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Therefore, this preliminary finding suggests a disorder in the enzymes or vitamins B12 involved in remethylation of homocysteine or in the metabolism of folic acid supplementation are as yet unknown. Folate and vitamin B6 are involved in the metabolism of homocysteine.

In fundamental biological processes that underly the preventive action of folic acid intervention studies suggest that periconceptional vitamin supplementation, deficiency or toxicity, and genetic factors. Results from case-control and cohort studies indicate that maternal hyperhomocysteinemia and occurrence of orofacial clefts in offspring, skin biopsy is an effective screening tool, while demonstration of impaired cholesterol esterification in skin fibroblasts. In conclusion, these cases illustrate the diverse, but common presentations of a rare disorder. With limited treatment options, establishing an early diagnosis is invaluable.


The female infant was the product of an uneventful 36-week pregnancy. Parents were non-consanguineous and healthy. At birth the child was jaundiced and had hepatomegaly with ascites. Laboratory studies revealed the following: total bilirubin 14.5 mg/dl (direct 0.5), albumin 1.7 mg/dl, prothrombin time 30% Factor II 16%, V 22%, VII 16%, X 22%, fibrinogen 114 mg/dl, amylase was normal. Serum ferritin concentration was 1,915 mg/ml. Urinary succinylacetone was absent. Alpha-1-antitrypsin deficiency was excluded. All viral and serologic studies and cultures were negative. The patient was treated conservatively and despite intensive management the child died on day 21 of life of diffuse uncontrollable cutaneous and mucous bleeding. This is not an uncommon disease; such analysis has not been previously reported in South-East Asia. In addition, we hope to develop rapid screening assays for mutations when the specific mutations have not been identified.

Identification of two novel polymorphisms in the glucocerebrosidase gene region: the first one consists of a tetranucleotide (AAAT) repeat upstream to the glucocerebrosidase gene, and the second is a series of a dinucleotide (CT) repeat in the intergenic region between the glucocerebrosidase gene and its pseudogene. These two polymorphisms, along with the previously reported PvuII polymorphism in intron 6 of the glucocerebrosidase gene, were analyzed in Gaucher patients (n=106) and two control populations (Akenzien n=72 and non-Jewish n=46). Strong linkage disequilibrium was found between the common haplotypes N370S/84GG mutations. We also found exceptions to previous reports that the N370S/644G genotype is always associated with a Pv1.1/-Pv1.1+ genotype. Several unusual cases of patients with unexpected haplotypes led to the recognition of two common N370S/644G mutations. Our work primarily consisted of a tetranucleotide (AAAT) repeat upstream to the glucocerebrosidase gene, and the second is a series of a dinucleotide (CT) repeat in the intergenic region between the glucocerebrosidase gene and its pseudogene. These two polymorphisms, along with the previously reported PvuII polymorphism in intron 6 of the glucocerebrosidase gene, were analyzed in Gaucher patients (n=106) and two control populations (Akenzien n=72 and non-Jewish n=46). Strong linkage disequilibrium was found between the common haplotypes N370S/84GG mutations. We also found exceptions to previous reports that the N370S/644G genotype is always associated with a Pv1.1/-Pv1.1+ genotype. Several unusual cases of patients with unexpected haplotypes led to the recognition of two common N370S/644G mutations. Our study of these markers may reveal possible ancestral chromosomes which led to affected alleles, and that may be diagnostically useful in Gaucher patients when the specific mutations have not been identified.

Spectrum of Mutations In 21-hydroxylase deficient form of Congenital adrenal hyperplasia in Singapore. Agnes Tay1, Kah-Yin Loke1, Larry Poh1, 2, Institute of Molecular and Cell Biology, 3Dept of Paediatrics, National University of Singapore.

Congenital adrenal hyperplasia is due to a deficiency in cytochrome P450 enzymes, the most common of which is 21-hydroxylase. This enzyme is encoded by the CYP21 gene on chromosome 6p. Our aim was primarily to determine the spectrum of genetic abnormalities responsible for this disease; such analysis has not been previously reported in South-East Asia. In addition, we hope to develop rapid screening assays for mutations common in our local population. Fourteen unrelated patients from the Endocrine Outpatient clinic were studied. A view of the mutations described in this report was extracted from peripheral leukocytes. The CYP21 gene amplified from genomic DNA using the polymerase chain reaction and the products of amplification were sequenced. Sequencing of six exons and intron 2 revealed mutations in 6 out of the 14 individuals. These included insertion of a single base pair creating an 8-bp deletion in exon 3 (1 patient), INN7 missense mutation in exon 4 (1 patient), and Q316X nonsense mutation in exon 8 (1 patient). For the intron 2, 2 mutation, allele-specific PCR and Tm ligation hybridization proved to be a reliable and rapid screening technique. Sequencing of the remaining exons is ongoing and we hope to infer genotype-phenotype correlations when we have catalogued the mutations in all the affected patients.