernest L. Mazzaferri and Juan F. Sotos. Depts of Peds and Med., College of Medicine, The Ohio State University and Children's Hospital, Columbus, Ohio.

Gastric Inhibitory polypeptide (GIP) given intravenously with glucose potentiates insulin secretion and improves glucose tolerance. Since patients with growth hormone (GH) deficiency frequently show alterations in oral glucose tolerance (GTT) and may have low insulin levels, the secretion of GIP in hypopituitary patients before and after GH administration for 6 months was studied. Glucose, insulin and GIP levels were obtained during an oral GTT. The results are expressed as ± the standard error of mean.

Time (min)		0	15	30	60	120
GIP(pg/ml)	Pre GH	378±72	809±68	809±87	750±92	780±100
	Post GH	306±69	677±118	745±123	677±95	623±91
Insulin	Pre GH	5.3±0.5	29±6	34±8	33±11	21±6
(μU/ml)	Post GH	5.6±0.5	20±5	31±8	31±10	19±4

There was no significant difference in the response of GIP, insulin, or glucose to an oral GTT before and after 6 months of GH administration (2 units I^m 3 times weekly). The levels of GIP are comparable to normal controls suggesting no impaired secretion of GIP in growth hormone deficiency. It does not appear that GIP plays a role in the carbohydrate abnormalities in growth hormone deficiency.

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338

A NEW TYPE OF RICKETS: UNRESPONSIVENESS OF BONE AND INTESTINE TO HIGH LEVELS OF ENDOGENOUSLY SYNTHESIZED 1,25-DIHYDROXYVITAMIN D_3 [$1,25(OH)_2D_3$]. John F. Rosen, Alan R. Fleischman, Laurence Finberg; Hector F. DeLuca. Albert Einstein Coll. Med., Montefiore Hosp. & Med. Ctr., Dept. Ped., New York; Dept. Biochem., Univ. of Wisconsin, Madison.

2 sisters, 3 (sib I) and 7 (sib II) years old, from consanguineous and normal parents, presented with active rickets, skeletal deformities and alopecia totalis after years of vitamin (vit) D_2 therapy (50,000 IU/d). Representative levels in serum for sib I and II, respectively, were Ca, mg/dl: 9.8, 8.9; P, mg/dl: 4.0, 2.9; 25-OHD, ng/ml: 47, 42 (normal 27±5); parathyroid hormone (PTH), μl-eq/L: 42, 44 (normal = < 40); $1,25(OH)_2D_3$, pg/ml, was >300 (normal = 46) in both sibs. Both sibs had a calcemic response to PTH: ↑Ca by 1.3 and 2.1 mg/dl and normal renal responses (P and cAMP) to PTH. The TRP in both was 77-80%. The mean balances, mg/d, in sib I for Ca was -55 and for P -95, while in sib II the value for Ca was -140 and for P -190. $1,25(OH)_2D_3$ treatment at doses of .04 and .06 μg/kg/d (.50 μg and .75 μg/d) failed to reverse the biochemical abnormalities or heal the ricketic lesions.

These 2 sibs have a new inborn error of vit D metabolism marked by intestinal end-organ unresponsiveness to supranormal levels of $1,25(OH)_2D_3$, endogenously synthesized, leading to malabsorption of Ca and P and rickets. Also, both sibs have hyporesponsiveness to $1,25(OH)_2D_3$ at bone in view of normocalcemia despite extremely high $1,25(OH)_2D_3$ and slightly elevated PTH levels in serum.

339

THE ONTOGENY OF GONADOTROPINS AND SEX STEROIDS IN THE SHEEP FETUS. C.A. Sklar, P.L. Mueller, P.D. Gluckman, S.L. Kaplan, A.M. Rudolph, and M.M. Grumbach. Dept. of Pediat., Univ. California San Francisco, San Francisco, Ca.

Using the chronically catheterized sheep fetus, the ontogeny of FSH, LH, testosterone (T), androstenedione (A), dehydroepiandrosterone (D), and D sulfate (DS) was studied in 84 fetuses from 70d to term (150d).

Gest. Age (days)	oFSH (ng/ml) Male	Female	oLH (ng/ml) Male	Female	T (ng/dl) Male	Female
70-90	1.7±0.4	2.6±0.6	1.0±0.4	2.3±1.0	(70-130 days)	
90-110	2.3±0.5	* 3.6±0.5	0.5±0.2	+ 0.9±0.3	+ 35±5.4	* 22.7±3.8
110-130	2.9±0.3	+ 2.4±0.3	+ 0.6±0.1	0.3±0.1		
130-150	1.5±0.3	1.8±0.2	0.2±0.1	0.3±0.1		
	A (ng/dl)**		D (ng/dl)		DS (μg/dl)	
90-110	11±5	18±5	69±7	54±17	4.9±.3	4.4±.3 +
110-130	12±4	19±7	104±42	69±14	---	7.8±.5
130-150	11±1	24±5	52±15	78±20	6.3±.7	6.2±.8

*Significant sex difference for age group; +Significant difference between gestational ages ($p<0.05$); **Total female group significantly higher than male group ($p=0.01$).

