728 LINKAGE ANALYSIS IN X-LINKED OCULAR ALBINISM. MaryAnn V. Volpe[1], John M. Graham, Jr.[1], Frederick S. Miller, III[2], Jeanette S. Risdahl[3], Richard A. King[4], B. deMartinville[3], (Spon. by R.Z. Klein). Dartmouth Medical School, [1]Dept. Mat. & Child Health, [2]Dept. of Surgery (Section of Opthalmology), Hanover NH 03756; and Univ. of Minn., Medical School, [3]Dept. Lab. Med. and Path., [4]Dept. Medicine, Minneapolis, MN 55455.

Preliminary work has suggested linkage of the Nettleship-Falls type of X-linked ocular albinism (XLOA) with three anonymous loci DXS85, DXS16, and DXS9; respectively defined by probes p782/EcoRI pXUT23/BglII, and RC8/TaqI (Amer. J. Hu. Genet. 37:A161, 1985). In this study, linkage of XLOA with DXS85 (p782) was demonstrated in 1 family (lod=3.4, conf. inter. 0-0.12), and localization of the XLOA locus to the region Xp22 to Xpter was suggested. Prior studies suggested loose linkage of XLOA to the dominantly-inherited Xg allele near Xpter. We studied 2 large families with XLOA via opthalmological exams, skin biopsies for macromelanosomes, & pedigree analysis. We analyzed segregation at 3 anonymous loci in addition to the Xg locus: DXS85 (p782), DXS9 (RC8), and DXS164 (pERT87-8/TaqI and pERT87-15/TaqI). Family 1 consisted of 108 members, including 12 involved in this study (2 affected males, 3 carrier females, 7 unaffected). Family 2 consisted of 122 members, including 45 involved in this study (8 affected males, 11 carrier females, 26 unaffected). Linkage of XLOA with DXS85 was confirmed for both families, while DXS9 was uninformative. Further studies with flanking markers (the Xg blood group and the pERT probes) are in progress. Since both families are informative at the pERT locus, it should be possible to define the relative distances between the XLOA locus and flanking loci.

729 EVIDENCE THAT CELL SURFACE HY ANTIGEN IS NOT THE SOLE MEDIATOR OF NORMAL HUMAN SPERMATOGENESIS. Sharon L. Wenger, Mark W. Steele, and Harry Ostrer, Univs. of Pittsburgh and Florida, Children's Hospital of Pittsburgh and J.H. Miller Health Center, Departments of Pediatrics, Pittsburgh, PA. and Gainsville, FL.

A 32 year old virile male was evaluated for sterility consequent to hypospermia. Physically he was a normal male other than that his right testis was firm and small.Blood FSH and LH were markedly elevated, testosterone was low normal,cell surface HY antigen was positive, and chromosomal analysis was 46,XY/47,XYY. Sperm ducts aspirates demonstrated 3-4 poorly mobile abnormal sperm per microscopic field but there was no sperm in ejaculate. The patient's Y chromosome was smaller than his chromosome #21. Compared to his chromosome #18, his Y chromosome was significantly smaller than like comparisons in 6 normal males (p=0.0002). Likewise, the patient's short and non-fluorescent long Y chromosome arms were the same relative size as in normal males (p=0.54) suggesting that the patient may have lost some Yq fluroescent DNA. Analysis by DNA probes confirmed no deletions in either the patient's short or non-fluorescent Y long arms and similar analysis for the Yq fluorescent arm is in progress. The patient's father was not available for evaluation. Studies by others suggest that the presence of gene(s) on non-fluorescent Yq are necessary for normal spermatogenesis and that cell surface HY antigen may be their product. Our data support this hypothesis and also suggest that fluorescent Yq may also somehow be involved in normal human spermatogenesis.

730 NEUROFIBROMATOSIS II (ACOUSTIC NEUROMA-MENINGIOMA) Wladimir Wertelecki, Duane W. Superneau, and Lois Forehand. University of South Alabama College of Medicine, University of South Alabama Medical Center, Department of Medical Genetics, Mobile.

Neurofibromatosis (NF) has been categorized as type I (von Recklinghausen) or type II (formerly "Central NF"), and other categories have been proposed (III-VII).

Our investigations concern a large kindred with NF II that spans 7 generations and includes over 300 members. Affected individuals do not fulfill the diagnostic criteria of NF I. Their symptoms and signs are direct byproducts of the emergence of nervous system neoplasia. Clinical and histologic data from 28 patients (14 males, 14 females) indicate that the most prevalent neoplasms are acoustic neuromas (AN) (15 cases) followed by meningiomas (MEN) (8 cases) and ependymomas (2 cases). MEN, if present, are diagnosed during puberty or shortly after (earliest onset 16 years) and tend to be multiple. Individuals developing symptoms later (latest onset 6th decade) tend to be free of MEN, and instead develop AN which most often are bilateral. None of the affected developed optic glioma or pheochromocytoma.

Molecular studies of MEN and AN tissue were indicative of a loss of genes on chromosome 22 (Seizinger et al, 1986), a strong clue to the chromosomal location of the defect. Molecular studies of this kindred by the same investigators are in process to determine whether the NF II gene is on chromosome 22.

