

● **449** VASOPRESSIN (VP) RELEASE IN FETAL NEWBORN AND ADULT SHEEP INDUCED BY HYPOXIA: CORRELATION WITH  $\beta$ -ENDORPHIN IMMUNOREACTIVITY (-EP) & PaO<sub>2</sub>. Raymond I. Stark, Salha A. Daniel, Kasim H. Husain, Sharon L. Wardlaw & L. Stanley James, Div. of Perin. Med., Depts. of Ped., Med., Coll. of P&S, Columbia Univ., NY.

To study the relationship of plasma VP (pg/ml),  $\beta$ -EP (pg/ml) & PaO<sub>2</sub> (mmHg) during hypoxic stress, we exposed pregnant ewes & lambs to an FIO<sub>2</sub> of 5 or 10% in N<sub>2</sub> for 30 min. In 11 fetuses of ewes exposed to 10% FIO<sub>2</sub>, VP increased from 1.7±0.5 to 56±17.8 (p<.001). In 6 newborn lambs with 10% FIO<sub>2</sub>, mean VP increased from 2.1±0.4 to 10.5±5.8 (p<.005) while with 5% FIO<sub>2</sub>, VP increased to 42±138 (p<.001). Exposure of 7 ewes to 10% FIO<sub>2</sub> produced no change in mean VP, yet with 5% FIO<sub>2</sub> mean VP increased from 1.7±5 to 38.9±15.7. There were significant negative correlations (p<.001) between PaO<sub>2</sub> and log VP in the fetal & newborn lamb.

Unlike VP control  $\beta$ -EP levels were higher (p<.01) in the fetus (134±31) & newborn (155±24) than in the ewe (50±11). Fetal  $\beta$ -EP increased during hypoxia to 544±81 (p<.01) & values were positively correlated (r=.63, p<.005) with log VP. Lambs & ewes exposed to 10% FIO<sub>2</sub> had no increase in  $\beta$ -EP, while with 5% FIO<sub>2</sub> mean  $\beta$ -EP increased to 532±158 & 150±17 (p<.01).  $\beta$ -EP levels correlated with VP (r=.91, p<.001). VP &  $\beta$ -EP values during hypoxia were higher (p<.02) in fetuses <130 days gestation than those >130 days.

We conclude that hypoxia strongly stimulates the release of VP &  $\beta$ -EP into the peripheral blood. With advancing gestation the fetus becomes more responsive to hypoxia. Data suggest parallel but independent release of VP &  $\beta$ -EP during hypoxia.

**450** ZINC (Zn) AND BIRTH DEFECTS (BD). Constance Stewart, Brad Katchan, Platon J. Collipp, Sanda Clejan, Scott Pudalov, and Shang Y. Chen. Nassau County Med Ctr., SUNY, Stony Brook Health Sciences Ctr., Department of Pediatrics, East Meadow, NY 11554.

Zn deficiency has been reported in infants with BD and in children born with achondroplasia. 304 families were studied comparing parental age, Zn nutritional status and infant weight at the time of birth.

Parental Age (years)	Hair Zn (ug/g)			Infant Wgt (g)	Infant Hair Zn
	Infant	Mother	Father		
14-20	192±23	174±33	142±28	< 2500	200±30
21-30	212±35	181±39	181±41	2500-3500	203±31
31-40	199±28	173±43	176±44	> 3500	192±24

There is a statistically significant correlation (p<.01) between infant hair Zn and maternal age at time of birth. The decrease in infant hair Zn seen with teenage (14-20) and elder mothers (31-40) may be related to the incidence of increased BD which occurs in these groups. Infant hair Zn was lowest in the heaviest infants and in a group with BD made up of porencephaly, anencephaly and microcephaly as the presenting sign (N=4; Zn=134±10). The heaviest children may represent the infants of potential diabetic mothers (who have more BD). Placental Zn was 18-19 ug/g and did not correlate well with maternal or infant hair Zn. Finally, diet did not explain parental Zn status since paired deficiencies did not occur. Therefore, an association between Zn levels, high-risk age groups and those children with BD is apparent.

● **451** INSULIN BINDING STUDIES IN THE ERYTHROCYTES OF DIABETICS IN ONE KINSHIP. Larry D. Stonesifer, M. Joycelyn Elders, Victoria L. Herzberg, J. Mark Boughter, Thomas J. Sziszak, and Donald E. Hill. University of Arkansas for Medical Sciences, Department of Pediatrics, Little Rock, AR.

Specific insulin binding to erythrocyte receptors has previously been reported to be unaltered in children and adolescents with insulin dependent diabetes mellitus (Ped. 66:385, 1980). We report here that five insulin dependent, fasting, non-ketotic juvenile diabetics from the same close kinship have a significant reduction in the percent insulin bound to erythrocytes (Normal % B/T=8.32±2.71, n=24±1SD vs 4.72±0.84 for the diabetic children). Three non-diabetic juveniles in the family have an intermediate value of 5.77±1.08. The youngest family member has normal binding. Scatchard analysis or two-site analysis indicate that the reduced binding is due to a decrease in the number of receptor sites/cell. There is no correlation with circulating plasma insulin values nor with the severity of the diabetes, however, the insulin dependent diabetics have an inordinate degree of ocular complications for the severity of the diabetes. Since diabetes mellitus is a heterogeneous disorder, there may be familial patterns to the abnormality seen with the erythrocyte receptor as in the above patients.

