† **835** CYSTIC FIBROSIS (CF): KNOWLEDGE AND ATTITUDES TOWARD PRENATAL DX (PND) AMONG PARENTS (PAR); AUNTS & UNCLES (A&U);HEALTH PROFESSIONALS; AND CLERGY (CL). M. Kaback, P. Boyd, R. Cantor, D. Zippin; Harbor/UCLA Medical Center, Torrance, CA

We have examined knowledge of CF and its genetics, perceptions of burden, and attitudes toward family planning and the use of CF-PND and carrier screening (HD) in 27 CF Center physicians (CF-MD); 55 ancillary Center staff (ST); 362 childbearing-age parents (PAR) of 214 children with CF; 245 aunts and uncles of these children (A&U); 80 family MD's (LMD); and 58 clergymen (CL) serving these families. Health professionals (CF-MD, LMD, ST) highly favor PND for CF (100%, 95%, and 96% respectively). PAR and A&U also favor this option (82%, 81%) while CL are less favorable (55%). HD also is highly desireable to all groups. Significant associations ($p<0.02$) were found between PAR attitudes toward PND of CF and: religion, religiosity, abortion attitudes, and number of children. PAR PND attitude was not influenced by: age, sex, prior death of a child with CF, education, family history, or CF burden. A&U perceived CF as more serious, burdensome, and emotionally stressful than PAR ($p<0.0001$). Increased knowledge of CF and its genetics, and acknowledged interaction with CF families (among non-Catholic CL) correlate highly ($r=0.85$) with more favorable attitudes toward PND. Wide utilization of such technologies is anticipated.

† **836** LD-B DOSE EFFECT IN TETRASOMY 12p PSEUDOMOSAICISM. Thaddeus E. Kelly, David E. Bruns, Theodore E. Mifflin, Joan F. Atkin. Departments of Pediatrics and Pathology, University of Virginia School of Medicine, Charlottesville, Virginia.

Pallister et al (BD:OAS XIII3B:103, 1977) described two profoundly retarded adults with normal lymphocyte karyotypes and an extra metacentric chromosome in fibroblasts. In a group of eight patients the phenotype was shown to be similar to the 12p trisomy syndrome (J Clin Dysmorphol I(3):1, 1983) under the eponyms of Killian and Teschler. Lactic dehydrogenase (LD) is a tetramer with α (chromosome 11p) and β (chromosome 12p) subunits. LD isozymes were analyzed by electrophoretic and immunochemical methods in serum, red cells, white cells and fibroblasts from two patients and their parents.

	SERUM			RBC	WBC
	LD1/LD2	β/α	%LD1	LD1/LD2	%β
AJ	.96	1.75	53.4	1.36	45
Mother	.54	1.08	30.8	0.85	43
Father	.49	1.06	28.4	0.95	49

Isozymes LD1 and LD2 are not expressed in fibroblasts. An estimate of subunits in LD4 and LD5 had a higher β/α in AJ than the parents. A similar pattern of isozymes in serum, red cells, white cells and fibroblasts was found in the M family.

These data support the identification of the metacentric chromosome as an isochromosome of 12p and demonstrate gene dosage effect in some tissues (serum, red cells and fibroblasts), but not in cells where the isochromosome was not found (white cells).

837 CONGENITAL CENTRAL HYPOVENTILATION SYNDROME: AN AUTOSOMAL RECESSIVE FORM WITH VARIABLE EXPRESSIVITY. Julie R. Korenberg, Christopher J.L. Newth, Tom Allerding and Seymour Packman. University of California, San Francisco, Department of Pediatrics; University of New Mexico, Department of Pathology.

Central hypoventilation syndrome may be congenital or appear later in life. At least two heritable forms have been reported. We have previously documented central alveolar hypoventilation in association with pyruvate dehydrogenase complex deficiency. In addition, a syndrome including congenital central hypoventilation, Hirschsprung's megacolon and disturbance of esophageal motility has been described in two infant sisters and an unrelated boy. We herein report congenital central hypoventilation in both a 4½ month old girl and her (deceased) 3½ month old brother. Almitrine, a peripheral chemoreceptor stimulant, did not affect respiration in the former. While the girl also manifested disturbed esophageal motility and Hirschsprung's disease, pre- and post-mortem histologic study of the large and small intestine revealed no abnormalities of ganglion cells. We conclude that the aggregate data support autosomal recessive inheritance for this syndrome. Further, the syndrome manifestations are variable in their expressivity, and the disorder---with its attendant 25% recurrence risk---must certainly be considered in babies with congenital central hypoventilation.

