

# Thalassemia in Southeast Asia

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Southeast Asia, consisting of 10 countries—Brunei, Indonesia, Kampuchea, Laos, Malaysia, Myanmar, the Philippines, Singapore, Thailand, and Vietnam—is a continent as large as the United States but with almost double its population—over 400 million people. The hematological hallmarks of Southeast Asia are the high frequencies of  $\alpha$ -thalassemias and hemoglobin (Hb)E, both of which have foci with densely concentrated prevalence. The focus of  $\alpha$ -thalassemia is between northern Thailand and Laos with frequencies of 30–40%, while that of Hb E is at the junction of Thailand, Laos, and Kampuchea with frequencies as high as 50–60%. These two abnormal genes are scattered throughout Southeast Asia with diluted frequencies further away from the foci.  $\beta$ -thalassemia and Hb Constant Spring are relatively common, but without clear foci, frequencies of the former being 3–9% and the latter 1–5%. The genetic nature of  $\alpha$ -thalassemia is rather homogeneous, while that of  $\beta$ -thalassemia is very heterogeneous. Southeast Asian  $\alpha$ -

thalassemias are characterized by a total deletion of the duplicate  $\alpha$ -globin gene cluster in  $\alpha$ -thalassemia 1 and a deletion equivalent to the loss of one  $\alpha$ -globin gene in  $\alpha$ -thalassemia 2. The genetic defects of the  $\beta$ -thalassemia are mostly point mutations and thus very heterogeneous, encompassing over 20 genotypes altogether.

The  $\alpha$ -thalassemia 1,  $\alpha$ -thalassemia 2,  $\beta$ -thalassemia, Hb E and Hb Constant Spring genes in different combinations lead to very complex thalassemia syndromes of over 60 genotypes with varying degrees of severity from completely asymptomatic to the total lethality of the Hb Bart's hydrops fetalis. The complex genotype-phenotype relationship causes diagnostic difficulty, especially for Southeast Asians settling around the world. With remarkable success in molecular biological characterization of the abnormal genes, the remaining task is to better understand the genotype-phenotype relationship and complications to apply better prevention and treatment.