331 MATERNAL-FETAL TRANSFER OF MELATONIN IN THE NONHUMAN PRIMATE. Steven M. Reppert, Ronald A. Chez, and David C. Klein (Spon. by Joseph D. Schulman), NICHD, NIH, Bethesda, Md.

Pregnant primates have been shown to have a large diurnal (24-hr) rhythm in circulating melatonin (MEL). We examined whether alterations in circulating maternal MEL could be transferred to the fetus by giving i.v. injections or infusions of MEL to pregnant monkeys. Three rhesus monkeys with timed gestations (± 1 d) underwent hysterotomy at 151 d gestation. [^{3}H]MEL levels were determined by chloroform-extraction and authenticated by TLC in the injection studies; MEL plasma levels were measured by RIA in the infusion studies.

Three min after a maternal injection of a trace amount of [^{3}H]MEL (1µg, 150µCi) fetal plasma [^{3}H]MEL levels were 84 ± 9% (SE) of maternal [^{3}H]MEL levels (168 ± 14 pg/ml). Parallel rates of disappearance occurred in both circulations over 30 min. Peak amniotic fluid [^{3}H]MEL levels of 17 ± 2% maternal plasma levels occurred at 30 min. Postmortem examination of CSF from 2 fetuses showed [^{3}H]MEL levels equal to fetal plasma levels.

To mimic endogenous changes in maternal MEL, 0.4 µg/min authentic MEL was infused to the mothers for 20 min. Prompt 6- to 12-fold MEL increments occurred in both circulations; parallel decrements occurred following the infusion.

These findings indicate the MEL, the putative pineal hormone, is rapidly transferred to the fetus in late primate pregnancy. The placental transfer of MEL may introduce the fetus to 24 hr periodicity and provide information about ambient lighting.

332 ACTION OF HUMAN GROWTH HORMONE (hGH) ON THE PERIPHERAL METABOLISM OF THYROXINE (T4). Iraj Rezvani, Angelo M. DiGeorge, Carlos J. Bourdony and Steven A. Dowshen. Temple University School of Medicine, Department of Pediatrics, St. Christopher's Hospital for Children, Phila., Pa.

In previous studies, we have shown that administration of hGH increases the half life of serum triodothyronine (T_3). We have now examined the effect of hGH on a loading dose of T_4 in 7 hypopituitary children (7 to 18 years of age). Before and after one month of hGH therapy (2 U t.i.w.) a single dose of T4 (1.2 mg/M$_2$) was administered orally, serum levels of T_3 and T4 were measured at 0,2,4,6,12,18,24 hrs. and daily thereafter for 6 days. Serum levels of T_4 peaked between 4 to 6 hrs. post ingestion and declined slowly to baseline values by the 6th day. The values for serum levels of T_4 were not affected by hGH therapy. There was a rise in serum levels of T_3 as early as 2 hrs. post ingestion but no uniform peak was discernable. The baseline values for serum T_3 were reached by the 6th day after several erratic fluctuations. Serum levels of T_3 were significantly higher after hGH therapy. This increase was more pronounced when the values were expressed as the ratio of T_3/T_4. These data indicate that hGH causes an increase in serum levels of T_3. Although this, in part, may be due to increase in half life of serum T_3, the long lasting elevation of serum T_3, as obtained in this study, can only be explained by an increase in extrathyroidal conversion of T_4 to T_3.

333 CONTINUOUS INFUSION OF AQUEOUS PITRESSIN FOR ACUTE TREATMENT OF DIABETES INSIPIDUS (DI). Iraj Rezvani, Angelo M. DiGeorge, Robert Rapaport and Henry G. Artman. Temple University School of Medicine, Department of Pediatrics, St. Christopher's Hospital for Children, Phila., Pa.

The management of DI in a patient who requires prolonged parenteral fluid therapy poses a great challenge to the clinician. Erratic absorption of pitressin in oil and the short action of aqueous pitressin make these preparations unsuitable for the purpose. We have used continuous infusion of aqueous pitressin in 2 patients (2 and 12 years of age) who developed DI immediately following resection of craniopharyngioma. Both patients required prolonged parenteral therapy. An I.V. priming dose (0.05 U) of aqueous pitressin was followed by continuous infusion of pitressin at the initial dose of 3 uU/kg/min. Both patients were kept on maintenance I.V. fluids and the rate of infused pitressin was adjusted until the optimum dose of pitressin was achieved. This was determined by monitoring serum and urinary sodium, urine volume and specific gravity and daily weights. The optimum dose of pitressin appeared to be 50 uU/kg/hr. No untoward side effects were observed. The short half life of I.V. aqueous pitressin renders the minute to minute adjustment of the dose a practical feasibility.

