1285 PLACENTAL DEVELOPMENT IN THE TRISOMY 16 MOUSE. John D. Gearhart, Mary L. Oster-Granite, and George Hatzidimitriou (Spon. by John W. Littlefield). Johns Hopkins University School of Medicine, Developmental Genetics Laboratory, Department of Pediatrics, Baltimore.

Survival and development in utero involve the intimate interaction of mother, placenta, and embryo or fetus. However, when chromosomal aneuploidy occurs in the placenta and/or embryo or fetus, intrauterine growth retardation and fetal death are frequent outcomes of the pregnancy. Placental insufficiency may play a role in these events. Specifically, insufficiency of the fetal circulation in a hypoplastic placenta may result in underperfusion of the fetus. To examine this, we have studied the development of the placenta in trisomy 16 (Ts16) mice. Ts16 mice were selected because homology has been demonstrated between portions of mouse chromosome 16 and human chromosome 21, specifically that portion of HSA 21 implicated to cause Down Syndrome (DS) when present in triplicate.

We examined 5 micron plastic section serial reconstructions of the placentas of Ts16 fetuses and their normal littermates from days 10 through 18 gestation. Morphometrically, the surface area ratio of fetal vasculature to that of the maternal sinuses was much less in the Ts16 fetus than its normal littermate but the ultrastructural characteristics of the placental barrier in the Ts16 fetus and its normal littermate were indistinguishable. The hypoplastic fetal vascular in the placenta could well lead to the underperfusion of the fetus, thus contributing to the aneuploid syndrome.

1286 DIABETIC EMBRYOPATHY: CORRECTED BY ARACHIDONIC ACID (AA) AND INFLUENCED BY H-2 HISTOCOMPATIBILITY COMPLEX. Allen S. Goldman, Lester Baker, Ronald Piddington, Barry Marx, Richard Herold, and Joseph Egler. The Departments of Pediatrics and Dental Medicine, University of Pennsylvania, Philadelphia, PA

Our work on teratogen-induced cleft palate in rodents indicates that a functional deficiency of arachidonic acid mediates the defect. Because of analogous embryologic processes, we have hypothesized that the failure of neural tube fusion seen in diabetic embryopathy may involve a similar mechanism. This hypothesis was tested in two animal models of diabetic embryopathy. Arachidonic acid (200-400 mg/K/d) administered subcutaneously to pregnant diabetic (streptozotocin-induced) rats during the period of organ differentiation significantly lowered the incidence of neural tube fusion defects from 11% to 3.8% ($p < .005$), the frequency of cleft palate from 11% to 4% ($p < .005$) and the incidence of micrognathia from 7% to 0.8% ($p < .001$). D-glucose (8 mg/ml) significantly inhibited neural tube fusion in B10.A ($H\text{-}2^a$) mouse embryo culture (13% vs 67% fusion, $p < .01$), but did not inhibit fusion (57%) in B10 ($H\text{-}2^b$) embryos. Arachidonic acid (1 or 10uG/ml) reversed the teratogenic effect of 8 mg/ml d-glucose in B10.A embryos (67% fusion). Thus, the teratogenic effects of hyperglycemia on neural tube fusion appear to be mediated by a functional deficiency of arachidonic acid. The differing effects of d-glucose in embryos of the B10.A and B10 strains suggest a role for the H-2 histocompatibility complex in determining susceptibility to hyperglycemia-induced teratogenicity, similar to its role in cleft palate.

1287 SYNDROMES ASSOCIATED WITH POLYDACTYLY AND HYPOPITUITARISM. John M. Graham, Jr., Mark Harris, Judith E. Frank, George A. Little and Robert Z. Klein, Dept. of Maternal and Child Health, Dartmouth-Hitchcock Medical Center, Hanover, NH, U.S.A.

We report two female infants with postaxial polydactyly and hypopituitarism of differing etiologies. The first infant was born at term to a 26-year-old gravida 6 para 2 abortus 4 woman who noted markedly decreased fetal movement and intrauterine growth retardation. She was delivered from a breech presentation with posteriorly rotated simplified auricles, short nose, flat nasal bridge, microglossia, micrognathia, cleft posterior palate, short limbs with dislocated hips, postaxial polydactyly of hands and feet, bilateral simian creases, and 2-3 syndactyly of the toes. She died at 21 hours of age and autopsy revealed hypothalamic hamartoblastoma, bilateral hypoplastic renal ectopia, bilateral pulmonary hypoplasia, and a bifid epiglottis. Family history revealed that the mother's sister had died at 17 hours of age with remarkably similar dysmorphic features (no autopsy done), and this is the first report of apparent familial recurrence for Hall-Pallister syndrome. The second infant was born by cesarean section at 42 weeks with postaxial polydactyly of the left hand and primary panhypopituitarism. This pregnancy in a 21-year-old gravida 2, abortus 1 woman was complicated by extremely low maternal estriols. Size at birth and a cranial CT scan were normal, and the family history was negative for other individuals with hypopituitarism or polydactyly. Postaxial polydactyly may be associated with hypopituitarism, especially when associated with cleft palate, choanal atresia, congenital heart disease, and basal brain anomalies.

