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## Clinical Genetics: Reproductive Genetics (Prenatal/Perinatal) *(continued)*

### 1185

**Alpha1-thalassemia majors: Outcome of 39 fetuses at risk; and PCR testing for 11 pregnancies.** Y.E. Hsia*, J.A. Hunt, J. Yuen, B.M. Chu, F. Miyakawa. U. Hawaii, Kapiolani Med. Ctr. Honolulu, HI, USA.

Among 1402 Filipino, 485 Chinese, and 372 Laotian adults screened for α or β thalassemias in Hawaii, 38 couples were at risk for homozygous $\alpha_1$-thalassemia; and 1 for severe Hemoglobin H/Constant Spring [CS] disease ($--/\alpha^{CS}\alpha$). Southern blots were used for diagnosis of Southeast Asian [SEA] ($--^{SEA}$) or Total ($--^{Tot}$) α-region deletions; and PCR with allele-specific oligomer [ASO] hybridization for ($\alpha^{CS}\alpha$).

In 92 fetuses at known risk for ($--^{SEA}/--^{SEA}$) or ($--^{SEA}/--^{Tot}$) 23 had hydrops, but in 17 known pregnancies at risk for ($--^{Tot}/--^{Tot}$) none was affected.

| Couples at Risk | | Chin | Fil | Lao | Fetus | Affected |
|---|---|---|---|---|---|---|
| ($--^{SEA}/--^{SEA}$) | 16 | 5 | 10 | 1 | 48 | 12 |
| ($--^{SEA}/--^{Tot}$) | 13 | 1 | 11 | 1 | 44 | 11 |
| ($--^{Tot}/--^{Tot}$) | 9 | | 9 | | 17 | 0 |
| ($--^{SEA}/\alpha^{CS}\alpha$) | 1 | | | 1 | 2 | 2 |

In 11 pregnancies at risk, we have detected 1 ($--^{SEA}/--^{Tot}$), and 3 ($--^{SEA}/--^{SEA}$) fetuses by PCR for the $\alpha_2$-gene, and 1 ($--^{SEA}/\alpha^{CS}\alpha$) by PCR with ASO.

For pregnancies at risk, rapid PCR tests can detect these fetal α-globin genotypes that are major causes of fetal mortality and morbidity in SEA.

### 1186 Poster Symposium 80

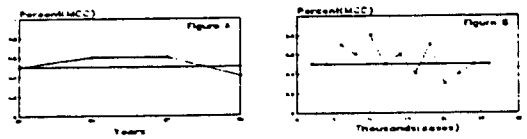
**A pilot study of maternal alpha-fetoprotein screening with dried-blood spot samples collected on filter paper.** K-J Hsiao* (1)(2), S-Y Lee (2), S-H Chiang (2), E-F Low (2), C-H Huang (2), M-F Huang (3), H-T Chen (4), and I-K Chen (5). (1) Institute of Genetics, National Yang-Ming Medical College, (2) Department of Medical Research, Veterans General Hospital-Taipei, (3) Taiwan Provincial Institute of Maternal and Child Health, (4) Nan Tou Public Health Bureau, (5) Tai Tung Public Health Bureau, Taiwan, Republic of China.

From Jan. 1988 to Dec. 1990, we conducted a pilot maternal alphafetoprotein (AFP) screening program in Nan Tou County, Taitung County and Taipei City, Taiwan. From 2 hospitals, 4 clinics and 35 health stations, a total of 8,800 pregnant women, were screened using the filter paper blood collecting technique. Of those screened, 3.6% of them were found borderline positive for neural tube defects (NTD) (2.0 < MoM < 2.5). The screening positive rates for NTD (MoM > 2.5) and Down syndrome (Down's risk > 1/100) were 2.6% and 3.6%, respectively. Except for those lost to follow-up, 6 (2.1%) of the borderline cases were confirmed to have serious pregnancy complications (porencephaly, fetal demise, and imminent miscarriage). Fourteen (8.1%) of the abnormal pregnancies, including 2 hydrocephalus, 2 anencephalus, 1 triploid and 5 fetal demise, were found in the NTD positive group. Nine (4.6%) anomalies (2 Down syndrome, 2 triploids, 1 hydatidiform mole, and 4 miscarriages) were detected in the increased Down's risk group. Totally, 29 adverse pregnancies, i.e. 0.33% (29/8,800) of the screened women, were confirmed in this screening program. From 2,836 post-delivery questionnaires completed, one false-negative case of Down syndrome was found, which had a Down's risk of 1/240 when screened. In this study, a public health and medical services network was incorporated in the screening system, and such a network may work well even in the remote areas of Taiwan. The results indicate that the use of the filter paper blood collecting technique for maternal AFP screening is practical. Currently, we are studying the possibility of using the same blood sample to screen other diseases (e.g. DM, thalassemia), which will make the screening program more cost effective.

### 1187

**Maternal cell contamination (MCC) in amniocytes: A constant frequency in 10 years and 26,000 cases.** LYP Hsu*, S Kaffe and B Tang. Prenatal Diagnosis Lab (PDL) of New York City/HHRA.

