- **1207** **FAMILIAL FACTORS IN SYNDROMIC AND NON-SYNDROMIC EAR MALFORMATIONS.** Celia I. Kaye, Beverly R. Rollnick, Samuel Pruzansky, Abraham Lincoln School of Medicine, Univ. of Illinois, Center for Craniofacial Anomalies, Chicago.

Ear malformations, minor or severe, occur in 1% of the population. When observed in combination with other anomalies, a wide variety of syndromes has been identified. We surveyed 350 patients with ear malformations, of whom 45 subjects with monogenic syndromes were identified. Of interest were families of probands with the Treacher Collins syndrome, an autosomal dominant (AD) disorder with incomplete penetrance; a high percentage of cases are assumed to result from new mutation. In 2/32 families, 2 affected siblings were born to phenotypically normal parents with negative family history, suggesting that caution be exercised in genetic counselling in this situation. Patients not identified as having monogenic syndromes are being evaluated to assess familial factors in the etiology of ear malformations. Ear anomalies were found to be familial in 32/84 families studied. In familial cases, pedigrees appeared to be suggestive of AD inheritance with incomplete penetrance, or of multifactorial inheritance. 8.8% (33/376) of first-degree relatives exhibited ear anomalies. The following conclusions are suggested: 1) The presence of an ear malformation should alert the clinician to the possible presence of a syndrome with a high recurrence risk; 2) Apparently non-syndromic ear malformations are often familial; genetic counselling with recurrence risk estimation is indicated.

Supported by grant DE02872, National Institutes of Health

- 1208** **INTRAUTERINE AND POST-NATAL GROWTH RETARDATION, BRANCHIAL CLEFT SINUSES, PREMATURE AGING AND UNUSUAL FACIES: A NEW SYNDROME WITH AUTOSOMAL DOMINANT TRANSMISSION.** W. Lee and A. Root. Univ. South Florida, Department Pediatrics and All Children's Hospital, St. Petersburg, Florida.

We describe a mother and son with the following findings: intrauterine and post-natal growth retardation, branchial cleft sinuses, premature aging and unusual facies. The propositus is an 8 year old boy whose term birth weight was 1.53 kg and length 40.6 cm. His present length is 108 cm (HA=4 yr), bone age 7 years. The mother is 39 years; birth weight was 2.10 kg; present height is 146.7 cm (HA=11.7 years); greying of her hair occurred at 18 years, and she now has an aged, wrinkled appearance and early cataracts. Both mother and son had bilateral congenital branchial cleft sinuses, obstructed tear ducts and strabismus, all of which required surgery. They have antimongoloid slant of the orbits, long eye lashes, bulbous nose, long philtrum, prominent and protruding upper lip, "cupid bow" mouth with down turned lips, and micrognathia. They have a slight problem with articulation, but are of normal intelligence. Routine hematological, biochemical and metabolic studies were normal as were the clinical and functional evaluations of the cardiorespiratory, gastrointestinal and urinary systems. No abnormality of anterior or posterior pituitary, thyroid or adrenal function was identified. Chromosomal karyotype, including banding analysis, was normal. This syndrome is probably transmitted as an autosomal dominant characteristic.

- 1209** **MESODERMAL INDUCTION DEFECT AS A POSSIBLE CAUSE OF EAR MALFORMATIONS.** Andrew Melnyk and Lester Weiss, Henry Ford Hospital, Department of Pediatrics, Detroit

Deafness due to inner ear anomalies is rarely associated with malformation of the auricles. Two brothers born of consanguineous parents, with profound congenital sensorineural deafness, malformed auricles, abnormal vestibular function and delayed motor development, had low-set, cupped, pointed auricles with folded helices, narrow external auditory canals and normal tympanic membranes. Caloric stimulation failed to elicit nystagmus. Temporal bone laminography revealed bilateral absence of the cochlea and normal ossicles. Since the external and inner ear originate from distinctly separate structures, the embryogenesis of this malformation association is less clear than the more common association of external and middle ear anomalies. In the latter, the first and second branchial arches are the common derivative of both structures. The association of auricular and inner ear anomalies, with sparing of the middle ear, can be explained on the assumption that mesodermal induction is responsible for differentiation of both otocyst and branchial arch ectoderm. A recessive mutant gene may be responsible for the production of a deficient mesodermal inductor substance or a deficient cell surface receptor of the target tissue, rendering it unresponsive. A similar mechanism may be involved in other multiple malformation syndromes, whereby a mutant gene acting during a specific period of organogenesis causes disruption of the normal induction competence relationship.

