	Phos. Excretion mg/24 hr/1.73 M^2	Phos. Clearance ml/min/1.73 M^2	Urinary CAMP 24 hr nanomoles	Urinary CAMP 24 hr μmoles per gm creat
Mean ± S.E.M.				
Day 1	7.86 ± 2.56	0.09 ± 0.03	53.2 ± 10.89	2.37 ± 0.41
Day 2	443.50 ± 77.12	3.49 ± 0.62	208.6 ± 37.00	6.93 ± 0.96

This 3–4 fold increase in cyclic AMP could reflect increasing PTH renal responsiveness and/or increasing secretion of PTH. One and 3 day old infants and adults were given a one hour PTH infusion (5 μ/Kg/hr) measuring urinary cyclic AMP in time periods before and after the infusions. Peak increases in responses from baseline of cyclic AMP were 1.64 ± 0.34, 7.15 ± 1.15 and 36.30 ± 0.73 μmoles/gm creatinine mean ± range on first day, third day and adults respectively with similar relationships of increasing phosphate excretion and decreasing % TRP. Thus, the development of newborn renal responsiveness to parathyroid hormone is on the cellular cyclic AMP level suggesting increasing maturation of the enzyme adenyl cyclase which forms cyclic AMP from ATP.

Pseudohypoparathyroidism without clinical stigmata. ROBERT M. CORWIN, GAETANO VISCO, and WILLIAM H. BERGSTROM. *State Univ. of New York Upstate Med. Ctr., Syracuse, N. Y.*

Five cases of pseudohypoparathyroidism without the usually associated clinical stigmata of short stature, mental retardation, brachydactylia and moon facies have recently been identified in Syracuse. Four of the cases are in the same family. The familial proband was a 12 year old, previously asymptomatic girl who, following a grand mal seizure, was found to have hypocalcemia, hyperphosphatemia, an elevated alkaline phosphatase and radiologic hyperparathyroidism. She was refractory to parathyroid extract but did respond to large doses of calciferol. Her father, brother, and two of her three sisters were clinically and biochemically normal. However, her 46 year old mother and 20 year old sister had biochemical pseudohypoparathyroidism. Investigation of this family has also revealed a maternal uncle with pseudohypoparathyroidism and a 79 year old healthy maternal grandfather with biochemical evidence of hyperparathyroidism. The fifth case is that of a tall, thin, highly intelligent black male who has been followed for 12 years with a history of grand mal seizures controlled with anticonvulsant medications (Dilantin, Phenobarbital and Mysoline). After a wrist injury, x-rays revealed unsuspected bone resorption. Subsequent studies disclosed hypocalcemia, hyperphosphatemia, elevated alkaline phosphatase, and generalized osteitis fibrosa cystica. He was refractory to parathyroid extract but did respond to large doses of calciferol with complete healing of the bone lesions. These five cases are presented to re-emphasize the fact that pseudohypoparathyroidism need not be associated with clinical stigmata.

Improved prognosis in congenital hypothyroidism treated before three months. Behavior concerns of parents of treated cretins. ALAN KLEIN, STEPHANIE MELTZER, and FREDERIC M. KENNY (Intr. by T. K. Oliver). *Univ. of Pittsburgh Med. Sch., Pittsburgh, Pa.*

We explored the possibility that a critical period exists during the first few months of life, when treatment should be started in order to obtain a normal IQ. Previous publications have not fractionated the first 6 months of therapy for comparison of IQ results by a single test procedure. Thirty-one cretins were tested by Stanford Binet after age 3 years. A significantly higher percentage had IQ > 85 when treated before 3 months (Chi-Square $p < 0.02$) indicating that thyroprevia is most harmful during the period that CNS neuronal number is increasing.

Age in Months When Treated	<3	3-4	5-6	>7
Number of patients with IQ > 85	7	1	2	0
Number of patients with IQ < 85	2	7	6	6

Questionnaires disclosed twice as many behavior concerns in parents of cretins with IQ < 85 than in those with IQ > 85 whose parents had no more worries than those of age matched normals. Parents had anxiety about punishment of these children who were characterized as "high strung, stubborn, contrary" and whose "feelings were easily hurt." Concern was high regarding future education and jobs.

Since clinical diagnosis of cretinism is difficult during the first 2 months of life, and since it is as common (1:8,000 live births) as phenylketonuria (1:10,000), a routine screening procedure is warranted. Systematic psychological counseling should be an integral part of therapy.