In amniocytes, MCC is usually detected through an admixture of XY and XX cells. In 1983, in our 1st 3,000 cases, we observed an incidence of 0.5% of MCC in comparison to a frequency of 0.123% of MCC in the nationwide MCC survey (Benn & Hsu, 1983). This difference could result from higher detection at PDL, and/or an actual higher MCC rate. In our first 26,000 cases (the first 10 years), we detected 132 cases with XY and XX admixture, i.e., a frequency of 0.5%. When the MCC percentages were examined for successive 3 year periods and for every 2,000 cases (Figure A&B), the incidence of MCC remained consistently around 0.5%. A dip in 1990 was statistically insignificant ($p > 0.25$). Among 132 cases, 25% showed only a single XX cell, 53.8% had multiple XX cells but restricted to one flask; and 21.2% had multiple XX cells from two or more flasks. We believe that the detectable MCC rate will remain around 0.5%. The true MCC incidence would be twice that, i.e., 1%, since MCC is usually not recognized when the fetal sex is female.




### 1188

Rate of chromosome 10 in balanced translocations. E.Hvozdíková, G.Kučerová, E.Nebesnáková. University Hospital, Košice, Czechoslovakia.

We have done a cytogenetic investigation in 279 conjugal pairs with unsuccessful reproduction in their history case. This analysis was aimed at occurrence of balanced translocation in one of the parents. Cytogenetic findings were positive in 7 couples/2,1%/, four pairs were the carriers of balanced translocation including chromosome 10 which it represents 1,4% out of the group investigated and 66,6% out of the balanced translocations which were detected. Rearrangements of chromosome 10 with autosomes 1,4,7 and 9 included the regions of short arm in the band 10p15 /1 couple/ and of long arm in the bands 10q23, 10q25 and 10q26 / 3 couples /.

Some tendency for chromosome 10 in the fragile sites expressed by the following joining with another autosomes is accounted for its increased rate in the chromosomal anomalies being examined.

### 1189

Prenatal identification of chromosome markers by fluorescent in situ hybridization. N.B.Isada (1), F.C.Koppitch (1), M.P.Johnson (1), M.I.Evans (1), J.Leana-Cox (2) and S.Schwartz (2). (1)Wayne State Univ., Hutzel Hosp., Detroit, MI and (2)Univ. of Maryland, Baltimore, MD.

Markers are de novo, extra, structurally abnormal chromosomes with variable clinical significance. We present 2 cases of chromosome markers identified prenatally using fluorescent in situ hybridization (FISH). Pt#1 underwent amniocentesis at 17 wks for maternal age. The karyotype showed a mosaic 45,X,9qh+/46,X,-(X or Y),9qh+,+marker. Parental karyotypes were normal. Y-specific DNA probes, DYZ3 and DYZ5 (Y-190), which localize to the Y centromere and Yp respectively, were utilized for a more detailed analysis. DYZ3 demonstrated that the marker chromosome had the Y centromere, while DYZ5 indicated the presence of 2 signals for Yp. We concluded this marker to be a Yp isochromosome (Ypter→cen→Ypter). The patient elected to continue the pregnancy, and delivered a phenotypically normal male infant, whose blood karyotype confirmed amniocentesis findings. Pt#2 underwent amniocentesis at 18 wks for maternal age. Karyotype showed 47,XX,+bisatellited marker. Parental karyotypes were normal. FISH was performed using a probe that localizes to the repetitive portions of 15p. This showed hybridization to both satellited regions, suggesting that this marker was an inverted partial duplication of 15 (15pter→q11:q11→15pter). After further counseling, the patient elected pregnancy termination at 22 wks.

Advantages of FISH include: 1) direct analysis from mounted slides using fluorescent molecular probes, a capability not possible with Southern blot, 2) fewer problems with contamination when compared to polymerase chain reaction, and 3) avoidance of radioactive reagents necessary for autoradiography. We conclude that FISH is useful for the prenatal characterization of chromosome markers.

### 1190 Poster Symposium 56

**A familial amino acid substitution in SRY can lead to conditional XY sex inversion.** R.J.Jäger* (1), R.A.Pfeiffer (2) and G.Scherer (1). Inst. of Human Genetics, (1) Univ. of Freiburg, FRG and (2) Univ. of Erlangen-Nürnberg, FRG.

Primary gonadal development in mammals is determined by the presence or absence of a gene on the Y chromosome encoding a testis determining factor, TDF. A candidate for TDF close to the Y pseudoautosomal boundary, termed SRY, encodes a protein with homology to a conserved DNA binding motif known as the HMG box. We and others have previously observed de novo mutations in SRY in XY gonadal dysgenesis; in addition, one XY female has been reported with a conservative amino acid change in the HMG box motif of SRY which is shared by her father (Nature 348: 448 and 452, 1990).

We have now identified a second inherited point mutation in the HMG box motif of SRY in an XY female. This mutation is clearly familial, because it is also present in the patient's normal male father, brother and uncle. The mutation, a T to C transition, results in a substitution of a Phe residue by Ser at position 52 in the HMG box motif. In contrast to the mutation mentioned above this substitution constitutes a non-conservative change at a highly conserved position. In all HMG box motifs known an aromatic residue is invariably found at the corresponding position. The mutation does not occur in more than 150 male controls. We conclude that this familial mutation is not a trivial polymorphism but causes conditional sex inversion depending on the genetic (or environmental) background.