New Mutation in a Swiss Girl
Leading to Clinical and Biochemical β-Thalassemia Minor

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Summary. Evidence is presented for the first observation of a new mutation in thalassemia. The diagnosis of thalassaemia minor was confirmed by hematological data, the elevated Hb A2, and the relative underproduction of β chains in the patient’s reticulocytes. All the above tests were negative in both parents and the three siblings. The paternity of the legal father was documented with 99.99% probability. The rarity of the condition is discussed.


The genetics of thalassemia has been elucidated by the classic work of Valentine and Neel in 1944, according to which thalassemia major is the homozygous, and thalassemia minor the heterozygous state of the same disorder (for reviews see Weatherall, 1969; Weatherall and Clegg, 1972; Second Conference, 1969). Although recent observations (Bargellesi et al., 1967; Conconi et al., 1970; Lehmann, 1970) suggest that the genetic background to different thalassemia types may be more complex, the above statement remains valid for classic Mediterranean β thalassemia (also called high-A2 thalassemia). Both parents of all children with thalassemia major (Cooley’s anemia) therefore carry the trait, which is detectable with the aid of appropriate examinations, whereas at least one parent of children with thalassemia minor always shows the same disorder. To date no exceptions to this rule have been observed.

The present report describes the case of a Swiss girl in whom we diagnosed β thalassemia minor. Surprisingly, neither of her parents showed any signs of the disease. The legitimacy of the patient was documented with an unusually
high degree of certainty. Since the diagnosis of thalassemia in the propositus and the exclusion of the condition in the parents were established by the application of the most stringent current criteria, we conclude that this case of the thalassemia syndrome was the result of a fresh mutation. A preliminary report of this case has already appeared (Tönz et al., 1973).

I. Case Report

The propositus is the youngest of 4 siblings. Her family originated in central Switzerland, and no Italian or other Mediterranean ancestors are known. The grandparents are no longer alive. It was first noted that she had moderate anemia when she was 9 months old. The diagnosis of β thalassemia minor was established when she was 2 years old. At that time the hemoglobin was 9.2 g%, the red cells count $4.5 \times 10^6$/mm³, hematocrit 31%, reticulocytes 18%, hemoglobin A₂ 5.1%, hemoglobin F 6.9%. (The hemoglobin F value decreased to 1.8% at the age of 5 years.)

The mean values of other hematological parameters are given in Tables 1 and 2. The blood smears exhibited hypochromia, polychromasia, aniso- and poikilocytosis, basophilie stippling and some target cells. The osmotic resistance was markedly increased, median corpuscular fragility being at 0.36% NaCl (see Fig. 1). Serum iron was 66 µg% at 2 years, 144 µg% at 5 years.

The parents of the child are healthy and were aged 45 (father) and 44 (mother) at the time of the patient's birth. On two occasions all blood parameters tested, including osmotic fragility, were normal (for mean values see Table 1 and Fig. 1). No morphological abnormalities were detectable on smears. Serum iron was 77 and 99 µg%. Hemoglobin electrophoresis and determination of the alkali-resistant hemoglobin F were performed twice in our own laboratory and once in another laboratory. All values were normal (Table 2).

The siblings' blood data, including osmotic fragility, hemoglobin analysis and serum iron levels were within the normal range, except for the hemoglobin F value of the sister, which was slightly elevated in several checks (Table 2). Hemoglobin F stained in blood films by the method of Kleihauer and Betke, was unevenly distributed in the red cells.

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Fig. 1. Osmotic fragility curves