●1272 CONGENITAL MALFORMATIONS ASSOCIATED WITH RHABDOMYOSARCOMA: AN ASSOCIATION WITH CENTRAL NERVOUS AND GENITOURINARY SYSTEMS ANOMALIES. A REPORT FROM THE INTERGROUP RHABDOMYOSARCOMA STUDY (IRS). F. Ruymann, H. Maddux, A. Ragab, E. Soule, N. Palmer, E. Gehan, and W. Newton, for the IRS Committee of CCSG and POG. Ohio State University College of Medicine, Department of Pediatrics, Columbus, Ohio 43205.

Congenital malformations in patients with rhabdomyosarcoma (RMS) eligible for IRS I and II were reviewed in the reports of 97 complete and 17 incomplete autopsies. Using the Collaborative Perinatal Project (CPP) for the baseline incidence, an increased number of central nervous system (CNS) and genitourinary (GU) anomalies were found. Four major and 5 minor CNS anomalies were found in 99 children including diffuse microgyria with hydrocephalus, myelomeningocele with hydrocephalus and Arnold-Chiari malformation, cerebral cortical atrophy, and an enormous corpus callosum. The CPP incidence of CNS malformations was 5.29/1000. Four major and 6 minor GU anomalies were present in 110 cases including medullary/cortical hypoplasia with decreased nephrons and a double ureter, single horseshoe kidney, a multicystic kidney with cortical hypoplasia, and a simple renal cyst. The CPP incidence of GU malformations was 7.29/1000. Two major cardiovascular (CV) anomalies occurred in 109 autopsies, including a tetracuspid pulmonic valve and two accessory coronary ostia, with a CPP incidence of 8.03/1000. One case was consistent with a diagnosis of Rubenstein-Taybi syndrome; another had presumptive neurofibromatosis. Two infants had congenital RMS. The association of congenital anomalies with RMS suggests that factors during development may be both teratogenic and oncogenic.

†1273 H-Y ANTIGEN DETECTED BY ENZYME LINKED IMMUNOSORBENT ASSAY (ELISA). A. Simpson, P. Saenger, S. Pang, C.A. Moreira-Filho, M. Brunner, S.S. Wachtel, Depts. of Peds., A. Einstein Coll. Med., Bronx and Cornell Univ. Med. Ctr., New York.

In a newborn (46,XX) with ambiguous genitalia and bilaterally descended gonads the presumptive diagnosis of true hermaphroditism (TH) was made using endocrinological methods and a newly developed ELISA system with monoclonal H-Y antibody. Evidence for cryptic testicular tissue was obtained by measuring male levels of testosterone in plasma (117 ng/dl). 17OH progesterone levels were normal thus ruling out congenital adrenal hyperplaisa.ELISA for H-Y antigen involves the reaction of monoclonal H-Y IgG antibody (AB) and cell borne or soluble antigen (AG). After that a 2nd AB (conjugated to peroxidase enzyme) is added. The amount of color (optical density) measured in a densitometer is a function of the interaction of AB and AG and consequential reaction of perioxidase with substrate. The patient tested positive for H-Y antigen but levels were less than those found in normal males. H-Y positive phenotypes in XX TH and XX male sex reversal obtained with this technique are consistent with the notion that the two conditions are variants of the same X-linked disorder and that the morphologic difference between the two may be related to the degree of inactivation of the X chromosome bearing the mutant gene. TH was confirmed at surgery when ovotestes were found. Conclusion: H-Y testing using ELISA technology can be performed rapidly with small amounts of blood (5 ml). Thus this assay is particularly useful in the evaluation of newborn infants with ambiguous genitalia where quick diagnosis is essential.

●1274 DELINEATION OF VARIABILITY WITHIN FAMILIAL NOONAN'S SYNDROME. David R. Witt, J.G. Hall, J.E. Allanson, D.R. Wilson, UBC Dept of Medical Genetics, Vancouver, B.C.

Attempts to characterize the Noonan syndrome/phenotype have been frustrating and confusing since published descriptions have been incomplete and family members have rarely been studied. At the David Smith Malformations and Morphogenesis Meeting in August 1983, a workshop was held to try to define the clinical features of the Noonan syndrome. After reviewing cases brought by the conference participants and literature reports, a comprehensive checklist was compiled which represented the spectrum of features which should be considered in assessing an individual with Noonan phenotype. Subsequently, using this checklist, we have re-evaluated our own 39 patients and were able to identify two distinct groups: 23 sporadic cases and 16 familial cases (in 4 families). The four families were re-examined in detail in an attempt to delineate the intrafamilial variability and the natural history of familial cases, and to determine whether any specific phenotypic traits were pathognomonic or diagnostic. In these four families we could identify a characteristic facies which changed with age, and a range of heart lesions, stature and I.Q. In comparing the features found in our four families to our sporadic cases, heterogeneity was obvious. At least 4 subgroups of the Noonan phenotype could be defined. Certain features were more commonly associated with the sporadic cases than with the familial. In addition, within our four families there was an increased number of affected individuals when compared to unaffected (2:1), and an increased number of affected males compared to affected females (2:1). These abnormal ratios are similar to the segregation ratios found in previously reported families.

