724 MAPPING THE HLA GENE CLUSTER WITH PARTHENOGENIC OVARIAN TERATOMAS. Frederick Hecht, Barbara Kaiser-McCaw, Theona Vyvial. The Genetics Center of Southwest Biomedical Research Institute, Tempe, Arizona and Arizona Blood Services, Scottsdale, Arizona.

The HLA gene cluster is known to be on chromosome 6. The distance between the centromere of chromosome 6 and the HLA gene cluster is, however, not known.

Ovarian teratomas were shown through combined cytogenetic and enzyme marker studies to be of parthenogenic origin by us in 1975. These tumors originate from a single female germ after first meiosis. Gene loci near the centromere which have not experienced recombination are homozygous, while genes further from the centromere which have experienced a recombinant event are heterozygous.

We have HLA-typed cells from two ovarian teratomas in tissue culture and compared their HLA types to data from lymphocytes and cultured normal cells from the same hosts. In both cases whenever the host had two HLA haplotypes, the teratoma cells had but one HLA haplotype and so was homozygous for HLA. This indicates no recombination between HLA and the centromere of 6 chromosome. Parthenogenic ovarian teratomas are thus a source of HLA-homozygous cells. The typing method is simple and will permit precise genetic mapping of the HLA gene cluster. This is the first use of parthenogenic human cells for immune gene mapping.

725 A NEW SYNDROME OF RETINITIS PIGMENTOSA, HEARING LOSS, MENTAL RETARDATION, AND DYSMORPHOLOGY, Joseph H. Hersh, Philip E. Podruch, and Bernard Weisskopf, (Spon. by Billy F. Andrews), University of Louisville School of Medicine, Department of Pediatrics, Louisville, Kentucky.

Two siblings born to nonconsanguinous parents were evaluated for mental retardation(MR). Findings included retinitis pigmentosa(RP), sensorineural hearing loss(HL) and similar dysmorphism.

JA was 4½ and LA was 2. There was delayed closure of the anterior fontanelle. Length and weight were 5th% and OFC for JA was 50th% and LA was 20th%. They had frontal bossing, downslanting palpebral fissures, epicanthal folds, flattened nasal bridge, lowset ears, and small feet. JA had strabismus and LA had proptosis. JA had small externalia genitalia. Both had hypotonia and hearing loss. Mental ages were 19 and 9 months. Both had extinguished ERG's, normal CT scans, amino acids, OGTT's and chromosomes. LA had normal skull films and thyroid studies.

RP is the common demoninator in a number of genetic syndromes with overlapping clinical characteristics:

	RP	HL	MR	HYPOGONAD	OGTT	OTHER
Laurence-Moon-Biedl	+	-	+	+	-	obesity, polydactyly
Alstrom	+	+	-	+	+	obesity
Usher's	+	+	+/-	-	-	
Edwards, et. al	+	+	+	+	+	
Present family	+	+	+	?	-	facies, feet

Although our patients shared some of these features, the dysmorphology separates them and reflects a new recessive syndrome which should be added to this group.

726 AUTOSOMAL DOMINANT ANTERIOR SEGMENT DYSGENESIS WITH VARIABLE EXPRESSIVITY: PROBABLE LINKAGE TO MNS BLOOD GROUP ON CHROMOSOME 4. Helen M. Hittner, Robert E. Ferrell, James H. Antoszyk, Frank L. Kretzer, (Spon. by Arnold J. Rudolph). Baylor College of Medicine, Departments of Pediatrics and Ophthalmology, and University of Texas Health Science Center, Center for Demographic and Population Genetics, Houston, Texas.

An autosomal dominant anterior segment dysgenesis (ADASD) with variable expressivity affecting members of at least eight generations was identified. One branch of the family involving five generations with 21 of 35 (60%) members affected was studied. This included sixteen affected (9 males and 7 females) who were still living. Clinical findings ranged from anterior Schwalbe's line with mild cataract to severe corneal opacification with moderate cataract while visual acuity varied from 20/20 to hand motion only.

The propositus had a corneal transplant and cataract extraction on one eye at age 6 weeks. Light and electron microscopic analyses demonstrated that the cornea had the following abnormalities: basal epithelial cell protrusions into a thickened Bowman's layer (22-60μ), activated keratocytes throughout the entire stroma, no Descemet's layer or endothelial cells, an aggregation of keratocytes posteriorly. The lens showed focal aggregations of vesicles in cortical fibers with extensive epithelial atrophy.