334 ELEVATED GONADOTROPINS, PERSISTENT MÜLLERIAN STRUCTURES, AND NORMAL TESTICULAR ULTRASTRUCTURE IN A GIRL WITH MIXED GONADAL DYSGENESIS: Barry H. Rich, Anne W. Lucky, Robert L. Rosenfield, Nanette Roche-Bender and Francis H. Straus, Univ. of Chicago Pritzker Sch. of Med., Wyler Children's Hospital, Dept. of Ped. and Path., Chicago.

A 7 month old child raised as a female had ambiguous genitalia with clitoromegaly, posterior labial fusion and a urogenital sinus. Her peripheral karyotype was 46 XY. She responded to hCG stimulation with an increase in serum testosterone from 59 to 211 ng/dl despite elevated basal gonadotropins (LH 34 ng/ml, FSH 736 ng/ml) which had suggested gonadal failure. At age 15 months, her LH (46 ng/ml) and FSH (670 ng/ml) remained high and she underwent laparotomy which revealed a septate vagina, a bicornuate uterus and fallopian tubes (Müllerian structures) as well as bilateral vasa deferentia (Wolffian structures). A right streak gonad contained multiple Müllerian ducts, whorls of collagen and hyperplastic steroid-secreting cells but no ova or follicles. A left intra-abdominal testis appeared normal by both light and electron microscopy with abundant germ cells and appropriate Leydig and Sertoli cell ultrastructure for age. No evidence for malignant change was seen.

The elevated FSH and persistent Müllerian structures in this child had suggested deficient inhibin and antimüllerian hormone, respectively. The Sertoli cell is the presumed source of these substances, however, no anatomic abnormality of the Sertoli cell could be demonstrated.

335 DEHYDRATION STUDIES AND RESPONSES TO CLOFIBRATE IN PEDIATRIC PATIENTS WITH DIABETES INSIPIDUS. Robert A. Richman, Douglas D. Notman and Arnold M. Moses (Spon. by Frank A. Oski) Departments of Pediatrics and Medicine, SUNY-Upstate Medical Center and VA Hospital, Syracuse, N.Y.

Some children with central diabetes insipidus (DI) may release ADH under certain conditions. We have studied 10 patients with central DI ranging in age from 3 to 18 years. Their evaluation included a dehydration test and a trial of clofibrate therapy.

During the dehydration test, hourly plasma and urine osmolalities (Posm & Uosm) were measured. When there was a plateau in Uosm, the patients received aq. Pitressin. Greater than a 9% rise in Uosm one hour later confirmed the diagnosis of DI. Four patients had a Uosm higher than their Posm revealing releasable ADH. This occurred with marked thirst associated with an elevated Posm. When the Posm exceeded 290 mOsm/l, the relationship of Uosm to Posm was always subnormal in our patients when compared to values obtained in 127 normal subjects. By comparing simultaneous Uosm and Posm values, the diagnosis of DI can be strongly suspected; and, the diagnosis will not be missed even in patients with DI who can release ADH when moderately dehydrated.

The 10 patients received clofibrate (500 mg q6h) for 3 to 7 days. Eight patients concentrated their urine 50 to 400% higher than previous levels during random hydration periods. These increases in Uosm were associated with decreases in daily urine volumes. Because Posm measurements during the trial of clofibrate were the same or even lower than during random conditions, we attributed this finding also to the presence of releasable ADH in most pediatric patients with central DI.

336 UTILIZATION OF THE ALTERNATIVE PATHWAY OF COMPLEMENT IN PATIENTS WITH THYROID DISEASE: PRESUMPTIVE EVIDENCE AGAINST A ROLE FOR ANTIBODY. Robert A. Richman, Ann E. Stitzel, Joan R. Urmson, Susan L. Loeffler and Roger E. Spitzer. State University of New York, Upstate Medical Center, Department of Pediatrics, Syracuse, NY.

Complement studies were performed on 21 patients, 2 months to 16 years of age, with various types of thyroid disease. Circulating antithyroglobulin or antimicrosomal antibodies were present in 12/21 (titers > 1:40). All sera were quantitated for C4 (classical pathway); factor B, properdin and properdin convertase (alternative pathway); C3 and C3-C9 activity (both pathways). In addition, functional assays were done by determining the extent of complement activation by an immune complex (classical pathway) or by zymosan, cobra venom factor, or rabbit erythrocytes (alternative pathway). Abnormalities were found in 16 patients, 11/12 with antithyroid antibodies and 5/9 without detectible antibodies. All but one of the abnormalities occurred in the alternative pathway. These consisted primarily of low serum levels (> 3 SD below the mean for age) of factor B and properdin or ineffective function with CoF. Such abnormalities suggest in vivo utilization of this pathway. No association, however, exists between the titers of antibody and any abnormality. Since C3 is deposited on the thyroid gland in many of these disorders, it would appear that it is the alternative pathway which is responsible for that deposition. Further, since antibody is not usually associated with alternative pathway activity, its role in that process is open to question.