The pattern of gonadotropins in the sheep fetus is similar to that in the human with higher FSH in the female and peak plasma levels of FSH and LH in mid-gestation. Higher T levels in males up to 130d most likely reflects fetal testicular activity and may explain the lower FSH in the male. The fall in gonadotropins in both sexes in late gestation may be a consequence of increasing hypothalamic-pituitary sensitivity to circulating sex steroids.

340

OVARIAN FAILURE FOLLOWING CANCER THERAPY IN THE PREPUBERTAL FEMALE. Robert Stillman, Isaac Schiff, Norman Jaffe, Demetrius G. Traggis, Frederick P. Li and Joel Greenberger (Spon. by David G. Nathan), Sidney Farber Cancer Inst., Children's Hosp. Med. Ctr. and Boston Hosp. for Women, Boston, MA 02115.

Long-term reproductive and gonadal steroid potential has been investigated in 10 female patients (pts) who were treated for a variety of abdominal malignancies before puberty. All pts presented with complaints of primary amenorrhea and lack of development of secondary sexual characteristics while off therapy and free of extant disease for 1-23 years. Evaluation consisted of assessment of pubertal development according to Tanner and by double antibody radioimmunoassay of serum gonadotropins according to Odell. All pts demonstrated significantly elevated serum gonadotropins indicative of ovarian failure: 24 mIU/ml to 85 mIU/ml LH and 78 mIU/ml to 156 mIU/ml FSH, with FSH consistently elevated above LH. The pts had been treated with between 1790-5500 rad to the abdomen and/or pelvis in fractionated doses as well as one or a combination of chemotherapeutic agents including vincristine, methotrexate, cyclophosphamide, actinomycin D or chlorambucil. Improved long-term survivorship from prepubertal malignancies necessitates consideration of future ovarian steroidal and reproductive function in therapeutic regimes. Evaluation of other pts to attempt to separate the effects of radio- and chemotherapy on gonadal function, as well as assessment of the effects of replacement estrogen therapies is planned. (Supported by Grant CA82002.)

341

EARLY CLINICAL FEATURES OF CONGENITAL ADRENAL HYPERPLASIA (CAH). Alfred Tenore, Fernando Cassorla and John S. Parks. University of Pennsylvania and The Childrens Hospital of Philadelphia, Division of Endocrinology, Philadelphia, Pennsylvania.

The newborn male with salt-losing CAH is at risk for mortality before recognition of the disease. To better define the clinical features of CAH in the newborn period, we have reviewed the records of 45 children with CAH diagnosed before age 4 weeks. In 14 of 27 (52%) families with older children there was a history of early death of a male infant. Affected infants had significantly greater birth length and birth weight than a group of 66 control term infants, and their upper-to-lower segment ratio (U/L) was significantly lower than that found in controls.

	CONTROLS	CAH	P
BIRTH WEIGHT (g)(mean ± sd)	3191 ± 440	3683 ± 560	<0.0005
BIRTH LENGTH(cm)(mean ± sd)	50.8 ± 2.2	52.0 ± 2.2	<0.01
U/L (mean ± sd)	1.70 ± .02	1.59 ± .11	<0.0005

In 17 of 19 salt-losing infants the initial sign of a metabolic abnormality was a decline in CO_2 content. Urinary 17-Ketosteroid excretion rose progressively from admission to initiation of therapy, but urinary Pregnanetriol excretion was uniformly low in the first week of life and did not permit distinction between different forms of CAH. The large for dates male infant with a low upper-to-lower segment ratio merits early diagnostic evaluation for CAH despite a negative family history of unexplained neonatal deaths.

342

ADRENAL ANDROGENS AND PUBERTY. Maria D. Urban, Peter A. Lee, Claude J. Migeon, Leslie P. Plotnick, A. Avinoam Kowarski and James P. Gutai. Johns Hopkins University School of Medicine, Baltimore, MD and University of Pittsburgh School of Medicine, Pittsburgh, PA.

To evaluate the possibility that adrenal androgens effect hypothalamic-pituitary maturation and the onset of puberty, several groups of patients have been studied who had increased or decreased adrenal androgens for age: 1/ 40 female patients with premature adrenarche were followed; 15% progressed to sexual precocity; in the other 85% the mean age ± SD of the onset of breast development and menarche was available for 21 (9.7 ± 1.3) and 17 (10.7 ± 1.4) subjects respectively. 2/ The mean age of the onset of puberty among 5 male patients with Addison's disease who were well-nourished and adequately treated was 12.3 ± 0.3 years. 3/ Mean levels of 24 hr integrated concentrations (ng/100 ml) of testosterone (T), androstenedione (Δ), 17-hydroxyprogesterone (17OHP), progesterone (P) and dehydroepiandrosterone (DHA) in 3 patients with Addison's disease, agonadal males, normal pubertal males were:

	T	Δ	17OHP	P	DHA
Addison	366	42	45	19	48
Agonadal	23	93	27	21	275
Normal Pubertal Males	227	101	54	29	271

Hence, the data suggest that adrenal androgens accelerate hypothalamic-pituitary maturation as shown by somewhat early development in female patients with premature adrenarche. However, this effect is not obligatory because puberty occurred normally in male Addisonian patients despite low levels of adrenal steroids.