PEROXISOMAL ENZYME DEFICIENCY IN THE CONRADI-HUNERMAN FORM OF CHONDRODYSPLASIA PUNCTATA. Ronald D. Holmes, Amiya K. Hajra, and Golder N. Wilson. William Beaumont Hospital, Divisions of Pediatric Gastroenterology and Genetics and the University of Michigan, Department of Biochemistry. Royal Oak & Ann Arbor, MI.

332

Heymans et al (New Engl. J. Med. 313: 187, 1985) have reported deficient dihydroxyacetone phosphate acyltransferase (DHAP-AT) in the autosomal recessive, rhizomelic form of chondrodysplasia punctata. We describe a partial deficiency of this peroxisomal enzyme in a female child with a dominant form of chondrodysplasia punctata (Conradi-Hunerman syndrome; chondrodysplasia calcificans congenita). Clinical manifestations in the child (age 7 months) included short stature, dysmorphic face with frontal bossing, shallow nasal bridge, shortened nose, brachycephaly and patchy alopecia; bilateral lenticular cataracts; asymmetric shortening of the left femur with scoliosis and multiple epiphyseal punctate calcifications; ichthyosis prominent at birth with residual swirls of hyperkeratotic skin. Her mother (age 39) had an adult height of 56 inches with similar clinical findings; she had a normal daughter by a different husband, two normal brothers, and no history of miscarriages or consanguinity. Activity of fibroblast DHAP-AT was 0.16 nmol per min per mg protein in the daughter and 0.46 in the mother compared to 0.50 in controls. Erythrocyte plasmalogens were normal in both patients. Other indices of peroxisomal dysfunction such as very long chain fatty acids, phytanic acid, and peroxisomal morphology were normal except for a qualitatively elevated urinary pipecolic acid in the child. These results add another disorder to the expanding spectrum of peroxisomal disease.

MATERNAL DRINKING AND FETAL CLUBFOOT. Silvia Iosub, Mahrukh Bamji, Richard K. Stone, Herbert Rich, Donald S. Gromisch, Edward Wasserman. (Spon. by Lawrence R. Shapiro). New York Medical College, Metropolitan and Lincoln Hospitals, Department of Pediatrics, New York.

●333

We studied the prevalence of clubfoot in 129 patients with Fetal Alcohol Syndrome (FAS) or Alcohol Related Birth Defects (ARBD) aged 1-24 years. The mothers were all chronic alcoholics who abused≥ 3 oz of absolute alcohol/day before and during pregnancy. They were divided in 2 groups: group I: alcohol abusers and group II: polydrug abusers (alcohol + narcotics ± cocaine). Group I comprised 55 mothers (40 blacks, 15 Puerto Ricans) and group II 30 (19 blacks, 11 Puerto Ricans). The socio-economic background, duration of alcoholism, average age at delivery and type of delivery were comparable in both groups.

Four patients (all males, 2 blacks and 2 Puerto Ricans) were found to have talipes equinovarus, as well as other anomalies. Three had bilateral and one unilateral clubfoot. All four were seen in the nursery, where the deformities were corrected, and two were followed in clinic. Two mothers belonged to group I and two to group II.

The occurrence of clubfoot in our study is significantly higher ($P<0.01$) than the accepted rate of 1.2/1,000.

In the embryo marked equinovarus is a normal stage of development. In the newborn it means permanent growth arrest, which might have been caused by various agents: viruses, radiation, thalidomide, etc. Since narcotic addiction during pregnancy does not result in congenital malformations in the offspring we submit that alcohol, a known teratogen, should be added to the above list

CONGENTIAL MALFORMATIONS INDUCED MY MONOCLONAL ANTIBODIES AGAINST RAT VISCERAL YOLK SAC. Marcela Jensen, Ivan Damjanov, Paz Vega, Thomas R. Koszalka and Robert L. Brent. Thomas Jefferson University and Hospital, Departments of Pediatrics, Pathology, Biochemistry and Anatomy, Phila, Pa.

334

Polyclonal antisera against rat visceral yolk sac (VYS) produces severe congenital malformations when injected into pregnant rats on the 9th day of gestation. To define and characterize the teratogen-stimulating antigen(s) from the VYS, monoclonal antibodies (MCA) against rat VYS were prepared. Spleen cells from BALB/c mice, hyperimmunized with VYS antigens purified by IEF and gel filtration were fused with two myeloma cell lines SP2/0-Ag 14 and P3x63 Ag. 8.653. Hybrids specific for VYS by indirect immunofluorescence were selected and cloned by limiting dilution and further expanded as ascitic tumor in BALB/c mice. More than 25 immunofluorescent hybrids for VYS have been selected and their biological activity defined. The first 12 clones were not teratogenic but since last year (1986) ascitic fluid from B-3 clone (IgG 2b type) induced CNS malformations and the clone D-4 (IgG 2a type) induced growth retardations when injected into pregnant rats on the 9th day of gestation. Each teratogenic MCA stained the apical portion of VYS endodermal cell, tubular kidney brush border and failed to react with kidney glomeruli, Reicherts membrane, long, lens capsule and liver tissue by immunofluorescence. Both teratogenic MCA's failed to recognize the VYS antigens by Western blots. Further studies will be directed toward using the teratogenic MAC's to study the mechanism of teratogenesis and the quantitative aspects of embryonic nutrition during early organogenesis. (Supported by NIH)