Placental transfer of thyronines and thyrotropin in sheep. JEAN H. DUSSAULT, JOSEPH J. DISTEFANO, and DELBERT A. FISHER. *UCLA Sch. of Med., Harbor General Hosp., Torrance, Calif.*

Data in a number of species suggest that placental transport of thyronine is limited in extent. Data regarding placental passage of TSH is indirect but suggests little or no transfer. The present studies were conducted to quantify T4, T3 and TSH transfer directly in both the maternal-fetal and fetal-maternal directions. Indwelling exteriorized fetal catheters and maternal jugular vein catheters were placed in pregnant sheep. Simultaneous tracer doses of 131-I-T4 and 125-I-T4 were injected into the fetus and mother, respectively, in one study (6 animals); 131-I-T3 and 125-I-T3 in another (6 animals); and 131-I-BTSH and 125-I-BTSH in a third (5 animals). Serial blood samples were collected for periods up to 96 hours. These were extracted with butanol (for T3 and T4) or ppt with specific BTSH antibody (for TSH), and counted in a double isotope counting system to assess placental transfer of labeled hormones. There was no significant transfer of labeled T4 or TSH. However significant transfer of labeled T3 occurred in both the fetal-maternal and maternal-fetal directions. By assessing maternal and fetal T3 kinetic data and assuming exchange between two compartments it was possible to quantify this transfer. Fractional transfer rates were 0.045 and 0.0023 hr.-1 in the fetal-maternal and maternal-fetal directions respectively. Since hormone pools and turnovers were measured it could be estimated that about 2 μg T3 were transferred daily in both directions. This approximated 0.5% and 2.0%, respectively, of total daily maternal and fetal thyronine turnover. These data further support the view that the fetal pituitary-thyroid axis functions autonomously of the maternal system.

Neonatal and early childhood hyperthyroidism: An expression of hereditary Graves disease. DOROTHY R. HOLLINGSWORTH, C. CHARLTON MABRY, and JOHN M. ECKERD. *Univ. of Kentucky, Lexington, Ky.*

We have studied six infants and young children with hyperthyroidism whose clinical course differs from the few reports of others. Neonatal and early childhood hyperthyroidism are usually thought of as separate, rare, and transient disorders seldom requiring long term treatment. 1) Our cases have not been transient: 2) they have occurred in families with a high incidence of adult Graves disease.

Four were born with Graves disease. Three continue to be hyperthyroid at ages 1, 5, and 6 years. Two developed Graves disease at ages 3 and 8 years and continue on anti-thyroid medication. Graves disease occurred in five of the six mothers and was apparent during gestation in four. The sixth mother, mother of a neonatal case, has never had overt Graves disease, but female members of four generations have had Graves disease. In all six kindreds there was a direct maternal line of affected patients for two or more generations.

Selected families were studied for the presence of latent thyroid disease using measurements of thyroid hormonal iodine. Some were screened for thyroid markers: PTC tasting and circulating thyroid antibodies. A rare unsuspected case was detected, but no thyroid marker pattern developed.

The occurrence of Graves disease in the very young in families with a high incidence of Graves disease suggests a hereditary factor. No goitrogens or use of medications were common to the families. We suggest that there is biologic unity between neonatal, early childhood and adult Graves disease. This unity is best explained by the presence of an autosomal dominant determinant with a predilection for the female.

Inhibition of masculine differentiation in male rat fetuses by two candidates for active-site-directed-irreversible (ASDI) inhibitors of 17α hydroxylase and C_{17-20} lyase. ALLEN S. GOLDMAN. *Children's Hosp. of Philadelphia, Philadelphia, Pa.*

