† **768** **VIRILIZATION IN A 45,X/46,Xr(X)/46,Xdel(X)(p21:;q11:) FEMALE,** SE Oberfield, LS Levine, S Pang, J Wedgwood, W Sweeney III, C Moreira-Filho, S Wachtel, MI New, New York Hosp-Cornell Med Ctr, New York, NY 10021

A 14 1/2 year old female with short stature, bone age 12, Tanner I breasts, pubic hair and clitoromegaly (3.5 x 1.5 cm), was studied. Lymphocyte karyotypes were 45,X/46,Xr(X)/46,Xdel(X)(p21:;q11). Abdominal and pelvic sonogram and CTT were normal. Elevated and fixed levels of serum testosterone were noted.

	T (ng/dl)	Δ4 (ng/dl)	DHEA (ng/dl)	FSH (mIU/ml)	LH (mIU/ml)
baseline	99	48	289	229	80
Dexamethasone (2 mg/d x 4 d)	93	15	41	355	169
Dexamethasone and HCG (5000 IU IM x 3 d)	98	20	36	---	---
Dexamethasone and Norlutin (30 mg/d x 3 d)	82	27	74	328	113

There was indication of expression of H-Y antigen in blood lymphocytes evaluated in the ELISA. Bilateral streak gonads were surgically removed and contained multiple clusters of Leydig cells. Postoperatively the T level decreased to 13 ng/dl.

Thus, in the patient's gonads there was evidence of functional Leydig cells in the absence of a Y line. Presence of H-Y antigen may define a group of patients with gonadal dysgenesis who are at risk for development of gonadoblastoma.

771 AMINO ACID CONCENTRATIONS IN MATERNAL AND FETAL BLOOD AND IN AMNIOTIC FLUID AFTER ADMINISTRATION OF A PHENYLALANINE LOAD IN PREGNANT FASCICULARIS MONKEYS. Siegfried M. Pueschel, Joan M. Boylan, Benjamin T. Jackson, and George J. Piasecki. Brown University Program in Medicine, Rhode Island Hospital, Department of Pediatrics, and Veterans Administration Hospital, Department of Surgery, Providence, Rhode Island.

The primary objective of this study was to obtain information on placental transfer mechanisms of amino acids in relation to their concentrations in amniotic fluid.

At 120 days of gestation fascicularis monkeys underwent an operative procedure: catheters were placed in a fetal common carotid artery, in the amniotic cavity, and in a maternal femoral vein. A priming dose of 200 mg/kg L-phenylalanine and 36 mg/kg p-chlorophenylalanine were administered followed by a two-hour infusion of 150 mg L-phenylalanine and 36 mg p-chlorophenylalanine. Maternal and fetal blood as well as amniotic fluid were sampled at 0, 1, 3, and 5 hours.

Comparing the amino acid concentrations in maternal and fetal blood and in amniotic fluid we observed that the amino acids in fetal blood significantly exceeded those in maternal blood and that the amino acid levels of the amniotic fluid were in most instances between the maternal and fetal blood amino acid concentrations. These differences were particularly striking when phenylalanine and tyrosine levels in the three compartments were studied. These data provide basic information on placental transfer mechanisms which will be of importance in the management of maternal phenylketonuria.

† **769** URIDINE MONOPHOSPHATE KINASE (UMPK)--A NEW GENETIC MARKER FOR SUSCEPTIBILITY TO HAEMOPHILUS INFLUENZAE TYPE B (HIB) DISEASE. GM Petersen, DR Silimperi, EM Scott, DL Hall, JI Rotter, JI Ward. Harbor-UCLA, Torrance, CA; and Arctic Investigations Laboratory, CDC, Anchorage.

The highest known risk for invasive HIB disease occurs in Alaskan Eskimos (10-50 times that in the U.S. population). Using a case-control design to study potential genetic explanations for this unique susceptibility, we examined 93 Eskimo HIB cases and an equal number of healthy Eskimo controls matched for age and village (exposure). We observed that allele 3 of the UMPK locus was positively associated with HIB disease, with a relative risk of 3.33 (McNemar matched pair, p<.01). Further, all UMPK 3-3 homozygotes in this study were HIB cases. This is consistent with an earlier suggestion of increased respiratory infections in a family with a UMPK variant (Giblett, AJHG, 30: 627, 1974).