18p- SYNDROME: CLINICIANS FANTASY: Debasis Kanjilal and Ram S. Verma (Spon. by Ramesh C. Jhaveri). Departments of Pediatrics, Laboratories and Medicine, Interfaith Medical Center - SUNY Health Science Center at Brooklyn, New York.

335

Since the advent of banding techniques, more than one hundred syndromes have been described based on just chromosomal abnormalities. In the majority of those cases a specific chromosomal abnormality could not be suggested by physical examination alone. However, after cytogenetic evaluation was completed, new syndromes were discovered. The 18p- syndrome is one such example whose clinical manifestations are so heterogeneious that by simply examining the patient, the abnormality of chromosome 18 was not even suspected. In fact, our patient was referred for cytogenetic evaluation to rule out Turner syndrome. The major clinical features included: mental and growth retardation, a few dysmorphic facial features, protruding ears, low hair line in the back, severe dental caries and behavioral problems. This is the first reported case of psychosis in this type of genetic abnormality. Primary and secondary amenorrhea are most frequently reported, however, our case had normal sexual development and normal menstruation. After reviewing the current literature, we concluded that it is impossible to establish a 18p- syndrome without chromosomal analysis.

FAMILIAL NEPHRITIS, PROXIMAL RENAL TUBULAR DYSFUNCTION (PRTD), DEAFNESS, PRURITIS, ECZEMA AND HEPATOSPLENOMEGALY: A NEW SYNDROME. Kaplan, P., Reece, E. and Kaplan, B.S. Department of Pediatrics, The Montreal Children's Hospital, Montreal, Quebec

●336

Passwell et al (J. Pediatr. 98:85, 1981) described the association of nephritis, deafness, and Fanconi syndrome in a 4 year old girl. We have cared for this girl (S. now 12 years) and her 9 month old sister (A.), and wish to describe this syndrome in more detail. Parents are first cousins and have a healthy son.

The following have occurred in both sisters: early onset nephritis PRTD, bilateral moderately-severe high frequency nerve deafness, pruritis, eczema, hepatoslenomegaly and osteopenia. Both are incapable of sustaining antibody responses to diphtheria and tetanus immunizations. In addition S. has recurrent infections, asthma, immunological abnormalities, and growth retardation and had vocal cord granulations. The immune dysfunction is characterized by low levels of IgG with low and unsustained antibody responses to diphtheria and tetanus immunization. There is skin test anergy despite generally normal in vitro parameters of cell-mediated immunity.

The renal and ear abnormalities are more severe in degree and have presented much earlier than is usual in Alports syndrome, especially for females. This unique constellation of findings is suggestive of an underlying biochemical defect. Mucopolysaccharides have been detected in skin and urine (S.) but this is equivocal.

HETEROGENEITY IN X-LINKED SPASTIC PARAPLEGIA

Laura D. Keppen, Mark F. Leppert, Jean-Marc Lalouel, Peter O'Connell, Yusuke Nakamura and Ray L. White. (Spon. by Terry Yamouchi) University of Arkansas for Medical Sciences, Dept. of Peds., Little Rock, AR. and University of Utah Medical Center, Howard Hughes Medical Institute Salt Lake City, UT.

337

We describe a family with pure X-linked hereditary spastic paraplegia (HSP) and report linkage to X-chromosome DNA probes. A 6-generation pedigree (K313) with 12 affected males is presented. Eight affected males and 7 mandatory female carriers were personally examined. The disorder is characterized by delayed motor milestones and development of the typical spastic gait in adolescence. Deterioration is gradual for 20-30 years and then nonprogressive. Adults generally require crutches by age 30 and a wheelchair by age 50-60. Intelligence, upper extremity function, and vision were normal. Carrier females had a normal gait and neurologic exam. Eight X-chromosome linked DNA markers were used to genotype K313 and linkage was observed with pYNH3 ($\theta = 0$, lod = 4.6) and DXS17 ($\theta = 0$, lod = 4.0). These markers map to the Xq21-22 region, distinct from the Xq28 locus for complicated X-linked HSP reported by Kenwrick. These findings strongly support the clinical delineation of two distinct disease entities: pure and complicated X-linked HSP. This has important implications for genetic counseling when using DNA linked markers.