ASDI inhibitors stoichiometrically bind to enzyme active-sites, have a high degree of "lock and key" specificity, cannot be removed from the active site by dilution and should have few side effects. Two synthetic steroids selected as ASDI candidates, 17β-ureidoandrosta-1,4-dien-3-one and 16β-bromo-5α-pregnan-3β,17α-diol-11,20-dione were found to inhibit the conversion of pregnenolone or progesterone to testosterone by adult rat testicular microsomes specifically at the level of both 17α hydroxylase and C_{17-20} lyase. When administered to pregnant rats at 30mg/kg daily from day 13 to day 21 each inhibitor significantly blocked penis formation in male offspring by reducing anogenital distance from 3.69 $\pm$ 0.24mm. (control) to 3.26 $\pm$ 0.22 (17β-ureide) and 3.32 $\pm$ 0.23mm. (16β-bromide). Testosterone production in vitro by experimental testes was only 25% of that of controls with either pregnenolone or progesterone as substrates. Abnormal accumulations of progesterone and 17-hydroxyprogesterone were present in incubations of experimental testes. Female fetuses and maternal and fetal adrenal size and steroid synthesis were unaffected. Each inhibitor obliterated C_{19} steroid excretion in urines and feces of adult female rats as analyzed by gas-liquid chromatography and mass spectrometry. Thus, these inhibitors appear to block sex hormone without affecting glucocorticoid synthesis in adult and fetal rats.

Rapid diagnosis of congenital adrenal hyperplasia (CAH) by plasma steroid determinations. ROBERT C. FRANKS. *Univ. of Texas Med. Sch. at San Antonio, San Antonio, Tex.* (Intr. by Michael J. Sweeney).

A semi-quantitative method for steroid determinations in a 0.5 ml plasma sample has been evaluated for the rapid (4–6 hr) diagnosis of CAH. Pet ether, benzene and methylene chloride extracts of plasma are quantitated by competitive protein binding using 17-hydroxyprogesterone (17-OHP), 11-deoxycortisol (cmpd S), and cortisol standards, respectively, for comparison. The observed plasma steroid concentrations are expressed as a ratio of "17-OHP" + "cmpd S" to "cortisol" since comparison of ratios, rather than absolute values, has been found to differentiate normals from patients more clearly.

Plasma samples have been obtained from six normal children aged 4 days–7 yrs following administration of ACTH, from six adults with 11-hydroxylation impaired by the administration of metyrapone, and from three children aged 11 mos, 6 yrs and 8 years with CAH due to deficient 21-hydroxylation (five samples). The ratios of "17-OHP" + "cmpd S" to "cortisol" for the respective groups have been determined:

	Range	Mean	1SD
Normals after ACTH	0.15–0.25	0.20	0.03
Normals after metyrapone	1.30–3.20	2.04	0.67
CAH	2.13–6.36	3.66	1.60

These preliminary results suggest usefulness of the procedure for rapidly ascertaining the presence or absence of the common variants of CAH, although further data from both normals and patients will be required for confirmation.

Urinary steroidal patterns in the adrenogenital syndrome. ALFRED M. BONGIOVANNI, WALTER R. EBERLIN, THOMAS MOSHANG, and HERBERT L. VALLET. *Univ. of Pennsylvania and Children's Hosp. of Philadelphia, Pa.*

The urinary steroidal pattern was reviewed in 7 cases of 21-hydroxylase deficiency (21-H) and 3 of 3β-hydroxysteroid dehydrogenase deficiency (3β-D). These were compared with 3 normals and 1 adrenal tumor of similar age. Pregnanetriol not only predominates in the urine of those with 21-H deficiency over Δ5-pregnene-3β,17α,21α-triol but in no instance did the latter substance exceed 0.9 mg./day and the ratio was 50:1 or greater. In 3β-D deficiency although pregnanetriol was found in each (in one case 34.6 mg./day) there was great elevation of pregnenetriol and the ratio was 2:1 or less. In one experiment 17-hydroxypregnenolone administered to a normal volunteer was converted exclusively into pregnanetriol. It is proposed that in 3β-D deficiency there may be peripheral conversion to pregnanetriol and careful measurement of these two triols can differentiate the two conditions. In addition pregnanetriolone was not found in 3β-D deficiency but was present in the 21-H deficiency and several steroids present in and peculiar to 3β-D deficiency were not found in 21-H deficiency. Gas chromatography was employed in these studies. The earlier hypothesis from this laboratory that pregnanetriol in 3β-D deficiency might represent a double defect no longer appears valid. (Drs. Maria I. New and Frederic M. Kenny kindly supplied specimens from 2 established cases)

Familial primary aldosteronism with delayed glucocorticoid responsiveness: A new syndrome? G. S. GIEBINK, R. W. GOTLIN, F. H. KATZ, and E. G. BIGLIERI (Intr. by H. K. Silver). *Univ. of Colo. Med. Ctr., VAH, Denver, Colo. and U. of Calif., San Francisco, Calif.*

Two brothers, ages 7 and 9, with systolic and diastolic hyper-