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PETI THUWAJIT: STUDIES IN CHLORIDE-BICARBONATE EXCHANGER GENE AE1 MUTATIONS IN SUBJECTS WITH SOUTHEAST ASIAN OVALOCYTOSIS AND DISTAL RENAL TUBULAR ACIDOSIS. THESIS ADVISORS : PRAPON WILAIRAT Ph.D., PA-THAI YENCHITSOMANUS Ph.D., RUTAIWAN TOHTHONG Ph.D., 220 p. ISBN 974-663-062-8.

Distal renal tubular acidosis (dRTA) is an endemic disease in Northeastern Thailand. It is associated with renal stone and causes public health problems, since only supportive treatment is available for this disease. Primary dRTA can be inherited in autosomal dominant and recessive patterns. Pathogenesis is the defect in urine acidification, which occurs in the distal part of the renal tubule at the intercalated cell type A. Kidney AE1 is a protein which plays a major role in this process (with anion transport activity). It is encoded by *AE1* gene, which also expresses erythroid AE1 (band 3). *AE1* mutations have previously been shown to be associated with both autosomal dominant and recessive dRTA. A common *AE1* mutation that results in a defect in anion transport activity is Southeast Asian ovalocytosis (SAO). Although an SAO itself cannot cause dRTA, it is hypothesized that dRTA can occur with SAO in autosomal recessive mode. Five dRTA patients with SAO were identified and studied. Two were adult manifestation with no evidence for *AE1* mutation in trans with SAO. Three patients were child manifestation. Two were compound heterozygotes for SAO and Bangkok I (G701D). Sulfate uptake of red blood cells from both probands did not differ from those of typical SAO red blood cells. Band 3 Bangkok I can function when expressed with glycophorin A (GPA) which is present in red blood cell but not in kidney intercalated cell type A. The remaining child form of dRTA was a compound heterozygote for SAO and R602H. A sibling had the same genotype also but with defect in urine acidification in the absence of clinical presentation (incomplete dRTA). Sulfate uptake of red blood cells from both SAO/R602H probands was half of that of typical SAO red blood cells. These data indicate that *AE1* mutations are polymorphic in the Thai population. Carriers for *AE1* mutations may have a selective advantage by being protected against *Plasmodium falciparum*, possibly by reduction of parasite invasion or prevention of cytoadherance of infected red blood cells to endothelial cells, and thereby are less likely to have fatal cerebral malaria.