● 474 SEX DIFFERENCES IN DETECTABILITY OF BIO(B)- AND IMMUNO(I)-LH IN EARLY PUBERTAL DEVELOPMENT: A LONGITUDINAL STUDY. Edward O. Reiter, Pierre C. Sizonenko, Mary F. Witt and Inese Z. Beitins. Baystate Med. Ctr. Univ. of Geneva, Univ. of Michigan, Depts. Peds., Springfield, MA., Geneva, SWZ., Ann Arbor, MI.

We examined and made hormonal measurements at 6 month intervals in 20 normal boys (M) and 15 girls (F) during a longitudinal study of puberty. Initial detectability of B- and I-LH, measured in highly sensitive assay systems, was related to chronologic (CA) and skeletal age (BA), pubertal stage and sex steroid levels. In prepuberty, the detectability of B-LH was similar in both sexes (M-27%,F-35%), but differed in I-LH (M-79%,F-40%; χ^2=10.026,p<.002). In pubertal stage II, detectability of both B-LH (M-91%;,F-48%;χ^2=18.701,p<.001) and I-LH (M-89%,F-49%;χ^2= 21.224,p<.001) differed. In contrast to measurability of I-LH in M at younger age and lower T levels than B-LH, no such difference existed in F when age, pubertal stage, E_2 or FSH levels were considered. BA (11.2 vs 9.9,p<.02), but not CA, and pubertal stage (2.2 vs 1.4,p<.005) were significantly later in F than M at the earliest I-LH, but not B-LH, above assay sensitivity. In conclusion: (1) Prepubertal detectability of I-LH was more frequent in M than in F; (2) although B-LH tended to be unmeasurable in Stage I, less than 50% of Stage II F had either B- or I-LH found, in contrast to 90% of M; (3) in view of discordant B- and I-LH pulses reported in adults, the detectable I-LH potency estimates in immature M must be reevaluated as to alpha-subunit or other assay interference, as well as to the problems of use of multiclonal antisera and impure standards.

475 ANALYSIS OF BIO(B) AND IMMUNO(I)-LH DURING PUBERTY: A LONGITUDINAL STUDY IN NORMAL BOYS. Edward Reiter, Pierre Sizonenko, Mary Witt and Inese Beitins. Baystate Medical Ctr., Univ. of Geneva, Univ. of Michigan, Depts. Peds., Springfield, MA., Geneva, SWZ, Ann Arbor, MI.

As part of a serial assessment of normal children throughout puberty, gonadotropins (B- and I-LH) were measured by sensitive RICT assay and RIA in 20 boys and related individually to chronologic (CA) and skeletal age (BA), stage of pubertal development and sex steroid levels. The boys were studied at 6-month intervals for 5 to 6 years. In overall data, B-LH and I-LH were highly correlated (r=.73,p<.001). In 52 samples during prepuberty, I-LH was detectable in 79%, but B-LH in only 27%(χ^2=28.13, p<.001). Time of initial detection of B-LH differed from I-LH in CA (11.5 vs 10.7,p<.02), BA (10.8 vs 9.9,p<.01) and in levels of testosterone (T) (17.8 vs 12.4,p<.04). A significant linear relationship existed between B-LH or I-LH and T in 70% of the boys. Fitting a quadratic model to these data significantly improved LH-T correlations, suggesting a plateau of LH after the early T rise. There was no significant relationship between B-LH or I-LH and E_2 in 13 individual boys. In conclusion: (1) I-LH is detectable by sensitive RIA more commonly than B-LH by sensitive RICT in prepubertal boys; (2) I-LH was measurable at a younger CA and BA, and at a lower T than B-LH; this discordance affirms that which has recently been described in analysis of pulsatile LH secretion, but does not clarify the role of the early pubertal increment of T upon a changing B/I ratio; (3) The relationship between I-LH and/or B-LH and T seems best described by a quadratic equation.

476 HORMONAL REGULATION OF SOMATOMEDIN SECRETION BY FETAL RAT HEPATOCYTES IN CULTURE. Robert A. Richman, Mark R. Benedict, James R. Florini, and Barbara A. Toly, Dept. of Pediatrics, SUNY Upstate Medical Center and Dept. of Biology, Syracuse University, Syracuse, N.Y.

To determine which hormones might regulate fetal somatomedin (SM) secretion, we measured SM levels in conditioned medium from primary cultures of fetal rat hepatocytes. We employed a bioassay (^{3}H-thymidine incorporation into DNA of chick embryo fibroblasts), a displacement assay (competition for binding of a radiolabeled rat IGF-II to the SM binding protein) for total somatomedin, and the radioimmunoassay for SM-C. Epidermal growth factor (EGF) and dexamethasone were the most active hormones tested, as measured by the displacement assay. Rat growth hormone (rGH) was much less stimulatory. Human placental lactogen (hPL), glucagon and insulin had little or no effect. Stimulation of SM secretion by both EGF and dexamethasone was time- and dose-dependent. The maximal response occurred at 48 hours, at a concentration of about 1×10^{-7} M of either hormone. In the bioassay, the stimulation by EGF, but not dexamethasone, could be detected. The steroid had enhanced the secretion of a heat-labile inhibitor that completely masked the mitogenic activity of the increased SM levels. The fetal SM secreted exhibited immunological cross-reactivity with human SM-C, but the levels were 500-fold less than those measured by our displacement assay. This suggests that the predominant fetal rat SM is not SM-C. We conclude that EGF and dexamethasone, but not rGH or hPL, stimulated the secretion by fetal hepatocytes of a fetal SM which resembled IGF-II.

