

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  $17\alpha$  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,  $17\beta$ -ureidoandrosta-1,4-dien-3-one and  $16\beta$ -bromo- $5\alpha$ -pregnan- $3\beta$ ,  $17\alpha$ -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  $17\alpha$  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  $3.69 \pm 0.24$ mm. (control) to  $3.26 \pm 0.22$  ( $17\beta$ -ureide) and  $3.32 \pm 0.23$ mm. ( $16\beta$ -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  $3\beta$ -hydroxysteroid dehydrogenase deficiency ( $3\beta$ -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  $\Delta 5$ -pregnene- $3\beta$ ,  $17\alpha$ ,  $21\alpha$ -triol but in no instance did the latter substance exceed 0.9 mg./day and the ratio was 50:1 or greater. In  $3\beta$ -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  $3\beta$ -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  $3\beta$ -D deficiency but was present in the  $21$ -H deficiency and several steroids present in and peculiar to  $3\beta$ -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  $3\beta$ -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-