**● 1213** TRACHEOESOPHAGEAL FISTULA AND ESOPHAGEAL ATRESIA IN NORTH CAROLINA: A STUDY OF CLUSTERING AND POSSIBLE ASSOCIATION WITH INFECTIOUS DISEASE. Carl D. Ozimek, Roger C. Grimson, and Arthur S. Aylsworth. (Spon. by Henry N. Kirkman) University of North Carolina School of Medicine, North Carolina Memorial Hospital, Departments of Biostatistics and Pediatrics and the Biological Sciences Research Center, Chapel Hill.

Two hundred and eighty-five cases of esophageal atresia with or without tracheoesophageal fistula (TEF/EA) occurring in North Carolina between 1952 and 1978 have been studied. Except for an increase of low birth weight and hydramnios in the study group, the cases are demographically representative of the general population. Cases without other malformations (isolated TEF/EA) and cases with other associated anomalies were analyzed separately. No significant clustering was found for the latter group while clustering over time was statistically confirmed for isolated TEF/EA cases. The dominant period for isolated TEF/EA was 8.3 years. Data compiled on 20 infectious diseases by the state of North Carolina were analyzed. A predominant period of 8.3 years was found for infectious hepatitis. The phase of the frequency curve for infectious hepatitis appears to coincide with that of the TEF/EA curve. Although these data do not allow us to conclude that a strong association exists between infectious hepatitis during pregnancy and the formation of TEF/EA in the fetus, they do suggest that this relationship should be studied further.

**1214** FAMILIAL SHORT STATURE: VARIANT OF THE SILVER-RUSSELL SYNDROME (SRS) OR A NEW ENTITY. Robert Rapaport, Lenore S. Levine, Maria I. New, CMDNJ-New Jersey Medical School, Newark and Cornell University Medical College, New York City, Departments of Pediatrics

We evaluated a 13 5/12 yr old boy for short stature (height age 8 yrs, weight age 7 1/2 yrs). His birth weight was 2.27 kg. He had high pitched voice, prominent forehead, frontal bossing, deep set eyes, fish-shaped downturning mouth, Kirner's deformity of the distal phalanges of the fifth finger, high metacarpal index, partial 2-3 toe syndactyly bilaterally, one pigmented nevus and asymmetrical kidneys. He was in early puberty (Tanner II); his bone age was 11 1/2 yrs. He had no organic, systemic, hormonal or chromosomal abnormalities. His baseline somatomedin and stimulated growth hormone (GH) levels were normal. Administration of Human GH, 1 u IM daily for five days, did not have any effect on the somatomedin levels or on his nitrogen, sodium, potassium, calcium or phosphorus balances. There is evidence (history and photographs) for the presence of this syndrome of short stature in 12 family members in five generations. We examined seven members of three generations. The six affected members reached adult heights of 128-150 cms. All had normal somatomedin levels. All had birth weights >2.0 kg, and three >2.5 kg. This family represents either a normal birth weight variant of the SRS, inherited as an autosomal dominant trait, or a new entity of familial short stature unaccompanied by significant growth retardation.

**1215** PROPRANOLOL INHIBITS BRAIN AND SOMATIC GROWTH IN THE RAT. Geoffrey P. Redmond (Spon. by L. F. Soyka). University of Vermont College of Medicine, Departments of Pharmacology and Pediatrics, Burlington.

Maternal use of the beta blocker propranolol (PRO) has been associated with intrauterine growth retardation (IUGR) in the offspring. Because mothers received the drug for hypertension or cardiac disease, it is uncertain whether the drug or the disease produced the IUGR. To determine whether PRO itself could inhibit growth, it was given to rats at various ages. Administration by gavage at a dose of 50 mg/kg to pregnant rats on days 17-21 resulted in significantly lower birth weight (5.76±0.28g vs. 6.41±0.63, $p<0.05$) even though mean litter size was also slightly reduced. In contrast, administration to pair-fed post-weanling rats had no effect on growth. Suckling rats given PRO 50 mg/kg by gavage starting on day 4 had a 22% deficit in body weight ($p<0.01$) and a 10% deficit in brain weight ($p<0.01$) in comparison to controls by day 16. A dose of 25 mg/kg did not affect growth while 75 mg/kg produced a 33% weight deficit on day 16.

Conclusion: PRO produces a dose-dependent impairment of somatic and brain growth in the absence of maternal disease. Administration after the completion of the phase of rapid brain growth had no effect.