477 GLYCOGEN STORAGE DISEASE TYPE Ib AND REGIONAL ENTERITIS. T. Roe, N. Schonfeld, J. Atkinson, H. Issacs, D. Thomas, and V. Gilsanz, Univ. of So. Calif. Sch. of Med., Childrens Hospital of Los Angeles, Dept. of Peds., Los Angeles. Sponsored by Gertrude Costin.

Glycogen storage disease (GSD) type Ib is a recently recognized variant with clinical features similar to GSD type Ia (glucose-6-phosphatase deficiency). In type Ib the transport of glucose-6-phosphate into hepatic microsomes is deficient. Neutropenia, a neutrophil (N) chemotactic defect, recurrent oral and anal mucosal lesions are characteristic. Inflammatory bowel disease has not been reported in GSD although abdominal pain is common. We investigated abdominal pain in 2 boys, ages 11 and 14 yrs, with biopsy-proven GSD type Ib. Both had mucosal lesions and gingivitis for 7-8 yrs. The older boy had 7 kg weight loss and growth failure. Both had neutropenia, anemia, hypoalbuminemia and increased erythrocyte sedimentation rates. Barium contrast studies showed irregularity of the distal ileal mucosa and fixed 50% narrowing of the cecum, indicative of regional enteritis (RE). Fecal alpha-1-antitrypsin was markedly increased in the older boy. He had a right colectomy for obstruction. The appearance of the bowel at surgery and on microscopic examination was totally consistent with regional enteritis (Crohn's disease). Skin tests for tuberculosis and stool examinations for pathogens were negative.

CONCLUSIONS: An association between RE and GSD type Ib is likely. The primary metabolic defect in GSD type Ib appears to involve N causing decreased chemotaxis. Since deficient N migration to inflammation is characteristic of RE, N dysfunction may play a role in both forms of enteritis.

● 478 GROWTH HORMONE (GH) RELEASE IN CHILDREN WITH SHORT STATURE: STIMULATION BY HUMAN PANCREATIC TUMOR GROWTH HORMONE RELEASING FACTOR-40 (hpGRF-40). A.D. Rogol, R.M. Blizzard, A.J. Johanson, R. Furlanetto, J. Rivier, W. Vale, M.O. Thorner, University of Virginia, Charlottesville, VA, Children's Hospital of Philadelphia, PA, and Salk Inst., San Diego, CA.

44 short children were evaluated for GH reserve after pharmacologic tests and a single IV injection of hpGRF-40. Four groups were studied 1) Idiopathic GH deficiency (IGHD) 2) Organic hypopituitarism 3) Intrauterine Growth Retardation (IUGR) and 4) Constitutional Delay (CD). A fifth category (unclassified) was included. Subjects were tested on 2 consecutive days 1) after IV arginine (0.5 mg/kg, 30 min) and oral L-DOPA (9 mg/kg) and 2) after hpGRF-40 (3.3 µg/kg IV bolus). A normal response to Arginine/L-DOPA was a GH level ≥ 7 ng/ml. The peak (±SE) GH (ng/ml) during each test is shown:

	n	Arg/L-DOPA peak	hpGRF-40 peak
1) IGHD	14	2.2±0.4	7.7±1.8
2) Organic	8	0.9±0.2	3.4±0.9
3) IUGR	5	12.0±4.3	14.2±6.4
4) CD	11	11.7±2.4	13.6±4.1
5) Unclassified	6	11.7±1.6	>25

The GH levels in groups 1 and 2 did not reach 7 ng/ml after Arg/L-DOPA, but some had marked increases after hpGRF-40. The lowest responses to hpGRF-40 were in children with Organic hypopituitarism and those with IGHD. The peak GH responses to hpGRF-40 in the children in groups 3-5 were widely variable (5->25 ng/ml). hpGRF-40 testing results suggest that pituitary GH deficiency is uncommon even in children with IGHD and Organic hypopituitarism.

● 479 DIMINISHED PULSATILE LUTEINIZING HORMONE SECRETION AND SUPERSENSITIVITY TO GONADOTROPIN RELEASING HORMONE IN AMENORRHEIC RUNNERS. Alan D. Rogol, Johannes D. Veldhuis, William S. Evans, Michael O. Thorner, Diane Wakat. Departments of Pediatrics, Pharmacology, Internal Medicine, and Physical Education, University of Virginia, Charlottesville, VA.

Menstrual irregularity is common in endurance-training women, although precise pathophysiological mechanism(s) remain unknown. To evaluate possible disturbances in the pulsatile mode of LH release, we sampled blood at 20 min intervals for 24 h in 10 amenorrheic long-distance runners. LH pulse frequency and amplitude were calculated using a computerized algorithm, and pituitary responsiveness evaluated by infusing graded submaximal doses of gonadotropin releasing hormone [(GnRH); 2.5,5,10 and 25 µg)] at 2 h intervals for 8 h. We observed that 6 women had very low frequency LH pulsations (5,1,3,4,2,6 pulses/24 h), and 4 others maintained normal LH pulse frequency (11,12,13 and 15 pulses/24 h). Reduced LH pulse *frequency* occurred despite normal mean and 24 h integrated serum LH concentrations, and normal early follicular phase levels of estradiol, testosterone and progesterone. Spontaneous LH pulse amplitude (% or absolute) was normal or accentuated and administration of submaximal doses of GnRH promoted greater release of LH in runners than in controls (P<0.001). We conclude that the women athletes exhibit normal or increased responsiveness of gonadotrophs to endogenous or exogenous GnRH. Thus, the decreased frequency of LH pulsations seems to reflect a defect in the hypothalamic GnRH pulse generator rather than the pituitary gland. These observations provide clear evidence for a brain defect in the regulation of LH secretion in certain long-distance runners.