●1248 ETHANOL NEUROTOXICITY IN VITRO. Kimberly E Dow and Richard J Riopelle. Queen's University, Depts. of Pediatrics and Medicine, Kingston, Canada. (Spon. by Michael W Partington)

Prenatal exposure to ethanol produces a characteristic phenotype and a constellation of nervous system abnormalities. Effects of ethanol on the developing nervous system occur during early neurogenesis when neuron-matrix interactions and process formation are proceeding.

An in vitro paradigm which quantitates both substrate interaction and process formation has been used to examine directly the effects of alcohol on embryonic neurons. Nerve Growth Factor (NGF) produces dose-dependent neurite outgrowth from responsive chick embryo neurons following attachment to an appropriate substrate (J Neurobiol 12, 175, 1981). Ethanol and its metabolite acetaldehyde produced dose-dependent inhibition of NGF-induced neurite outgrowth. The 50% toxic dose (TD 50) of ethanol was 175 mg/100ml (38mM) and the TD 50 of acetaldehyde was 2.5mg/100ml (0.6mM). No effects were seen on neuron attachment to the substrate or on neuron viability at 24hrs. These data suggest that ethanol is toxic to neuron process formation at concentrations considered moderate in the human circulation. Consistent with in vivo experimental studies there was a rank order of toxicity with acetaldehyde having greater toxic effect than ethanol on a molar basis.

Ethanol may exert its toxic effects on neuronal development by interfering with the ability of neurons to respond to trophic influences within their environments. Further studies using this paradigm may contribute to an understanding of the teratogenic potential of alcohol, anticonvulsants and other xenobiotics.

1251 CUTIS LAXA, HYPOSPADIAS AND OLIGOHYDRAMNIOS SEQUENCE IN A NEWBORN: A DISCRETE SYNDROME. Ellen M. Bifano, Lytt I. Gardner, Karen J. Sanders, Rita M. Ryan, James S. Pergolizzi and Shiraz G. Sunderji. SUNY Upstate Medical Center, Depts. of Pediatrics and OB-GYN, Syracuse, New York.

This boy's birth weight was 2960 gm. Sonogram done at 14 weeks gestation was normal; at 30 weeks sonogram showed no amniotic fluid. Cesarian section at 35½ weeks revealed a deformed infant with loose folds of skin hung around his head in an "elephant man" appearance. A cape-like fold drooped from the nape of his neck, and redundant skin hung from his trunk and extremities. Hands and feet were puffy like little balloons. On the right was a "Potter ear", and the palate was high-arched. The shoulders, radial heads and hips were dislocated. The digits appeared to dislocate in various directions. There was a left club foot. The phallus had a swollen foreskin, with 3rd degree hypospadias. Scrotum was hypoplastic with palpable right gonad. Karyotype was 46,XY. Renal, abdominal and head sonography were normal, as were echocardiography and EKG. The case closely resembles that of Kaye et al. (AJDC.127:115,1974). Experimental oligohydramnios in animals results in multiple articular deformities (including club feet), high-arched or cleft palate and primitive digits (DeMyer and Baird, Teratology 2:33 1969). Our patient shows many of the deformities seen in human oligohydramnios sequence. We propose that this clinical picture may be explained by a genetic defect (?single gene disorder) mediating the genital anomaly, cutis laxa and oligohydramnios, and that the various deformations follow in the train of the oligohydramnios.

●1249 PSEUDODIASTROPHIC DYSPLASIA: A DISTINCT NEONATAL SKELETAL DYSPLASIA. DJ Eteson, GR Beluffi, C Belloni, F. Paolillo, S Sherman, RS Lachman, and DL Rimoin, Harbor-UCLA Medical Center, Torrance, CA; Universita di Pavia, Pavia, Italy; Ospedale Maggiore, Lodi, Italy; and Children's Hospital, Oakland, Ca.

In 1974, Burgio et al. described pseudodiastrophic dysplasia (PDD) as a distinct neonatal skeletal dysplasia which superficially resembled diastrophic dysplasia (DD). The two sisters reported died in infancy of unexplained hyperthermia. A third case, reported by Canki in 1979, also died in infancy.

We wish to report three new, unrelated cases of PDD, including two children who have survived infancy, the oldest now 4 years old. Clinical features include: relative macrocephaly, flat midface, abnormal pinnae which do not undergo cystic enlargment, small chest, scoliosis, rhizomelia, flexion contractures of the hands, and club feet. Unique radiographic features include proximal interphalangeal joint dislocations and platyspondyly. The metacarpals are short but normally modelled. In the older children, the hand and foot abnormalities have improved with physical therapy alone, which also distinguishes PDD from DD. Scoliosis has been progressive, and the oldest child has recently undergone spinal rodding.

Morphologic examination of chondro-osseous growth plate of one of the original cases and our oldest patient revealed non-specific changes. The focal degeneration of cartilage with intracartilaginous ossification characteristic of DD was not seen. The pathogenesis of this unique, apparently autosomal recessive, neonatal skeletal dysplasia remains to be elucidated.

