An Individual with “Miyada”-Like Hemoglobin Indistinguishable from Hemoglobin A₂

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Received 5 Feb. 1973—Final 20 Apr. 1973

The hemoglobin of a 24-year-old man of Italian descent who has the phenotypic characteristics of thalassemia intermedia contains about 12% hemoglobin F, 73% hemoglobin A, and 15% hemoglobin A₂. Chemical analysis definitely identifies the last as hemoglobin A₂. So elevated a percentage of hemoglobin A₂ has not been reported before. In addition, the amount of hemoglobin A is unusually large for an individual with presumed homozygosity for β-thalassemia. Although the evidence is indirect, it is suggested that he is heterozygous for two conditions: β-thalassemia and a “Miyada” type of gene that produces a hemoglobin indistinguishable from hemoglobin A₂.

INTRODUCTION

It is well known that the non-α chain of the hemoglobins Lepore (Hb-Lepore) has an N-terminal portion with the sequence of the δ chain and a C-terminal portion with the sequence of the β chain. Baglioni (1962), who first made this

The work was supported in part by grants HL-02558 and HL-05168 and Training Grant HD-00048 from the National Institutes of Health, U.S. Public Health Service, as well as funds from the Southern California Chapter of the Cooley’s Anemia Blood and Research Foundation.

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observation, concluded that the cause was nonhomologous crossing over of the δ and β genes with deletion. Many studies have since substantiated this conclusion and have shown, for example, that the Lepore δ-β chain is 146 residues in length, as are the β and δ chains (Labie et al., 1966).

The original Hb-Lepore (LeporeWashington) has a crossing over between residues 87 and 116. On the other hand, LeporeHollandia has the crossing over between residues 22 and 50 (Barnabas and Muller, 1962) and LeporeBaltimore between residues 50 and 86 (Ostertag and Smith, 1969). Recently, the anti-Lepore type, a β-δ fusion, has been detected by Ohta et al. (1971); it is termed Hb-Miyada and has the crossover between residues 13 and 21. In the Miyada type, parts of two genes have been duplicated rather than deleted.

Smithies (1964) has pointed out in some detail that the product of crossing over at certain residues will have the charge and presumably the electrophoretic properties of either Hb-A or Hb-A₂. However, the product of some crossings over near or at the N- and C-termini would be chemically indistinguishable from Hb-A or Hb-A₂.

The individual about whom we report has the phenotypic characteristics of thalassemia intermedia and about 15% Hb-A₂. We conclude that he is heterozygous for β-thalassemia and for an Hb-Miyada-like condition in which the "Miyada" hemoglobin is chemically identical to Hb-A₂.

MATERIALS AND METHODS

Blood samples were collected in Alsever's solution and immediately refrigerated. Hematological examination was made by standard methods.

Hemoglobin components were examined by starch gel electrophoresis in

![Fig. 1. Pedigree of family B.](image-url)