TYPICAL FACIES AND NORMOVOLEMIA IN BARTTER'S SYNDROME, Thomas James, Nancy H. Holland and David Preston, Dept. of Med., Temple Univ. Sch. of Med., Philadelphia, Pa., and Dept. of Ped. and Radiation Therapy, Univ. of Ky. Sch. of Med., Lexington, Ky.

Bartter's Syndrome (BS) was diagnosed in two female infants presenting with failure to thrive, hypokalemic, hypochloremic alkalosis, hyper-renism and secondary hyperaldosteronism without associated edema or hypertension. A lack of response to angiotensin II infusion was demonstrated in one infant. Similarity of facial characteristics in the two infants was recognized: large head relative to the body, triangular facies with protruding pinnae, large eyes, a "pouting" expression with drooping mouth possibly related to potassium depletion. Reference to the literature showed a resemblence to the other infants with BS.

The association in these infants of normotension, increased plasma renin and hyperaldosteronism has been explained on hypovolemia secondary to a renal tubular defect in sodium reabsorption. Plasma volume was measured in the two infants with BS and in two control infants by the dilution method using radioiodinated human serum albumin. Plasma volume in both BS infants was normal or even increased compared to predicted values relative to weight. Control infants had plasma volumes equal to or less than the predicted volume. These measurements suggest that hypovolemia may not be present in all cases of BS and that an alternate mechanism such as impaired vascular responsiveness to angiotensin may be operant.

THE PLACENTAL BARRIER TO HUMAN INSULIN-I-125 IN INSULIN DEPENDENT DIABETIC MOTHERS. Satish Kalhan, Robert Schwartz and Peter Adam. Dept. Ped. Case Western Reserve Univ. at Cleveland Metropolitan General Hosp.

Although the normal human placenta is impermeable to insulin, the effect of anti-insulin antibodies upon the placental barrier to insulin has not been defined. The placental transfer of human insulin-I^{125} was examined in normal (n=4) and insulin-dependent diabetic mothers (n=4) by infusing human insulin-I^{125} at a constant rate for 60-90 min. prior to delivery and measuring immunoprecipitable insulin-I^{125} radioactivity in the maternal and umbilical venous plasma at delivery. In normal mothers plasma insulin-I^{125} radioactivity was 683 ± 110 cpm/ml (Mean$\pm$SEM) in the maternal vein and 6 ± 2 cpm/ml in the umbilical vein. In three diabetic mothers with high plasma insulin binding capacity (1850-8400 μU/ml) the umbilical venous insulin-I^{125} was 10 ± 10 cpm/ml when the maternal plasma insulin-I^{125} was maintained at 1388 $\pm$356 cpm/ml., even though the antibodies were present in the fetal plasma. In another insulin-dependent diabetic mother with negligible anti-insulin antibodies, no placental transfer of human insulin-I^{125} was demonstrated. Thus, in both normal and diabetic mothers, placental transfer of human insulin-I^{125} is negligible and the presence of maternal anti-insulin antibodies does not induce insulin transfer.

METABOLISM AND EFFECTS OF GONADOTROPIN RELEASING HORMONE(GnRH) IN CHILDREN AND ADULTS. Robert P. Kelch, L. Edward Clemens, and Mara E. Markovs, (Intr. by William J. Oliver), Univ. of Mich., Dept. of Ped., Ann Arbor.

The purpose of this study was to compare the metabolism and effects of synthetic GnRH (Parke-Davis) in children and adults. Eight prepubertal children, 1 pubertal male, and 1 adult male received 10 $\mu g/m^2$ i.v.; 2 adult females were given 100 μg i.v. Blood samples were drawn at frequent intervals. GnRH concentrations were determined by a highly specific radioimmunoassay. Sensitivity of this assay is 1 pg/tube or 5 pg/ml plasma. Serum LH and FSH were determined by RIA. No correlation was found between physiological state or serum gonadotropin values, and endogenous GnRH values: n=64, X=11$\pm$1.2 (SE) pg/ml. Many plasma samples fell beneath the sensitivity of the assay. Peak GnRH concentrations occurred at 1 or 2 min. (4.42$\pm$0.4 ng/ml, 10$\mu g/m^2$, 20 and 19.5 ng/ml, 100μg); baseline values returned by 90 min. Initial $t_{\frac{1}{2}}$ was 2.9$\pm$.3 min. in children and 3.6$\pm$.3 in adults. Initial distribution volumes were also similar; children 6.6$\pm$0.8; adults 5.9$\pm$0.9 % body weight. The plasma disappearance curve of GnRH was described best by a double exponential function: $t_{1\frac{1}{2}}$=2.8$\pm$.2 min.; $t_{2\frac{1}{2}}$=18.9$\pm$.9 min. Blunted serum LH responses were seen in all children when compared to our adult standards. These data indicate: 1)that endogenous GnRH levels are lower than previously reported; 2)children and adults metabolize GnRH similarly and 3)dosages of GnRH in comparative studies should be based on weight rather than surface area.

