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PRENATAL DIAGNOSIS OF DIFFERENT FORMS OF PHENYLKETONURIA

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Phenylketonuria (PKU) is an autosomal recessive disorder of phenylalanine hydroxylation. For the hydroxylation to function normally, phenylalanine hydroxylase (PAH) and tetrahydrobiopetrin (BH4) are required. The PKU phenotype may be caused by either defect in PAH or deficiency of BH4. The incidence of Chinese PKU in Taiwan was estimated to be about 1 in 32,000. The BH4-deficient form of PKU was found to be around 20% among Chinese PKU population in Taiwan, which was more prevalent than that in Caucasian population. DNA analysis, enzyme assay of aminocytes or fetal blood, and measurement of pterins in amniotic fluid is possible in aid of prenatal diagnosis of various forms of PKU. By linkage analysis of restriction fragment length polymorphisms (RFLP) at PAH locus, approximately 44% Chinese PAH deficient PKU families were informative for prenatal diagnosis, which was significantly lower than in Caucassians. Prenatal diagnosis of a Chinese PAH-deficient PKU (haplotypes 44 and 4) with chorionic villi sampling was made successfully by the RFLP linkage analysis. Point mutations at codon 408 of PAH gene were identified on Chinese PKU alleles of haplotype 4,41,44, which could be applied to prenatal diagnosis with the aids of polymerase chain reaction of DNA amplification and allele-specific oligonucleotide hybridization. BH4-deficiency may be caused by defects in BH4 synthesis or the BH4 regeneration enzyme, dihydropteridine reductase(DHPR). Defect in 6-pyruvoyl-tetrahydropterin synthase (6PTPS) involved in BH4 synthesis was found to be the most common form of BH4-deficiency in Chinese. Analysis of pterins in amniotic fluid by high performance liquid chromatography resulted in successful prenatal diagnosis in four pregnancies at risk of 6PTPS deficiency. One affected homozygote, one heterozygote, and two normal homozygotes were detected. Prenatal diagnosis of DHPR deficient PKU could be performed by determining DHPR activity in amniocytes or chorionic villi. RFLP linkage analysis of DHPR gene locus in two Chinese DHPR deficient families were informed informative which could be applied to prenatal diagnosis of DHPR deficiency as well.

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GENETIC FACTORS IN GASTRIC AND DUODENAL ULCER DISEASE

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Peptic ulcer has a lifetime prevalence of 10% for males and 5% for females. Elucidation of specific genetic abnormalities is difficult, as environmental, psychologic and physiologic variables may interact differently. Concordance of peptic ulcer is higher (but not 100%) in monozygotic than in dizygotic twins, and twins share either gastric or duodenal ulcer. Association with various genetic traits is evident in duodenal ulcer patients: individuals with blood group O, non-secretors of ABO blood group antigens, patients with HLA antigens of the B 5, B 12 and the BW 35 phenotype. Duodenal ulcer is not a single disease with a complex pattern of inheritance interpreted as polygenic, but is characterized by genetic heterogeneity. Subclinical markers of peptic ulcer are: maximum acid secretion, serum pepsinogen 1, gastric emptying, gastrin response to a meal. Potential markers are: Serum pepsinogen II, gastric secretion, gastrin, duodenogastric reflux. A bimodal distribution of serum pepsinogen I concentrations was found in duodenal ulcer patients. Pepsinogen I levels are elevated in 50% presenting a significant risk factor for the disease. 40% of siblings with duodenal ulcer and hyperpepsinogemia I had also duodenal ulcer, whereas only 12% of siblings of normopepsinogenic I [illegible]