

## SICKLE CELL DISEASE IN THE KINGDOM OF SAUDI ARABIA: EAST AND WEST

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Two articles in this current issue deal with sickle cell diseases from the Eastern and Western Provinces of Saudi Arabia, and present interesting but different information about these hereditary hemoglobinopathies.<sup>1,2</sup> Nasserullah and associates performed electrophoresis from cord blood samples on infants born in hospitals in Qatif and Al Hasa over a one-year period of study.<sup>1</sup> A small subset of the study included a group of infants from primary health centers using capillary blood. These studies establish gene prevalence in their region.

The proportions of the various sickle genotypes in infants from Qatif and Al Hasa are very similar to those documented by Al Awamy in his comprehensive studies from Dammam and Qatif.<sup>3</sup> Data from both studies indicate that in the Eastern Province, 20% to 30% of Saudi newborns are heterozygous for the sickle gene (FAS, FAS-Bart's), and 1.6% to 2.3% may be homozygous (FS, FS-Bart's). If, as is likely, about the same frequency of heterozygotes is present in the adult Saudi population, it can be calculated that the frequency of homozygosity for sickle cell genes (SS) should be about one in 100 births, or 1.0%. The observed frequency of presumed SS, based upon a hemoglobin FS or FS-Bart's pattern in cord blood, was in fact slightly higher than this. This increased frequency probably results from inclusion of newborns with Hb S  $\beta$ -thalassemia who have the same neonatal electrophoretic pattern (FS) as sickle cell anemia, as well as consanguinity.

Nasserullah et al.<sup>1</sup> refer to American experiences that indicate a high early morbidity and mortality of Hb SS disease.<sup>4</sup> However, it is well known that the sickle cell disease seen in many patients from the Arabian Gulf areas has distinct clinical and electrophoretic differences from that observed in the United States and Africa.<sup>5,6</sup> These differences include a less severe hemolytic process (higher hemoglobin levels and lower reticulocyte counts), fewer and less severe vaso-occlusive symptoms and longer survival. These patients usually have high levels of fetal hemoglobin which persist into adolescence and adult life. It has been shown by DNA gene polymorphism analyses that the sickle cell gene that is prevalent in the Arabian Gulf area probably originated in Asiatic India. This has been designated the "Indian" sickle cell mutation, and it is believed to have entered the gene pool of the Gulf region

following ancient maritime trade routes hundreds of years ago.<sup>7</sup>

The second article in this issue, by Hawasawi and associates from the Maternity and Children's Hospital in Madina, describes some of the morbidity associated with Hb SS disease in their area of Western Saudi Arabia.<sup>2</sup> They retrospectively analyzed 53 patients with sickle cell diseases who were admitted to their hospital over a one-year period. The most frequent indications for hospitalizations were painful vaso-occlusive crises, infections and acute chest syndrome. This clinical pattern of morbidity is very similar to what is seen in Africa and the Western Hemisphere. Although hematologic data of their patients were not reported in this paper, it is likely that they were different than the findings in many patients from the Eastern Province. The sickle cell genes in Western Saudi Arabia were probably imported from Africa.

I believe that the most important message of these two articles is that sickle cell genes are prevalent in the Kingdom, but that their clinical and hematological manifestations may vary considerably in different regions. Because of this the rationale for neonatal testing and intense follow-up may vary considerably. One example may illustrate this. In Hb SS infants associated with homozygosity for African sickle cell genes, one can predict a generally severe course. Functional hyposplenism develops early and causes a marked susceptibility to overwhelming pneumococcal sepsis and meningitis, which has a high mortality. These children benefit markedly from early diagnosis and prophylactic treatment with penicillin, which reduces the incidence of invasive pneumococcal disease by 85%.<sup>8</sup> The clinical course associated with homozygosity in the Gulf area is generally less severe. Many Hb SS infants from this area maintain splenic function at least into adolescence and so do not have a high incidence of severe pneumococcal disease and early mortality.<sup>3,8</sup>

The major rationale for neonatal testing for sickle cell is to prevent early morbidity and mortality by identifying severely affected homozygotes who are at risk, and providing these children with penicillin prophylaxis. It would seem that newborn screening can be easily justified in those areas of the Kingdom where the African sickle

cell genes are prevalent. The case for newborn screening may be less strong in regions where the Indian sickle cell gene predominates. However, to make this kind of public health decision, much more genetic information will be necessary. A high priority should be given for studies to determine the epidemiology of the sickle cell genes throughout the Kingdom. The availability of the DNA polymorphism testing for the various sickle cell genes would also be of great value for establishing the prognosis of an individual sickle cell patient.

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