

## Glucose 6 Phosphate Dehydrogenase Deficiency and Dengue Hemorrhagic Fever

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OBJECTIVE : To determine if Glucose 6 Phosphate Dehydrogenase (G6PD) deficiency is related to the occurrence and/or course of dengue virus infection in man.

BACKGROUND : Despite a world wide distribution of dengue viruses, dengue hemorrhagic fever (DHF) and its severe manifestation, dengue shock syndrom, (DSS) appear to be major problems only in Southeast Asia. It has been suggested that this may be due to the simultaneous circulation of two or more dengue virus serotypes in this part of the world. However, more than one serotype of dengue virus type is endemic in Africa and in the Caribbean and no DSS has yet been reported (Personal communication : COL Philip K. Russell, M.D.). Other factors which may be associated with the occurrence or the severity of dengue infections must also be studied. Glucose 6 Phosphate Dehydrogenase deficiency is a genetic enzyme deficiency which is an x-linked recessive trait. Although the enzyme deficiency has been observed in several tissues, it is recognized mainly in the erythrocyte, where it causes hemolytic anemia following exposure to certain drugs, food stuffs or infections. The disorder is fully expressed in hemizygous males and in the homozygous females. In the heterozygous female the expression varies and is dependent on the degree of expression of the normal gene.

In Thailand, G6PD deficiency has been reported in up to 14% of the Thai population (1). This condition has been found to occur more frequently in patients with bacterial infections such as typhoid fever or pneumococcal pneumonia than in non-infected control subjects. G6PD deficiency has been associated with viral as well as bacterial diseases. Morrow *et al.* (2) have pointed out a relationship between G6PD deficiency and the incidence as well as the severity of viral hepatitis. Since G6PD deficiency and DHF occur frequently in Thailand, a relationship was sought between the enzyme deficiency and the occurrence and/or severity of disease.

METHODS : Children hospitalized at the Bangkok Children's Hospital with signs and symptoms compatible with the diagnosis of DHF were studied for G6PD deficiency. G6PD was examined using the methemoglobin technique of Gall *et al.* (3) which allowed for the determination of the patient's genotype. Patients were considered to have DHF if they met the laboratory criteria for diagnosis. A confirmed diagnosis was based on the isolation of the dengue virus and/or a

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four-fold or greater rise in antibody titer to dengue virus antigens. A presumptive diagnosis called for a fixed hemagglutination inhibition antibody titer  $\geq 1:640$  to two or more dengue virus antigens between the acute and convalescent sera. DHF presents a spectrum of severity. Grading of severity used established criteria (4).

Patients in this study were divided into two groups based upon the severity of illness. Those without circulatory failure and those with shock.

RESULTS : Eighty patients who met the laboratory diagnostic criteria for DHF were studied for G6PD deficiency. The frequency of G6PD deficiency in these patients was compared to a group of 131 controls collected in the well-baby clinic of the Bangkok Children's Hospital (Table 1).

Table 1. Glucose 6 Phosphate Dehydrogenase Deficiency in Dengue Hemorrhagic Fever Patients and Controls.

Subjects	No.	G6PD Deficiency*	
		No.	Percent
Patients	80	9	11.2
Controls	131	13	9.9

Chi square (1 d.f. = 0.0053; p not significant)

\* Includes all individuals homozygous, hemizygous or heterozygous for G6PD deficiency.

There was a 11.2% prevalence of G6PD deficiency in patients with DHF while in the control group 9.9% were affected. There was no significant differences in the frequency of G6PD deficiency between the DHF groups and control groups. The frequency of homozygosity and hemizyosity for G6PD deficiency in the two populations was also not significantly different.

An association was sought between the presence of G6PD deficiency and the severity of dengue infection (Table 2). Of the 80 patients with DHF, nine were G6PD deficient. Of those nine with G6PD deficiency, seven developed shock, as compared to 41 out of 71 patients without G6PD deficiency. This difference was not significant.

The results show no significant relationship between G6PD deficiency and the occurrence of DHF. The relationship of G6PD deficiency and severity remains a question. Although there was no clear or significant relationship demonstrated this may have been due to the small number of G6PD deficient patients with shock that were studied. This project is now completed.

Table 2. Glucose 6 Phosphate Dehydrogenase Deficiency and the Severity of Dengue Infections.

Dengue Patients	Total	Shock	
		No.	Percent
G6PD deficient*	9	7	
G6PD normal	71	41	
Total	80	48	

Chi square (1 d.f.) = 0.6310; p not significant

\* Includes all individuals homozygous, hemizygous or heterozygous for G6PD deficiency.

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