NEONATOLOGY

1275 MABP IN THE FIRST 48 HOURS OF LIFE IN PREMATURE INFANTS WITH IVH. M.A. Adams, L. Benson, J.F. Pasternak, T.G. Gardner (spon. by C. Hunt), Dept. Peds., Div. Neonatology, Evanston Hospital, Evanston, IL.

The pathophysiology of intraventricular hemorrhage (IVH) in premature infants remains unclear. Recent evidence has implicated increased cerebral blood flow (CBF) and specifically systemic hypertension as a major determinant of increased CBF. Hypotension alone has not been implicated as an etiologic factor of IVH. We monitored continuously true mean arterial pressure (MAP) via an umbilical artery catheter with a pressure transducer and module interfaced with a microcomputer in 9 premature infants with IVH grades II-IV and 9 gestational age matched controls. Continuous recording was initiated by one hour of age in 7 infants, two hours in 6, and in all infants by eight hours; 3600 MAP determinations were stored sequentially each hour. The 1st 48 hours of data were subjected to statistical analysis. Hourly means of the 9 IVH infants were consistently lower than the means of the control infants although the difference did not reach statistical significance. The slope of the two regression lines of MAP verses postnatal age for the IVH infants and the controls was the same (.12 mmHg/hour) but with difference intercepts, (35 mmHg verses 31 mmHg). Variability was assessed by comparing mean hourly variances of the two groups. The mean hourly variance of the IVH group was consistently lower than the control group although the difference was not great. Our data suggests that MAP and variability in the first 48 hours after delivery and before the occurrence of IVH is not greater in the infants with IVH than in those without.

●1276 BILIRUBIN ASSOCIATED ABNORMALITIES OF THE AUDITORY BRAINSTEM RESPONSE IN AN INFANT RHESUS MONKEY MODEL. Charles E. Ahlfors, Craig T. Shoemaker, Stephen H. Bennett and William G. Ellis. School of Medicine, Department of Pediatrics University of California, Davis, California

Neonatal bilirubin toxicity (kernicterus) frequently results in deafness. The auditory brainstem response (ABR) has used as a hearing screening tool for newborns. We studied the potential usefulness of the ABR for detecting neonatal bilirubin toxicity using a rhesus monkey infant model.

Five rhesus monkey infants aged 1,6,20, 35, and 40 days received up to 300 mg/kg of intravenous bilirubin over four hours with ABR monitoring. The one day old infant was a non-asphyxiated premature with hyaline membrane disease. If no bilirubin induced ABR change occurred, sulfisoxazole (200 mg/kg), a bilirubin displacer with no effect on the ABR, was given. Progressive ABR flattening was observed in the premature (bilirubin only) and in the 6 day old (bilirubin and sulfisoxzole). The total bilirubin concentrations at the time of ABR flattening were 33 and 60 mg% for the premature and 6 day old, respectively. The ABR in the 6 day old partially recovered in 24 hours. However, the Wave I-V latency had increased from 3.31 msec initially to 3.75 msec and the I/V amplitude ratio decreased from 2.0 to 0.7. No yellow staining was found in the brains of these two animals. No bilirubin induced ABR changes occurred in the 3 older animals.

The auditory evoked response may be a sensitive, early indicator of reversible bilirubin toxicity, and the infant rhesus monkey may be a useful paradigm for studying bilirubin toxicity.

1277 ESTIMATE OF CREATININE CLEARANCE IN PRETERM INFANTS DURING THE FIRST MONTH OF LIFE. Arie L. Alkalay, Jeffrey J. Pomerance, Murugesa Thangavel, Mary Buechlein, and Sergio J. Farber. UCLA School of Medicine, Cedars-Sinai Medical Center, Department of Pediatrics, Los Angeles, California.

Previous work enables us to derive an equation for estimating creatinine clearance based on body length and serum creatinine in children and infants beyond the first month of life.

The purpose of the present study was to derive a simple equation for measuring creatinine clearance in appropriate for gestational age, preterm infants during the first month of life. To date, approximately one-half of the study has been completed. In 33 infants, 28-36 weeks' gestation, creatinine clearance was calculated from measurements of serum and urine (24 hour collection) creatinine. Post-natal age ranged from 4-30 days.

Gestational age, post-natal age, sex, Apgar Scores, weight, length, head circumference, serum creatinine, and aminoglycoside therapy, were subjected to multiple regression analysis. The ratio of body weight to serum creatinine had the best correlation with creatinine clearance ($r = 0.63$; $p < 0.01$). The regression equation is $y = 7.92033 + 0.00665$ weight/serum creatinine (standard error of the estimate = 6.39). The predicted creatinine clearance differed from the observed creatinine clearance by [0.09-15.11 ml/min/1.73m^2]. The addition of more patients will likely improve the ability to determine a stable coefficient for predicting creatinine clearance. Validation of the regression equation on a prospective sample will then be performed.