Proc. of 5th International Congress of IEM, Monterey, 1990

W4.2

PRENATAL DIAGNOSIS OF DIFFERENT FORMS OF PHENYLKETONURIA (PKU)

K.J. Hsiao, T.S. Su, T.T. Liu, T.F. Tsai and M.L. Yang*.
Depts. of Medical Research and Obst. & Gyn.*, Veterans General Hospital; Taipei, Taiwan 11217, Republic of China

Using human phenylalanine hydroxylase (PAH) cDNA probe, the restriction fragment length polymorphisms (RFLP) at PAH locus have been identified with 7 restriction enzymes. By RFLP linkage analysis approximately 44% Chinese PAH deficient PKU families are informative for prenatal diagnosis, which is significantly lower than in Caucasians (Chen et al. Hum Genet 1989;81:226). Recently, prenatal diagnosis of a Chinese PAH deficient PKU (haplotypes 44/4) with chorionic villi sampling was made successfully by this analysis. Furthermore, analysis of the polymerase chain reaction amplified DNA demonstrated that the mutation in Chinese haplotype 44 is a single-base substitution (Arg408-Trp408) corresponding to the mutation associated with haplotype 2 in northern-European Caucasian (Tsai et al. Hum Genet 1990;84:in press).

Tetrahydrobiopterin (BH4) deficient PKU is reported to be a rare variant forms of PKU in Caucasian. However, approximately 50% of Chinese PKU in Taiwan are caused by BH4 deficiency. The most common form of BH4 deficiency is found to be deficient in 6-pyruvoyl tetrahydropterin synthase (PTPS) activity. Analysis of pterins in amniotic fluid by HPLC resulted in successful prenatal diagnosis in pregnancies at risk of BH4 synthesis deficiency. Reference ranges (n=40) of biopterin (B;pmol/mL), neopterin (N;pmol/L) and total biopterin ratio (B%=B/(B+N)) in amniotic fluid (gestational age: 12-24 wks) were determined to be 6.0-25.6, 22.1-103.1 and 9.3-36.3%, respectively. Two cases, one heterozygote and one normal homozygote, were diagnosed prenatally.