320 BECKWITH WIEDEMANN SYNDROME PRESENTING IN PREMATURE INFANTS. David A. Chitayat, Avi Rotschild, W. Emily Ling, James D. Dimmick and Judith G. Hall, University of British Columbia, Departments of Genetics and Pediatrics, Vancouver, B.C. Canada

Beckwith-Wiedemann syndrome (BWS) is characterized in most reported cases by the triad of Exomphalous, Macroglossia and Gigantism (EMG syndrome). However, these major manifestations probably represent the extremes of this syndrome while cases with minor or time-dependent manifestations are usually not published. We present the variable expressions of BWS syndrome in 3 preterm infants.

The first had 75th percentile measurements at her birth (32 weeks) with macroglossia, large fontanel, ear creases and omphalocele. At corrected age of 7 months she was diagnosed to have hepatoblastoma.

The second had 60-75th percentile measurements at her 28 week birth. Dysmorphia was not noted at birth or during life. At corrected age of 2-1/2 months, she developed signs of puberty, and at 4 months, hepatomegaly. The liver histologically showed extensive hepatoblastoma. At autopsy adrenal cytomegaly, pancreatic islet cell hyperplasia and umbilical hernia were also noted to be present.

The third had 97% weight, 75% height and 30% OFC at his 32 week birth. No anomalies were present at birth. Four weeks after birth he developed an umbilical hernia, facial coarsening and macroglossia (causing difficulty in breathing and feeding) but no visceromegaly. By the age of 3 months, the clinical presentation was highly suggestive of BWS. Extensive investigation failed to show any metabolic or endocrine abnormality.

●321 TANDEM DUPLICATION OF CHROMOSOME 1q IN FRYNS SYNDROME. RD Clark, T Mohandas, M. Fenner-Gonzales, (Sponsored by LJ Shapiro) Harbor-UCLA Med. Ctr, Depts of Peds and Pathology, Torrance, CA.

A newborn male with Fryns syndrome (FS), a lethal autosomal recessive condition, also had mosaic tandem duplication of chromosome 1q. Multiple malformations were noted at birth including diaphragmatic hernia, cleft palate, microglossia, hypoplastic digits, micrognathia, long philtrum, thin upper lip and short nose. The baby died at 5 hrs. of age. Autopsy revealed absent right middle lobe, bilateral renal cysts, hypoplastic renal arteries, urethral stricture, hydronephrosis and aortic coarctation. Chromosome analysis showed an abnormal constitution in 63% of lymphocytes: 46,XY/46,XY, dup(1) (q24q31.2). Parental chromosomes were normal.

Possible explanations for a chromosomal abnormality in an autosomal recessive syndrome are (1) the chromosome anomaly could be coincidental, (2) partial trisomy for 1q could produce a phenocopy, (3) the gene for FS may be on 1q. This structural abnormality could have transformed a heterozygous carrier state into an hemizygous state with full expression of FS by disrupting the normal allele. Alternatively, the abnormal allele may have been amplified by the duplication here. This case poses many interesting questions regarding the relationship between chromosomal anomalies and mendelian traits.

●322 TERATOGENS FROM WEEKLY ORAL ETHANOL EXPOSURE IN A NON-HUMAN PRIMATE. Sterling K. Clarren, Douglas M. Bowden, Susan J. Astley. University of Washington School of Medicine, Departments of Pediatrics and Psychiatry and Behavioral Sciences, Seattle, WA.

Ethanol has been orally administered once per week to 54 gravid pigtailed macaques (M.nemestrina) in doses of 0.0, 0.3, 0.6, 1.2, 1.8, 2.5 or 4.1 gm/kg from the first week in gestation or in doses of 2.5, 3.3, or 4.1 gm/kg from the sixth week. Peak plasma ethanol concentrations (PPEC) ranged from 24 ± 6 mg/dl at the 0.3 gm/kg dose to 549 ± 71 mg/dl at the 4.1 gm/kg dose. An increased rate of spontaneous abortion occurred at and above the 1.8 gm/kg dose (mean PPEC = 205 mg/dl) and no viable infants were born in cohorts receiving 2.5 gm/kg or 4.1 gm/kg ethanol from the first week in gestation. Thirty-three viable infants were followed from birth to 6 months of age. No animal had any major malformations. Mental retardation and craniofacial dysmorphisms were identified nearly consistently in the animals achieving PPEC's of 150 to 250 mg/dl from the first week in gestation. Animals with higher PPEC's and exposures only after 40 days gestation were less consistently abnormal. The data demonstrated the teratogenicity of weekly ethanol exposure with an apparent period of teratogenic vulnerability in the first 6 weeks of gestation.