- **1210** **ACETYLCHOLINESTERASE (AChE) ASSAY FOR PRENATAL DIAGNOSIS OF NEURAL TUBE DEFECTS (NTDs).** Aubrey Milunsky and Victor S. Sapirstein, Harvard Medical School, Eunice Kennedy Shriver Center, Depts. Pediatrics & Biological Chemistry, Boston.

Amniotic fluid (AF) alpha-fetoprotein (AFP) assay has for some years been the most reliable test for the prenatal diagnosis of NTDs. Recently AChE assay has been proposed as either an alternative or adjunctive diagnostic tool. The non-specificity of AFP and the spurious results that occur with fetal blood contamination have spurred the search for a better diagnostic tool. We have assayed for AF AChE in 196 mostly retrospective cases using polyacrylamide gel electrophoresis and compared the data with our AFP results from a background experience of > 27,000 cases. High AFP and an AChE band was present in all 61 NTDs. No AChE was observed in clear (19) or bloody (21) normal AFs. Uninterpretable results from AFs (49) with fetal blood + high AFP were resolved in 80% when no AChE band was found. The remaining 10 had fetal death (2), Meckel synd.(1), normal outcome(4) and pending(3). An AChE band was seen in only 7 (15%) of 46 AFs with high AFP and "no" fetal blood. These 7 had AChE in association with omphalocele(1), Turner synd.(2), open abdominal defect(1) and normal fetuses(3). Neither total cholinesterase nor AChE bands were seen in 1 fluid probably of cystic hygroma origin. AChE was found to be stable after multiple (10) freeze-thawing and assays after 5 days at room temperature. AF AChE assay is a valuable adjunct (to AFP) for prenatal diagnosis of NTDs, and requires more study.

- **1211** **SHORT CORDS, LONG CORDS... WHO CARES?** Adrien C. Moessinger (Spon. by W.A. Blanc). Depts. of Pediatrics and Pathology, Columbia Univ., New York.

Both short and long umbilical cords have been associated with obstetrical complications but the factors controlling longitudinal cord growth have remained unknown. Recent observations suggest that cord length is a reflection of fetal movements. If this were true, cord length should be a useful diagnostic tool and could suggest specific congenital anomalies.

Using pregnant Sprague-Dawley rats in the last third of gestation, we induced the following experimental situations: A fetal restraint by oligohydramnios (n=17), B fetal paralysis with curare (polyhydramnios, n=18), C extrauterine pregnancy with fetus free in the abdominal cavity (n=18) and D, as in C but fetus fixed to the uterine horn, close to the placental implantation site (n=8). At term, the cords were measured with a fine caliper under standard conditions. When compared to littermate controls, A & B fetuses had shorter cords (p<.01), C fetuses had longer cords (p<.01) and in D fetuses the cords were either shorter or unaffected.

These results support the contention that longitudinal cord growth is governed by tensile forces and depends both on fetal motion and available intrauterine space (Ped. Res. 14:586, 1980). A short cord may be a useful marker of conditions associated with impaired fetal movement such as neuromuscular disease or oligohydramnios. Similarly, long cords may signal fetal hyperkinesia.

- 1212** **LEFT VENTRICULAR AND CORONARY ARTERY MORPHOLOGY IN THE HYPOPLASTIC LEFT HEART SYNDROME** William O'Connor, James Cash, Carol Cottrill, Gregory Johnson, Jacqueline A. Noonan, University of Kentucky School of Medicine, Lexington, Kentucky.

Myocardial sinusoids have been noted angiographically to communicate with the small LV of infants with hypoplastic left heart syndrome (HLHS). These may represent egress of blood at high pressure from the completely obstructed chamber into the coronary vasculature when aortic valve atresia is present with intact ventricular septum. In order to further characterize these channels we examined microscopically transverse subserial sections from 12 autopsy specimens of HLHS. The mean age at death was 5.8 days. Gross anatomic defects were: Aortic valve atresia 9/12; Critical aortic stenosis 3/12; Mitral valve (MV) hypoplasia 11/12; IV atresia 1/12; VSD 2/12; Premature closure (PC) of foramen ovale (FO) 3/12; FO under 2 mm. 5/12. The mean LV chamber diameters were 13 x 9 mm. compared with 25 x 20 mm. for the RV. The mean LV wall thickness was 7 mm. Microscopic findings included: Calcification of the myocardium 11/12; Thick walled LV with prominent endocardial fibroelastosis 9/12; Medial hypertrophy/intimal proliferation of coronary arteries 9/12; Multiple direct communications between LV cavity and coronary arteries 9/12 (absent in both VSD cases and one combined atresia case); Spongy capillary network in midzone of LV wall 7/12 (4 cases FO under 2 mm. and 3 cases PCFO). This study provides morphologic evidence of widespread developmental abnormalities of LV myocardial vascular structure in HLHS.