

Growth Patterns in the Hemoglobinopathies: (I) Growth Patterns by Age and Sex in Children With Sickle Cell Disease and (II) Growth and Sexual Maturation in Thalassaemia Major

The first report evaluates by age and sex the growth patterns of 133 children enrolled in the Sickle Cell Anemia program at Children's Hospital in Pittsburgh. These children were representative of the total population aged 1 to 18 years with sickle cell disease (SCD) in the metropolitan area. Eighty-three children (62.4%) had homozygous sickle hemoglobin (SS) and 50 (38.6%) had a variant hemoglobinopathy, such as sickle-cell hemoglobin C disease (SC), sickle cell thalassaemia (S-Thal), and sickle cell plus hereditary persistence of fetal hemoglobin (S-HPF).

The median height and weight of males fell below the 50th percentile at all ages between 2 and 18 years. Height and weight deficits increased with age, with values eventually falling below the fifth percentile in the 14- to 17-year age group. The median height and weight of female patients at ages 2 to 18 years followed a similar pattern, with median height and weight falling below the 50th percentile at all ages. A trend toward increasing deficits with increasing age was also seen. The overall growth deficit in the female patients was less pronounced at all ages. This basic growth pattern was seen in all patients with SCD (regardless of subtype), except for significantly higher weight in female patients with a variant hemoglobinopathy.

This study provides evidence of growth impairment in a large sample of children with SCD. The growth deficit, which increases with age, is more pronounced in males. Height and weight deficits appeared to begin as early as 2 years of age; the increasing deficits in height and weight noted in males between the ages of 14 and 17 years and in females between 10 and 12 years of age were associated with delayed onset of puberty. The authors constructed growth velocity curves that demonstrated the significance of the delayed pubertal growth spurt; maximum height and weight velocity occurred later and the magnitude

of the spurt was depressed. Final adult heights of these patients were significantly decreased, with the mean height and weight of adult males falling below the tenth percentile.

In the second report, growth and sexual development were evaluated in 250 adolescents with β thalassaemia major. These represented all patients above the age of 10 with transfusion-dependent thalassaemia major who were receiving treatment at the thalassaemia clinics of five teaching hospitals in northern Italy. Mean pretransfusion hemoglobin concentrations had been kept at greater than 9.5 g/dl during the previous five years and desferrioxamine had been administered for the previous seven to ten years. Thirty-seven percent of the thalassaemic children were found to be 2 SD below the mean for normal height. After age 14 years, the percentage of children with short stature reached 62% for males and 35% for females. As in the normal population, thalassaemic children with parents of short stature tended to be shorter than those with taller parents. Throughout childhood and adolescence, children with thalassaemia were shorter than normal, but their weight was found to be adequate for their height.

Eighty-three percent of the males and 75% of the females had delayed skeletal maturation. Pubescent changes were absent in 30% of the females and 67% of the males between 12 and 18 years of age. Indeed, only 11% of females less than 18 years of age had experienced menarche. Cardiac arrhythmias were reported in 22% of the patients and cardiac failure in 5.6%. Several patients had diabetes, and thyroid function was frequently lower than normal.

Thus, growth retardation and delayed or absent puberty are common findings in children with transfusion-dependent thalassaemia. The authors suggest that patients with lesser iron levels because of more intensive chelation therapy do not

fare any better than those on less adequate chelation therapy with regard to sexual maturation. Menarche does not seem to be any more prevalent today among girls between ages 12 and 14 who are on chelation therapy than it was in a group of female patients now older than 18, but not receiving adequate chelation therapy.

Phebus CK, Gloninger MD, Maciak BJ: *J Peds* 1984;105:28-33, and Borgna-Pignatti C, De Stefano P, Zonta L, et al: *J Peds* 1985;106:150-155.

Editor's comment—As these two reports demonstrate, short stature and delayed adolescence are common problems in the hemoglobinopathies. This, of course, is true of all chronic disorders, be they hematologic, infectious, gastrointestinal, or cardiopulmonary in origin. In transfusion-dependent thalassaemia, however, much of the growth delay had been attributed to a defect in the hepatic biosynthesis of somatomedin and to iron deposition in the pituitary, resulting in deranged function of the hypothalamic-pituitary axis. Thus, hemosiderosis had been considered one of the major problems resulting in growth and sexual delay (and other endocrine problems) in thalassaemia. Hemosiderosis, however, was not significant in the sickle cell study, although growth was significantly retarded in the SCD subjects. It is clear from these studies that individuals with SCD do not achieve normal adult height, in contrast to earlier reports from Jamaica suggesting that adults with SCD may attain normal or even greater than normal height. The specific reasons for the poor growth and delayed sexual development in children and adolescents with SCD, however, are not clear.