731 PARENTS' ATTITUDES TOWARD PRENATAL DIAGNOSIS OF CYSTIC FIBROSIS AND PHENYLKETONURIA, H. A. Williams, H. Ostrer, and S. Chesrown, University of Florida, Colleges of Nursing and Medicine, Gainesville, Florida (Sponsored by E. Ayoub)

Recent advances in molecular genetic research have made possible prenatal diagnosis and carrier detection for phenylketonuria (PKU) and for cystic fibrosis (CF). All of the families currently followed in our PKU and CF Clinics were surveyed to test the hypothesis that parents' willingness to use prenatal diagnosis correlates with their perception of burden of disease (i.e. risk of long-term handicap and/or mortality). A questionnaire was mailed to 66 families of children with CF and 37 families of children with PKU. Knowledge about the disease and about clinical genetics in general were examined. Socioeconomic status, level of education, and religious affiliation were ascertained to determine if these were significant predictors of parental responses. The responses from each individual were subjected to multi-variant analysis. In addition, qualitative data were examined utilizing content analysis. The response rates were 56% for CF and 59% for PKU. The overwhelming majority of parents of children with PKU ranked their children as being mildly ill or not ill at all. None indicated that they would use prenatal diagnosis. By contrast, 37% of parents of children with CF ranked their children as being moderately ill; 19% of parents of children with CF indicated that they would consider using prenatal diagnosis within the next five years. Many of the parents were still unsure about how the test would alter their plans. The study supports the notion that perception of burden of disease is a major determinant of parental attitudes toward prenatal diagnosis.

732 CHROMOSOMAL LOCATION OF THE CMT I GENE BY CBG-BANDING Lowell L. Williams, Richard Stallard (Spon by Dwight A. Powell) Depts. Ped. and Cytogenetics. Ohio State Univ. Col. Med. Children's Hospital, Columbus, Ohio.

The gene for the familial peripheral neuropathy Charcot-Marie-Tooth disease, Type I (HMSN I) is assigned to the proximal long arm of chromosome #1 within 10 centimorgans of the Duffy locus (FY) (Povey et al.Hum. Gene Map 8,1985). We report on the location of the CMT I gene in 6 families by examination of the heteromorphic, CBG-positive 1qh region which intervenes between FY and the #1 centromere. At least 10 pairs of straight,flat, well-differentiated CBG-banded #1 leukocyte chromosomes were evaluated. The 1qh regions were interpreted as approximately equal or unequal in length. Lengths of 1qh were estimated by comparison to the short arm of chromosome #16. In Family A the 1qh regions could be distinguished in cells from an affected proband. Two affected daughters carried the proband's #1 chromosome with the larger qh. Two fetuses from one of them also carried the identifiable 1qh at amniocentesis. Each affected member of Family B in 3 generations was recognized blindly through an identifiable 1qh. Linkage of CMT I to FY was confirmatory in Family A, but not informative for Family B. Blind cytogenetic analysis of Families C and D are in progress. Since 1qh heteromorphism was not present in 2 other CMT I family probands, these families were not further studied.

These data support assignment of CMT I gene to proximal 1g. Further, cytogenetic assessment of 1qh may provide information for counseling pre-symptomatic carriers and for prenatal diagnosis in affected CMT I families.

●733 A RECOMBINANT CHROMOSOME 9 DERIVED FROM A MATERNAL PARACENTRIC INVERSION: CYTOGENETICS, INTERPHASE NUCLEAR PROJECTIONS, AND IN SITU HYBRIDIZATION USING CENTROMERE AND PARACENTOMERE PROBES. Maria J. Worsham, Dorothy A. Miller, V. Ramesh Babu, Lester Weiss, and Daniel L. Van Dyke. Medical Genetics and Birth Defects Center, Henry Ford Hospital and Molecular Biology and Genetics, Wayne State University, Detroit.

The two year old proband has multiple malformations and severe developmental delay. Her karyotype is 46,XY,-9,+rec(9),dup p,inv(9)(q22.1q34.3)mat, with a net duplication of 9pter→q22.1 and deficiency of distal 9q34.3→qter. The rec(9) was derived by two crossovers, one within the inversion loop. The mother's karyotype is 46,XX,inv(9)(q22.1q34.3). Her chromosomes 9 differ in that the #9 with the inversion has some heterochromatin in the short arm as a normal variant. In the proband's rec(9), the variant centromere is now attached to the normal 9q, which indicates that during maternal meiosis there was a crossover between 9q12 and 9q22. The rec(9) was present and stable in over 300 lymphocyte metaphase cells. Most rec(9)'s had one primary constriction at the centromere within the normal 9q segment. This centromere was Cd-positive, and the second centromere was Cd-negative, but 18% of routine Giemsa-stained cells had two primary constrictions. In the proband's fibroblast cells harvested in situ without colcemid, nuclear projections were observed in 10% of interphase cells. Such nuclear projections have been observed whenever a chromosome with one active centromere and one latent centromere is present, suggesting that there was at least some spindle-fiber activity of the latent centromere (Am J Hum Genet 26:83, 1974 & Proc Clin Biol Res 26:181, 1978). In situ hybridization with a centromere specific probe (p82H) and a paracentromere specific probe (L6) revealed no differences between the two C-band regions of the rec(9). This suggests that there was no interstitial deletion of heterochromatic or centromeric material. The present case confirms that a stable recombinant chromosome derived from a paracentric inversion can lead to malformations and suggests that prenatal diagnosis should be made available to families with paracentric inversions.