Maximum likelihood analysis between ADASD and 14 biochemical and serological markers showed probable linkage between ADASD and the MNS blood group on the long arm of chromosome 4 (Z = 3.48).

● **727** GENERALIZED SIALIC ACID STORAGE DISEASE. A.L. Horwitz, L. Hancock, G. Dawson and M.M. Thaler. University of Chicago Medical Center, Depts. of Ped. and Biochem., Chicago, Il and University of Calif. Med. Center, Dept. of Ped., San Francisco, CA (Spon. by A. Dorfman).

A male infant born prematurely with fetal hydrops died suddenly at the age of 5 months with persistent hepatomegaly and abdominal ascites but no skeletal abnormalities. Alcian blue staining inclusions were noted in placental trophoblast and liver cells. Electron micrographs of liver and cultured skin fibroblasts revealed vacuolated cells with granular and floccular material within lysosomes. Lysosomal enzyme activities (including neuraminidase) in liver and fibroblast extracts were within normal limits. Analysis of aqueous extracts of autopsy brain and liver samples by gas liquid chromatography revealed large amounts of sialic acid; an average of 4.4μmole/g of brain and 21.0μmole/g liver. Normal tissues had undetectable amounts of this sugar. Gel filtration and thin layer chromatography confirmed that the major storage material was free sialic acid. Cultured skin fibroblasts incubated with [^{3}H]glucosamine demonstrated an accumulation of a radioactive component with chromatographic properties and charge consistent with sialic acid. (Supported by NIH grants HD06426 and HD09402).

728 EFFECTS OF PHENYTOIN ON THE FREQUENCY OF SISTER CHROMATID EXCHANGES IN HUMAN LYMPHOCYTES. Marsha H. Hunke, Nancy J. Carpenter and B. Say. Children's Medical Center, Department of Clinical Genetics, Tulsa, OK.

Sister chromatid exchanges (SCE) are an indication of DNA damage, and the BrdU-labeling technique used to detect them constitutes a sensitive method for assaying the clastogenicity of various chemical agents. This method was used to investigate whether the drug phenytoin sodium (Dilantin), a commonly prescribed anticonvulsant, produces clastogenic effects. The frequency of SCE was determined in normal human lymphocyte chromosomes treated in vitro with various concentrations of phenytoin and differentially stained with acridine orange. The SCE frequency was significantly increased at 30 mcg/ml of phenytoin. SCE frequencies were also determined from lymphocyte cultures for six control subjects and for ten patients undergoing monotherapy with phenytoin for a maximum of eight years. Serum phenytoin levels ranged from 3.8 mcg/ml to 29.5 mcg/ml in the therapy group. There was no significant difference between the frequency of SCE in the phenytoin-treated patients and the control subjects.

729 CYSTINE STORAGE IN I-CELL AND CYSTINOTIC FIBROBLASTS. Adam J. Jonas, Edward A. Bump, Erik Harms, Ocean L. Pellett, and Jerry A. Schneider. Univ. of California, San Diego, Department of Pediatrics, La Jolla, California 92093.

I-cell (MLII) fibroblasts have a high free-cystine (cys) content. As in cystinotic (C) cells, the cys is in lysosomes. In cystine-free media with 1mM cysteamine, both cell types lose 50% of their cys in 6-9 min. The rate of loss changes with time, and by 60 min the decrease of cys is 88-97% in C cells but only 54-64% in MLII cells. Following removal of cysteamine and replacement with complete medium, cys reaccumulation in the first 8 h. is much greater in C cells (0.27-0.48 nmol/mg prot/h.) than in MLII cells (0.02-0.04 nmol/mg/h.). From 8 to 24 h. the rates of reaccumulation of both cell types are similar (0.06 nmol/mg/h). Reaccumulation of cys in complete medium containing 30 mM glutathione-cysteine disulfide (GSSC) is increased 380% in C cells, but only 140% in MLII cells. With 50 μM chloroquine, the reaccumulation of cys in complete medium is inhibited in both cell types. Chloroquine does not inhibit the marked increase in cys reaccumulation with GSSC seen in C cells, but does in MLII cells. This suggests that the mechanism of cystine storage differs in the two cell types and that protein degradation is a more important source of cys in MLII than in C cells.