●1252 A NEW AUTOSOMAL DOMINANT NEUROECTODERMAL SYNDROME. Mahin Golabi, Elizabeth B. Crawford, Seymour Packman, Mary L. Williams, Robert B. Jaffe, Department of Pediatrics and Reproductive Sciences, University of California and Mt. Zion Hospital, San Francisco, CA

This report describes three males and four females in three generations of a family with a new, progressive neuroectodermal syndrome. The principal features are: seizure (6/7); cerebral vascular accident (1/7); generalized hirsutism (7/7); low frontal hair line and temporal projection of scalp hair onto forehead (7/7); coarse facies (7/7); redundance of skin of the eyelids (blepharochalasis) (5/7); thick lips (6/7) hyperplasia of tissue in anterior palatal region (4/7) and cutis verticis gyrata (5/7). Abnormalities are more marked in males. No corneal leukoma, clubbing of the digits, periostosis or mental retardation are present. Androgen profiles and FSH/LH ratios in the two cases tested are normal. The occurrence of this disorder in three generations with male-to-male transmission documents autosomal dominant inheritance. This condition has features in common with pachydermoperiostosis, however it lacks clubbing and periostosis. Pashayan et al. (1973) reported on a family with blepharo-naso-facial syndrome; these individuals have many similarities to our cases, yet they have marked dystopia canthrum, torsion dystonia, and mental retardation which are not present in our cases. Gingival fibromatosis-hypertrichoses syndrome differs by having extensive gingival fibromatosis and mental retardation. Autosomal dominant syndrome of cutis verticis gyrata and thickening of the oral mucosa (Hughes, 1983), has many features in common with our cases but lacks hirsutism. We conclude that our cases represent a new syndrome.

1250 BLOOD DISORDERS AND CARDIAC MORPHOGENESIS. Charlotte Ferencz, Judith D. Rubin, Robert J. McCarter, Phillip D. Wilson, Joel I. Brenner, Catherine A. Neill, Lowell W. Perry, Seymour I. Hepner, John W. Downing, (Spon. by Glenn C. Rosenquist). University of Maryland School of Medicine, Department of Epidemiology and Preventive Medicine and The Baltimore-Washington Infant Study Group, Baltimore, Maryland.

An epidemiologic study of congenital heart disease (CHD) is in progress in the Baltimore-Washington area of 85,000 annual births. Infants with CHD are studied in comparison to a representative sample of the birth cohort. Family histories of 696 cases and 908 controls reveal heritable blood disorders (HBD) in 1% of CHD infants and/or parents, including hemophilia, von Willebrand's disease (v. W's), spherocytosis, thalassemia and sickle cell disease (SCD); only SCD occurred in 2 controls. Additional cases gathered from pediatric cardiologists and the literature suggest that transposition of the great arteries and valve lesions are predominant with HBD. An etiologic association is biologically plausible: cyanotic and acyanotic CHD occur with various coagulopathies and with familial fibrinogen and coagulation factor deficiencies; v. W's is linked with mitral valve prolapse and teleangiectasias.

Two possible morphogenic mechanisms include a gene induced alteration of early cardiac endothelium which also secretes factors VIII and v. W's (Jaffee, E.A., N. Engl. J. Med. 296:377, 1977) and/or alterations of osmosis of embryonic blood causing the teratogenic "edema syndrome" (Grabowski, C.T., J. Exp. Zool. 157:307, 1964). The studies suggest HBD as a potential risk factor for CHD.

●1253 EFFECT OF PHENCYCLIDINE (PCP) ON THE FETUS. N.L. Golden, B.R. Kuhnert, S. Martier, R.J. Sokol. Case Western Reserve Univ., Cleveland Metropolitan General Hospital Dept. of Pediatrics and OB/GYN - (Spon. by S. Kalhan).

The purpose of this study was to report the effects of maternal PCP use on the fetus. 94 neonates whose mothers had a history of PCP exposure were compared with 94 control infants. Mothers of study and control patients were matched by maternal date of recruitment, ethnicity, weight, parity, weeks gestation at registration, and tobacco smoking behavior. PCP using women tended to be multiple drug abusers compared to non PCP users (mean number of drugs used 1.4±1.12 vs 0.6±0.8) [$p < 0.001$]. PCP use was assessed by questionnaire and repeated urine testing. Infant growth, neurological function, physical characteristics, behavior, and hospital course were assessed by a single examiner blind to the maternal history. Study infants had a mean of 4.5±2.7 abnormalities while control infants had a mean of 3.6±2.4 abnormalities [p (2 tailed)< 0.005]. Non parametric tests were used to determine which abnormalities differentiated the study from the control infants. Study infants were more likely to have poor attention, hypertonia, and depressed neonatal reflexes [$p < .05$]. Growth was normal and anatomic abnormalities were not found. The contribution of 7 classes of abused substances (narcotics, depressants, marijuana, stimulants, cocaine, glue, and alcohol) to the total number of abnormalities was assessed using stepwise multiple regression. Only PCP accounted for a significant percentage of the variance ($f = 4.38$; $p < .05$). This study indicates that maternal PCP alone may lead to abnormal neonatal neurobehavior.