**● 1216** MULTIPLICATION RATES OF ENDODERM/MESODERM IN HEAD PROCESS-TO 17-SOMITE-STAGE CHICK EMBRYOS. Glenn C. Rosenquist, Children's Hospital National Medical Center and George Washington Univ. School of Medicine, Washington, DC, 20010

Study of chick embryos in early stages of development has shown that the rate of cell multiplication slows as organ differentiation begins. We calculated the rate of doubling of cells in the endoderm/mesoderm layer from Hamburger-Hamilton stage 5 to stage 12+ (head-process to 17-somite stages, 24-47 hours of incubation). Equally-sized tritiated-thymidine-labeled transplants were excised from the endoderm/mesoderm layers of donor embryos, and placed in homologous positions in 12 pairs of recipient embryos. One recipient of each pair (the control embryo) was fixed as soon as the transplant had healed, and the other was reincubated for 4-23 hours before fixing. All embryos were embedded in paraffin, serially sectioned and mounted. The slides were radioautographed with exposure times of 5-42 days, and the labeled cells in each embryo were counted. In each pair of embryos, the number of labeled cells in the control embryo was compared to the number of labeled cells in the embryo reincubated for a longer period. The resulting ratios were plotted on a graph against the number of hours of reincubation; the ratios were grouped at 4, 15-16, 18-18.5 and 21.5-23 hours. The resulting growth curve indicated that the number of endoderm/mesoderm cells had doubled at five hours of reincubation (approximately the one-somite stage) and again 12 hours later. These multiplication rates are within the range of rates calculated by previous investigators from mitotic or radioactive indices.

**1217** NEONATAL PROGERIA IN SIBLINGS. Uma T. Salcedo, Andrew Hsu, Alfredo J. Herrera, Maria Paz D. Ruiz, (Spon. by Allen Glasgow), St. Agnes Hospital, Department of Pediatrics, Baltimore, Maryland.

Progeria (Hutchinson-Gilford Syndrome) is classified among the very rare childhood diseases (1:8,000,000 births according to DeBusk's estimation). After 60 cases had been documented in medical literature by DeBusk in 1972, 5 more cases have been reported. There are only 4 reports in siblings up to this date, only 2 reports (4 cases) that clinical pictures appeared at birth and only 1 of these reports presented as a neonatal progeria in siblings without consanguinity in the family. The rarity of the disease prompted us to report our patient - a 1500 gm white female infant born at 35 wks. gestation with the phenotype typical of progeria patients described in literature along with the radiographic evidence of clavicles resorption at birth. The 1st pregnancy 8 yrs. ago also terminated at 35 wks., 1690 gm male with the same features as our patient, with evidence of clavicles and humeri changes in x-ray at 1 mo. Our patient developed natal tooth at the lower incisor area on the 5th day (also reported in 4 cases with typical phenotype at birth). She died at 7 days of age from heart failure and sepsis. (Sibling died at 6 wks. of age from congestive heart failure). There are 2 normal children. No consanguinity in the family. Our patient had the lowest birth weight reported. Typical phenotype and x-ray changes at birth, early dentition and early death may represent a new "neonatal progeroid syndrome" or just represent the most severe form of progeria.

**1218** A FAMILIAL X-LINKED MENTAL RETARDATION SYNDROME ASSOCIATED WITH MULTIPLE CONGENITAL ANOMALIES, MEGALO-GENITALIA AND A FRAGILE X CHROMOSOME. Siegfried M. Pueschel, Ross Hays, and Teresita Mendoza (Spon. by Leo Stern). Brown University, Program in Medicine, Rhode Island Hospital, Department of Pediatrics, Providence, Rhode Island.

The availability of improved diagnostic services for mentally handicapped persons and the recent development of refined cytogenetic techniques have permitted the identification of subgroups within the general diagnostic category of familial X-linked mental retardation.

We studied a unique Azorian family whose three affected sons ages 17 (A), 22 (B), and 30 (C) years displayed moderate to severe mental retardation, speech disorder and self-stimulating behaviors. They had atypical facial features with a prominent glabella, large nose, abnormally structured ears, high arched palate, broad alveolar ridges, malocclusion, clinodactyly of the fifth finger, and single palmar creases. The most outstanding features were large genitalia [length of penis 112mm (A), 130mm (B), and 94mm (C); length of testes, left/right 70/75mm (A), 82/80mm (B), and 80/85mm (C)].

The cytogenetic analyses revealed a fragile X chromosome (Xq27 FRA) in all three sons [8% (A), 4% (B), and 2% (C)].

The phenotypic characteristics of the probands with familial X-linked mental retardation, fragile X chromosome and megalogenitalia have not been described previously. It is conceivable that these patients present another subgroup of the familial X-linked mental retardation category.