323 BONE FRAGILITY, CRANIOSYNOSTOSIS, HYDROCEPHALUS AND OCULAR PROPTOSIS: FURTHER OBSERVATIONS ON A NEWLY RECOGNIZED TYPE OF OSTEOGENESIS IMPERFECTA (OI). David E.C. Cole and Thomas O. Carpenter, Depts of Pediatrics, Dalhousie University, Halifax, NS and Yale University School of Medicine, New Haven, CT.

We reported 2 unrelated infants who presented with bone deformities and multiple fractures reminiscent of OI, but also displayed ocular proptosis, orbital craniosynostosis, hydrocephalus and distinctive, strikingly similar facial features. Both were unaffected at birth but suffered multiple metaphyseal compression fractures of the long bones at 2 to 4 months of age. This was accompanied by extensive demineralization and recurrent diaphyseal fractures that were most frequent in the second year of life. Communicating hydrocephalus and orbital craniosynostosis were also noted in the first year of life. In one patient, a shunt was installed and craniofacial surgery was undertaken to correct proptosis and dysmorphic features. At 3 and 5 years of age, intellectual performance is unimpaired in both, but they are dwarfed, kyphoscoliotic, and markedly handicapped by bony deformities. Bone biopsy reveals decreased bone volume and increased bone resorption without compensatory new bone formation. Although neither electron microscopy nor fragment mapping of fibroblast collagens is abnormal, clinical features, including enamel hypoplasia, high-pitched voice, blue sclerae, joint laxity, thin skin with easy bruising, and poor wound healing, all suggest generalized connective tissue involvement. Cytogenetic and extensive biochemical investigations have failed to suggest an etiology; further elucidation requires identification and study of new cases.

324 ASSOCIATION OF VISCERAL MYOPATHY WITH VESICO-INTESTINAL FISSURE. Linda H. Cripe, Frank A. Mitros, Robert T. Soper, Kevin C. Pringle, and James W. Hanson. University of Iowa College of Medicine, University of Iowa Hospitals and Clinics, Departments of Pediatrics, Pathology, and Surgery, Iowa City, IA.

Vesico-intestinal fissure (extrophy of the cloaca, OEIS complex) is a pattern of multiple malformations including extrophy of the bladder with epispadias, extrophy of the cecum with rudimentary colon and imperforate anus. Other commonly associated anomalies include omphalocele, intestinal duplication, meningomylocele and hydronephrosis. Current pathogenetic theories postulate fusion of genital tubercles caudal to the normal position leading to interruption of migration of the infra-umbilical mesoderm with secondary abdominal wall rupture.

Patients with vesico-intestinal fissure have a poor prognosis. Abnormal bowel motility with malabsorption often contribute to death. Histopathologic observation of a visceral myopathy suggestive of an embryologic insult to smooth muscle development in a recent patient with a negative family history for familial visceral myopathy, prompted review of all cases of vesico-intestinal fissure since 1966 at this institution. Results suggest abnormal morphogenesis of intestinal smooth muscle may be an important part of the pathogenetic sequence. This is consistent with an early insult to the lateral plate mesoderm from which arise the intra-embryonic splanchopleure and the intra-embryonic somatopleure. These structures form the smooth muscle of the GI tract and the ventral body wall, respectively. Intestinal biopsy and electrophysiologic motility studies may help to define the extent of such defects and contribute to the successful clinical management of these patients.

325 COMPARATIVE STUDY OF CONGENITAL MALFORMATIONS. Kenneth W. Dumars, Bui Loan, Chanthan Chea, Hanh D. Nguyen. (Spon. by Thos. L. Nelson) University of California, Irvine, College of Medicine, Irvine, California.

There are no good data providing frequency of congenital and genetic disorders occuring in those from Vietnam, Cambodia, and Laos. Life threatening diseases and malnutrition; injury or death due to warfare exhausted health resources. Because of these realities, a population study has been started to determine those genetic and/or congenital disorders occuring in the Vietnamese, Cambodian, Lao and Hmong. Preliminary data from birth, death, hospital records(*), and screening of a random sample of population for thalassemia reveals following.

	SEA	Asian	Black	Hispanic	Anglo
Birth prior to 20 yrs of age	54	18	115	150	58
Birth after 35 years of age	100	121	63	66	82
Congenital Malformations	13	9	7	10	7
Infant deaths prior to 1 yr	7	6	10	7	6

*Expressed per 1,000 live births in 1984.

Screening for hemoglobinopathies reveals approximately 10% of Vietnamese population to be carriers for thalassemia.

In comparison with Black and Hispanic, those from Southeast Asia and from Asia have fewer births prior to 20 years of age, but more frequently continue reproduction after 35 years of age. The numbers and types of malformations reveal some ethnic/racial variation. Thalassemia may require increased medical attention.