● **451A** TREATMENT OF CUSHINGS DISEASE (C.D.) BY TRANSPHENOIDAL MICROADENECTOMY (Tr.M.) IN CHILDHOOD AND ADOLESCENCE. D.M. Styne, J.B. Tyrell, F.A. Conte, S.L. Kaplan, M.H. Connors, G.P. August, C.B. Wilson, and M.M. Grumbach. Dept. of Pediatrics, Univ. California San Francisco, CA.

The efficacy of Tr.M. in the treatment of C.D. in children and adolescents has not been assessed. We treated 7 patients (7-6/12 to 18-9/12 years old) with C.D. before epiphyseal fusion with Tr.M. (followup 2-72 months postoperatively). Growth failure and weight gain were the first signs of C.D.; pubertal delay, virilization and fatigability were variable features. Preoperative evaluation showed elevated but highly variable urinary free cortisol and no diurnal variation in plasma cortisol or ACTH values; high dose dexamethasone therapy suppressed excretion of urinary free cortisol. Two of 7 patients lacked definite radiographic evidence of a pituitary adenoma. Transphenoidal exploration revealed 1-4 mm adenomas in 6 of 7 patients; no definite adenoma was noted in the 7th patient in spite of CT scan evidence of adenoma. Postoperative complications were limited to transient diabetes insipidus. The 6 treated patients had low cortisol and ACTH secretion postoperatively and required replacement glucocorticoid therapy for 6-12 months. Weight loss, growth and pubertal progression without recurrence of C.D. were noted in 5 patients with long term followup. Our experience indicates that ACTH secreting microadenomas are the principal cause of C.D. in childhood and adolescence and suggests that transphenoidal microadenectomy is the initial treatment of choice for Cushing's disease in young patients.

**452** DIRECT DETERMINATION OF 17 $\alpha$ -HYDROXYLASE (17OHase) DEFICIENCY IN A MALE PSEUDOHERMAPHRODITE BY IN VITRO STUDIES OF TESTICULAR STEROID BIOSYNTHESIS. A. Vargas, E.O. Reiter, K. Kula, L.J. Rodriguez-Rigau, E. Steinberger, A.W. Root. Univ. South Florida, Dept. Pediatrics, Tampa and Univ. Texas Health Sc. Ctr., Dept. Reprod. Med. and Biol., Houston.

A 4 year old male (46XY) pseudohermaphrodite with 17OHase deficiency (Ped. Res. 13:387A, 1979) underwent bilateral orchiectomy 2 days after 3 days of HCG (2,000 u/day IM), during which serum levels of testosterone, dihydrotestosterone, androstenedione, 17OH-progesterone (17OHP) and estradiol did not increase while progesterone increased from 52 to 69 ng/dl. Teased testicular tissue was incubated with 10uCi (3.3 nmol) of <sup>3</sup>H-pregnenolone or <sup>3</sup>H-17OHP in 3 ml NADP fortified KRB buffer, pH 7.4, for 3 hr. at 37°C with and without 100 IU/ml HCG.

Metabolite	pmol/20 mg tissue		
	<sup>3</sup> H-pregnenolone		
	-HCG	+HCG	Normal Adult Male
Progesterone	66.0	566.0	19.6
17OH-Pregnenolone	37.0	60.0	221.8
17OHP	0.9	66.6	115.0
Testosterone	0.2	4.0	22.1
	<sup>3</sup> H-17OHP		
Androstenedione	0.3	81.0	
Testosterone	59.0	96.0	

Thus the testes of this patient were unable to metabolize pregnenolone, but were able to metabolize 17OHP. The data are consistent with deficiency of 17OHase activity.

**453** SALT WASTING WITH POSTERIOR URETHRAL VALVES. John S. Venglarcik, Dale Doerr, Virginia H. Peden, James A. Monteleone. St. Louis University School of Medicine, Cardinal Glennon Memorial Hospital for Children, Department of Pediatrics-Adolescent Medicine, St. Louis, MO.

Clinical manifestations of posterior urethral valves (PUV) may vary widely. Biochemical abnormalities have not been emphasized. Seven male infants (mean age 6 weeks, range 9 days to 6 months), seen over a ten year period, presented with laboratory evidence of salt wasting suggesting adrenal insufficiency. Admission sodium, potassium, BUN, creatinine, serum pH, and urine pH and specific gravity were recorded. When available simultaneous urine and serum electrolytes were noted. In all cases PUV were confirmed by voiding cystourethrogram. The mean sodium on admission was 117 ± 11 mEq/L (range 95-127) while the mean potassium was 7.9 ± 1.3 mEq/L (range 6.5-9.6). The BUN and creatinine were 76 ± 42 mg/dl (range 27-136) and 3.7 mg/dl (range 2.2-5.8) respectively. The mean specific gravity of the urine was 1.007 ± .004 (range 1.005-1.017). In four patients simultaneous serum and urine electrolytes were determined. The mean serum sodium was 132 while the mean urine sodium was 9.25 mEq/Kg/L. All of the patients manifested an impaired ability to conserve water and sodium. In addition, an impaired ability to excrete acids into the urine resulted in acidosis and hyperkalemia. The sodium, potassium, water and acid imbalance is not due to aldosterone deficiency but reflects a glomerulus-tubular dysfunction.

Infants presenting with hyponatremia and hyperkalemia who have a very high BUN should have a urethral catheter implaced and a diagnosis of PUV ruled out.