●1288 CONOTRUNCAL DEFECTS IN CHARGE ASSOCIATION: EVIDENCE FOR NEURAL CREST INVOLVEMENT. John M. Graham, Jr., Edward Meill, Roberta A. Pagon, Joseph R. Siebert, and Larry Kaplan (Spon. by Robert Z. Klein), Dept. of Maternal and Child Health, Dartmouth-Hitchcock Medical Center, Hanover, NH; Children's Orthopedic Hospital and Medical Center, Seattle, WA; Children's Hospital Medical Center, Boston, MA.

Defects in CHARGE association may include choanal atresia, coloboma, cardiac anomalies, growth and mental deficiency, genital hypoplasia, and ear anomalies, as well as other facial defects such as cleft palate, micrognathia, facial palsy and velopharyngeal problems. Previous studies have demonstrated that cephalic neural crest plays a major role in facial morphogenesis. Recent studies using quail/chick chimeras have shown that mesenchyme of the aorticopulmonary septum is also derived from cells of the cephalic neural crest. There is overlap between CHARGE association and DiGeorge Syndrome, and when tissue from cephalic neural crest is ablated, conotruncal septation defects and thymic deficiency may result. We hypothesized that abnormalities in the formation, proliferation, or migration of cephalic neural crest cells might result in an association between craniofacial and conotruncal anomalies in CHARGE association. We tested this hypothesis by examining the types of cardiac defects among 34 previously published and 17 new CHARGE association patients with congenital heart disease. Conotruncal defects were present in 35% of these patients, versus an expected prevalence of 16-22% in large series of patients with congenital heart disease. These data suggest a possible pathogenetic link between certain craniofacial and cardiac defects that may involve the cephalic neural crest.

† 1289 A PROSPECTIVE CLINICAL AND CYTOGENETIC STUDY OF DiGEORGE SEQUENCE. Frank Greenberg, David Ledbetter, John Kirkland, William Shearer, Howard Rosenblatt. (Spons. by Arthur L. Beaudet, M.D.) Baylor College of Medicine Houston, TX., Department of Pediatrics.

DiGeorge Sequence (DGS) is a multifactorial defect in development of the third and fourth branchial arches. 24 patients with DGS were ascertained prospectively between 1982-84 by presentation with specific cardiac defects, persistent hypocalcemia, family history, or thymic aplasia at surgery or autopsy. Peripheral blood lymphocyte or skin fibroblast chromosome studies were done to determine the frequency of abnormalities, primarily monosomy 22q11. T cell function studies and parathyroid hormone levels were studied when possible.

Of the 24 cases, 21 were ascertained by their cardiac defect. Two presented with persistent hypocalcemia and seizures. One was detected only at post-mortem. Two cases were familial. One patient with retinoic acid teratogenicity syndrome had decreased T-cell function.

High resolution chromosome studies were done on 23 cases and were normal in 20. The three abnormal studies revealed monosomy 22q11, monosomy 18q, and monosomy 10p. The familial case with monosomy 22q11 was previously reported (Hum Genet 65:317, 1984). The other familial case in our series had normal chromosomes.

These findings are consistent with DGS as an etiologically and clinically heterogeneous condition with a chromosomal etiology in about 10% of cases. DGS should be suspected and evaluated in all patients with any third and fourth branchial arch defects.

1290 EXTERNAL HYDROCEPHALUS IN WEAVER SYNDROME. Sue Hahm, Luis Alvarez, Shlomo Shinnar and Harold M. Nitowsky. Department of Pediatrics, Albert Einstein College of Medicine, Bronx, New York 10461

The Weaver syndrome is a rare disorder of overgrowth, characterized by accelerated somatic growth and osseous maturation, increased head size and unusual facies. Excessive macrocephaly is a striking finding that differentiates Weaver from other overgrowth syndromes. We report a male infant who had the characteristic features of Weaver syndrome including rapid growth. His facial features included round face, frontal bossing, wide bifrontal diameter, hypertelorism, downslanted palpebral fissures, epicanthi, flat nasal bridge, long prominent philtrum, retromicrognathia and large ears. At birth his length (Lt) was 63.5cm and weight (Wt) 5.8kg. At age 2 months Lt was 72.5cm and wt 8.3kg. Carpal bone age was advanced to 6-9 months. At age 3 months his head circumferance (HC) was 50.4cm. A CT scan showed large bilateral extracerebral fluid collections. A repeat CT at 4 1/2 months showed a decrease in this collection and a picture more consistent with external hydrocephalus. A subdural tap confirmed that the fluid was normal CSF under no increasure pressure. No intervention was done. We have seen a similar CT abnormality in at least one patient with Soto syndrome and in several patients with benign familial macrocephaly. Based on the observation in patients with benign familial macrocephaly, we suggest that the CT appearance may be a relatively benign finding, common to syndromes with rapid head growth in early life.