To investigate further the nature of this susceptibility, serum levels of total HIB antibody (AB) were measured by radioimmunoassay. While no relationship was found between antibody and the UMPK phenotypes in the controls, a positive correlation was observed between antibody level and UMPK type in the HIB cases. Log AB levels increased with the number of UMPK-2 and -3 variants (p<.04), both in the overall sample and after adjusting for age:

UMPK Genotype:	1-1	2-1	3-1	3-3
HIB Cases (log ng HIB AB/ml)	5.56	6.11	6.35	7.61

This study has identified a genetic marker associated with susceptibility to HIB disease and suggests that a relationship may exist between UMPK enzyme activity, HIB disease susceptibility, and specific humoral antibody response.

772 CHROMOSOME INSTABILITY IN THE SYNDROME OF TRIPHALANGY OF THUMBS, ONYCHODYSTROPHY, DEAFNESS, SEIZURES AND MENTAL RETARDATION. Q.H. Qazi, C. Madahar, B.S. Nangia and T. Sheikh. SUNY, Downstate Med. Ctr., and Methodist Hospital, Depts. of Pediatrics, Brooklyn, N.Y.

Triphalangy of thumbs associated with onychodstrophy, deafness, seizures and mental retardation is a rare autosomal recessive disease. We have observed high frequency of chromosomal breaks in lymphocyte cultures from two affected children and their phenotypically normal mother. Blood samples were obtained simultaneously from all individuals on three separate occasions. Cultures were established and harvested by standard procedures. The slides were stained with giemsa and 50 cells were examined in detail from each culture. The only abnormality detected was a high frequency (P<<.0001) of chromatid and isochromatid breaks in both patients (0.24 and 0.22 breaks/cell, respectively) compared to that in 50 laboratory controls (0.02 breaks/cell). The frequency of breaks in the mother (0.08 breaks/cell), nearly one-third of that in her children, was still higher (P=.0001) than that in the controls.

Chromosomal instability is an integral feature of several autosomal recessive disorders such as ataxia telangiectasia, Bloom syndrome and Fanconi anemia. Its occurrence in a syndrome characterized by skeletal, skin and central nervous system abnormalities is an unusual observation, the significance of which remains to be determined.

770 X-LINKED RECESSIVE MYOTUBULAR MYOPATHY. Siegfried M. Pueschel, Mary M. Ambler, Charles Neave, Barbara G. Tutschka, Jay M. Orson, and Don B. Singer. Brown University Program in Medicine, Rhode Island Hospital, Departments of Pediatrics and Pathology, and Women & Infants Hospital, Department of Pathology, Providence, Rhode Island.

We studied a family with four neonatal deaths due to X-linked myotubular myopathy. The cardinal features of the two index patients included low Apgar scores, weak respiratory efforts requiring intubation and positive pressure ventilation, flaccidity, lethargy, hypotonia, reduced muscle mass, no spontaneous movements, poor grasp, suck, and Moro reflexes, absent deep tendon reflexes, cephalohematomata, narrow chest with thin ribs, undescended testes, and various minor congenital anomalies.

Light microscopy studies revealed variation in cell size and fiber hypotrophy. Fiber typing showed that the small fibers were both Type I and II cells; 90% of larger fibers were Type II A and B. Muscle nuclei appeared prominent and were located centrally in both large and small muscle cells. Small fibers showed prominent hollow centers with thin marginal rims of myofibrils. Larger fibers also had altered myofibril-free centers.

Electron microscopy examinations also noted fiber size variation and central nuclei. The myofibril-free areas contained glycogen and vacuoles. Complex stacks of cylinders comprised of membranes with granular material resembling junctional complexes abutted the central pale regions. Both rough endoplasmic reticulum and ribosomes aligned along the myofilaments were observed.

773 Promoter-terminator fusions of E. coli ribosomal RNA operons have been constructed on multicopy plasmids in order to study regulation of RNA transcription. Previously, we have identified a small (80bp) DNA region that when transcribed, produces anti-terminating RNA polymerase transcripts. We presume this means that the RNA polymerase elongation complex passing through this region becomes modified such that ordinarily efficient terminator sites downstream are ignored. We also found that the ribosomal RNA terminator region contains a pair of terminator sites (T1 & T2) that have a special property of being able to stop even anti-terminated transcripts. We are attempting to define the DNA sequence determinants of this special property, called "super-termination".

Super-termination could occur simply as a linear additive effect of two inefficient terminators or alternatively as a more complex cooperative function. By sequencing bisulfite induced mutations in the super-terminator, functions of T1 alone and T2 alone related to termination can be defined. These are compared to mutant sites found to interfere with super-termination. In all cases terminator mutants are selected using a galactokinase detector gene and sequenced using dideoxy techniques with ml3 templates.

In eukaryotes the existence of extremely large heteronuclear RNA transcripts suggests transcription antitermination and super-termination mechanisms may also occur.