838 MATERNAL HISTIDINEMIA: STUDY OF FAMILIES IDENTIFIED BY ROUTINE CORD BLOOD SCREENING Harvey L. Levy and Rachel Benjamin, Harvard Medical School; State Lab. Inst., Mass. Dept. of Public Health; Children's Hosp., Depts. of Neurology and Pediatrics, Boston.

The adverse effect of maternal PKU on the fetus has led to concern about the potential for fetal damage in other maternal inborn errors of metabolism. Maternal histidinemia has been associated with lowered intelligence among offspring, and in mice, with a balancing defect and inner ear changes in offspring. We routinely screened filter paper cord blood specimens for histidine by the Guthrie assay and identified seven mothers with histidinemia among 230,362 specimens. Assuming 40% rescreening, this is a frequency of 1:20,000. Five families could be studied. Maternal plasma histidine ranged from 586 uM to 1023 uM. All mothers had absent skin urocanic acid. Among 14 untreated pregnancies, 13 produced liveborn full-term offspring, and one ended in spontaneous abortion. Eleven of 13 offspring had normal measurements at birth, including head circumferences; 2/13 were SGA. Congenital anomalies included bilateral clubfoot in one infant and hip dislocation in another. Three offspring in one family also had histidinemia. At the time of evaluation (age 4.4 ± 3.0 yrs), all offspring except one had normal weight, height, and head circumference; one was FTT. IQ among offspring (n=9) was 103.8 ± 18.0 (range 82-139) compared to maternal IQ (n=5) 102.0 ± 18.7 (range 80-130). Offspring DQ (n=3) ranged from 106-128. There were no physical defects, and neurological assessments were normal. Maternal histidinemia seems to have no adverse effect on the fetus.

● **839** USE OF OLIGONUCLEOTIDES WITH NON-HUMAN SEQUENCES FOR PROBING HUMAN DNA. Karla J. Matteson, Mickey S. Urdea, Bon-chu Chung, Mu Lan Lim and Walter L. Miller Department of Pediatrics, University of California, San Francisco and Chiron Corp. Emeryville, CA.

Short, chemically synthesized mixed-sequence oligonucleotides have been used to identify cDNA and gene clones. Recently, pairs of 19 to 23 base unique-sequence oligos differing at a single base have been used to identify disease-causing point mutations in human DNAs. Both techniques rely on the requirement of short oligonucleotides to have a perfect match with the probed gene in order to hybridize. We have used long oligonucleotides containing non-human sequences with unknown mismatches for the same purpose. Using a unique new DNA synthesizer (DNA 3:401, 1984) we produced a 63-base and 3 72-base oligonucleotides corresponding to various regions of the bovine cDNA for P450scc (20, 22 desmolase) the enzyme converting cholesterol to pregnenolone. All four oligos hybridize to Northern blots of human adrenal mRNA in the same pattern. Two of these oligonucleotides hybridize to Southern blots of normal human genomic DNA in identical patterns indicating the human genome contains a single P450scc gene. As the two non-hybridizing oligos hybridize to mRNA but not genomic DNA, they probably span introns. Southern blots of genomic DNA from 3 patients with 20, 22 desmolase deficiency (congenital lipoid adrenal hyperplasia) hybridize with the oligos in the same pattern as DNA from normals, implying the disease is not due to a detectable gene deletion. Advances in DNA synthesis may permit gene studies in human diseases without requiring the tedious intermediate cloning steps.

840 CHROMOSOME ABNORMALITIES IN OSTEOSARCOMA DEVELOPING THIRTEEN YEARS AFTER TREATMENT FOR RETINOBLASTOMA. Lee G. Meyers, Karen A. Michalski (Spon. by Giulio J. Barbero), University of Missouri Health Sciences Center, Department of Child Health, Columbia, MO.

There is a high incidence of second malignancies, especially osteosarcoma, in survivors of hereditary retinoblastoma. The retinoblastoma "gene" which has been assigned to chromosome region 13q14 has been proposed to be a more generalized cancer gene and the link between these two diverse tumors. Non-random abnormalities, primarily deletions, have been seen in the 13q14 region in a significant number of retinoblastoma tumor cells and is felt to be the second event. Osteosarcoma tumor cells of a right temporal bone from a 13-year-old female who had received radiation therapy (5000 R) at age 12 weeks for bilateral retinoblastoma was grown in culture and analyzed. The patient had received high-dose methotrexate 2 months before the tumor resection. Cytogenetic analysis of primary cultures show 15% with abnormalities of the #13 chromosome with 5/15 with a deletion in the 13q14 region. Other clonal abnormalities were also noted. Simultaneous examination of peripheral lymphocytes and skin fibroblasts show 46XX normal female chromosome complement. This patient provides evidence for a common chromosomal connection between these two tumors.