LH & FSH RESPONSE TO LUTEINIZING RELEASING FACTOR (LRF) IN CLYCLOPHOSPHAMIDE TREATED MALES. Rebecca T Kirkland, David Cornfeld, Alfred Tenore, Vanitha Vaidya, John S. Parks, Alfred M. Bongiovanni. Univ. of Pa. Dept.of Pediat. Children's Hosp. of Phila.

Testicular damage associated with cyclophosphamide (CX) therapy of steroid-dependent nephrosis prompted assessment of 5 pubertal males, 15-18 yrs, to identify those who may have gonadal injury as a result of medication. 3 who had received CX for 4 months and 2 for a total of 9 and 10 months between the ages of 12-1/2 to 16 yrs (2-4 yrs before testing) received LRF, 100 ugm. Basal serum testosterone (T) values in 4 were within the normal range for age, mean 507 (400-900 ngm/ml) and one was low, 246.

Responses to LRF in 3 with normal T showed higher basal levels of LH, mean 46.3 mIU/ml, and peaks to 101-119. Mean basal levels of FSH were 25.7 mIU/ml and had sustained elevation rather than a significant peak. 1 with normal T and 1 with low T had mean basal LH 18.5 mIU/ml and mean basal FSH 1.4. After LRF a 3-4 fold rise of LH and 8-10 fold rise of FSH occurred. The LRF test caused no untoward reactions and does identify those who require further evaluation of their gonadal status. These studies showed that testesin CX-treated males may be under higher LH and FSH stimulation to maintain normal T.

PATTERNS OF LH & FSH RELEASE STIMULATED BY LUTEINIZING HORMONE RELEASING FACTOR (LRF) IN 18 CHILDREN. Rebecca Kirkland, Alfred Tenore, Vanitha Vaidya, John S. Parks and Alfred M. Bongiovanni. Univ.of Pa. Dept. of Pediat. The Children's Hosp. of Phila.

18 subjects, 5-20 yrs, received LRF to determine if the responses of serum LH & FSH might be useful in specific situations. The subjects who received LRF, 50-100 ugs IV, had hypopituitarism, intrasellar mucocoele (A); constitutional delay, normal female (B); delayed puberty & anosmia, anorchia & encephalocoele (C); obesity (D); anorexia nervosa (E) & gonadal dysgenesis (F).

Pt.#	Age-Yrs	Basal-LH-Peak		Basal-FSH-Peak	
A-3	6-20	11.3	25.0	10.0	5.5
B-3	12-13	11.3	43.7	6.7	14.8
C-2	12,16	<2,11.1	N,17.5	9.7,4.5	N
D-1	5	18.0	N	21.2	N
E-2	14,18	4.8	13.8	12.1	35,N
F-7	6-15	29.8	106.9	44.6	89.8

A prepubertal hypopit had FSH 0.7 mIU/ml (peak 4.5); LH was basal 16.0 (peak 31.7). B had no LH, FSH abnormality. LH did not rise in anorchia; C had no FSH peaks. D had no peaks but basal LH, FSH were higher than expected for age. E had low LH & no rise in FSH (N) in one. F had elevated LH,FSH. The LRF test is useful for evaluation of suspected hypothalamic-pituitary disorders.

LH & FSH RESPONSES TO LRF IN GONADAL DYSGENESIS (GD) AFTER ETHINYL ESTRADIOL (EE). Rebecca T. Kirkland, Alfred Tenore, Vanitha Vaidya, John S. Parks and Alfred M. Bongiovanni. Univ.of Pa. Dept.of Pediat. The Children's Hospital of Phila.

Subjects with GD have elevated LH & FSH and achieve greater rise in both after LRF (Silver,Yen 1973). Estrogens exert inhibitory action on FSH & LH release (Yen et al 1972). To ascertain an effect of estrogen on LH and/or FSH to LRF in GD, 8 females 7-20 yrs, were studied; 4 XO, 1 XO/XY, constitutional delay, hypopituitarism, normal female. LRF, 50-100 ugm IV, was followed by 0.1 mgm EE daily 3-7 days, with 1-7 days off EE prior to second LRF test. In 3 young XO GD, 7 days EE decreased basal FSH (mean 17.6 mIU/ml before EE, 6.1 after EE) and the FSH peak to LRF (mean FSH peak 64.1 before EE, 16.1 after); LH was not significantly affected. With 3 days EE, a 7 yr. XO/XY had no change in LH,FSH responses. An older XO had an LH rise to LRF after 3 days EE, with a decreased FSH responsiveness. LH levels with LRF (after EE) were decreased in a normal female and constitutional delay. The younger child with GD lacks ovarian feedback mechanism and may have chronic endogenous secretion of LRF which induces pubertal LH response, as shown in these studies. LH & FSH responses to EE varied with age.