

tension; normal growth; absence of virilism; hypokalemic alkalosis; elevated urinary aldosterone (UA), tetrahydroaldosterone (THA), tetrahydrocorticosterone; low plasma renin activity (PRA); and high plasma aldosterone (PA) were studied. Mild elevation of urinary 17-ketosteroids (KS) and marked elevation of 17-ketogenic steroids (KGS) was noted intermittently in both boys. Plasma cortisol (F) was low-normal in the older and normal in the younger subject. Spironolactone in the younger corrected the hypokalemic alkalosis without lowering the BP. Dexamethasone therapy, 8 mg/day for one week, also corrected the hypokalemia and lowered the BP within the first week in both subjects; correction has been sustained for four months with prednisone, 5 mg/day in the older and 2.5 mg/day in the younger subject. THA remained elevated but PRA became normal during the first 2 weeks of treatment. THA and UA fell to normal levels and F was suppressed by the fourth week, but KS and KGS remained intermittently elevated. The unique features in these cases are: a.) occurrence in male siblings; b.) lack of biochemical data supporting a complete or partial 11, 17, or 21-hydroxylase deficiency; c.) rapid fall in BP elevation and rapid correction of PRA and PA abnormalities with large doses of glucocorticoids; d.) delayed fall of THA excretion and e.) persistent elevation of KGS and KS. The findings of a generalized adrenocortical hyperactivity not totally suppressed by glucocorticoid therapy are consistent with adrenocortical adenomata.

FSH induction of sensitivity to LH: One mechanism for control of puberty. WILLIAM D. ODELL, RONALD S. SWERDLOFF, and HOWARD S. JACOBS. *UCLA Sch. of Medicine, Harbor Gen. Hosp., Torrance, Calif.*

It is postulated that the immature hypothalamic-pituitary unit is more sensitive to inhibition by gonadal steroids and that sexual maturation results from a decrease in this sensitivity. However, we have reported separately that in the *male* rat there is no difference in threshold dose of testosterone for feedback inhibition of LH and FSH at the time of sexual maturation. We now wish to report data in the female rat which provides a possible alternate explanation for puberty. These data indicate that the immature ovary is insensitive to LH stimulation and that this sensitivity is restored by FSH treatment. Hypothalamic-pituitary sensitivity to feedback suppression was tested as in the male. To study ovarian sensitivity to gonadotropin stimulation, immature (21 days) and mature (87 days) females were hypophysectomized. Five days later graded doses of LH (NIH-P7) were administered. Since only LH was administered, specificity of response was not important. Uterine weight increased in *mature* animals by all doses over 5  $\mu\text{g}/100$  grams body weight, but was unaffected by doses as large as 2000  $\mu\text{g}/100$  grams body weight in *immatures*. Sensitivity to LH in *immatures* could be made equal to *matures* by pre-treatment with FSH. When a constant dose of LH was administered with graded doses of FSH, a dose response to the LH effects was observed. The threshold dose of FSH for ovarian weight increase was similar in *matures* and *immatures* and uterine sensitivity to estrogen also was similar. Thus in the female rat FSH induces LH responsiveness of the gonad which in turn results in sexual maturation.

The pituitary-gonadal axis in the female child during infancy and at puberty. JEREMY S. D. WINTER and CHARLES FAIMAN. *Univ. of Manitoba and Children's Hosp. of Winnipeg, Manitoba, Canada.* (Intr. by James C. Haworth).

Serum FSH and LH (radioimmunoassay), estradiol (radioim-

munoassay), and testosterone (competitive protein-binding) were studied in 120 healthy females aged 0-20 years, and correlated with physical development. Prepubertal girls (4-9 years) showed low levels of FSH (6-12  $\mu\text{g}$  LER-907%), LH (0.5-2.5  $\mu\text{g}\%$ ), estradiol (<1 ng%) and testosterone (<20 ng%). Puberty (thelarche and pubarche) was accompanied by a rise in all these variables, reaching adult levels by age 14-16. The earliest hormonal change (age 9-11) was a rise in serum FSH, together with estradiol and testosterone; serum LH rose later (around age 12). These data resemble our previous findings in males. In 0-2 year old females, serum FSH (8-40  $\mu\text{g}\%$ ) and LH (1.3-3.0  $\mu\text{g}\%$ ) levels were higher than those in male infants (FSH 4-10  $\mu\text{g}\%$ ,  $p < .01$ ; LH 0.5-2.0  $\mu\text{g}\%$ ,  $p < .01$ ). Female FSH and LH levels diminished from age 0-8 years, while in boys these values increased slightly during this time. Estradiol and testosterone levels were not elevated in infancy. Serial determinations of FSH and LH in infant chimpanzees demonstrated similar constant low values (FSH 5-9  $\mu\text{g}\%$ , LH 2.2-3.1  $\mu\text{g}\%$ ) in males; female chimps had higher values (FSH 13-40  $\mu\text{g}\%$ , LH 2.2-6.1  $\mu\text{g}\%$ ). Moreover the females showed day-to-day cyclicality of varying amplitude (with 6-14 day periodicity). This sex difference in hypothalamo-pituitary function in infancy possibly represents an effect of differing intra-uterine exposure to endogenous androgen. This is the first demonstration of an endocrine sex difference in primates prior to puberty.

#### INFECTIOUS DISEASE

Acquisition of type-specific antibodies following exposure to *Hemophilus influenzae* b meningitis. G. PETER, S. GREENFIELD, V. M. HOWIE, and D. H. SMITH. *Children's Hosp. Med. Ctr. and Beth Israel Hosp., Boston, Mass.*

Type-specific antibodies (Ab) to *Hemophilus influenzae*, b (H. i.) are believed to confer protection against invasive infections by this organism. The rising incidence of Ab with age is generally cited to explain the decreasing incidence of H. i., b infections after age 3 yrs., but the antigenic experience responsible for eliciting Ab has not been defined. To investigate this question the incidence of hemagglutinating and bactericidal Ab among 4 groups of children was examined. (1) In a Day Care Center in which a 2 yr. old girl developed H. i., b meningitis, 7 of 8 of her classmates demonstrated markedly elevated Ab titers. H. i., b was cultured from the nasopharynx of only 3 of the 8 and this carriage was transient in 2 of 3 cases. In contrast, Ab titers were observed in (2) only 5 of 28 control children (2-4 yrs. old); (3) only 2 of 7 children with culture proven H. i., b otitis media; and (4) only 5 of 17 children (<4 yrs. old) hospitalized with H. i., b meningitis, epiglottitis, or arthritis. These data suggest that acquisition of type-specific antibodies correlates more closely with intense exposure to H. i., b infection than with clinically significant *Hemophilus influenzae* infection.

Studies of children with natural infections with *H. influenzae* antibacterial serological test vs. type B. SARAH H. SELL and RICHARD B. JOHNSTON, JR. (Intr. by David T. Karzon). *Vanderbilt Univ. Sch. of Med., Nashville, Tenn., and Univ. of Ala., Birmingham, Ala.*

Polyribose phosphate (PRP) antigen from *H. influenzae*, type b, is available for clinical trials for prevention of serious infections, such as septicemia and meningitis. It is therefore critical to document bacteriological and serological events in natural infections. 20 normal children were followed from birth through 5 years