HEMOGLOBIN ''PORTO ALEGRE''

ESTRUTURA MOLECULAR DA HEMOGLOBINA "PORTO ALEGRE". By CASEMIRO VICTORIO TONDO. (Porto Alegre: Universidade Federale do Rio Grande do Sul, 1974. Pp. 120.)

In recent years, new and useful molecular biologic methods have improved our knowledge of the structure and function of normal and pathologic hemoglobins. A number of different hemoglobins that have been identified appear to be the product of mutant genes. Structural differences are either a result of selective synthesis of one type of polypeptide chain (as in thalassemia), of a consequence of substitution of an amino acid in the structural sequence of the chain (as in sickle-cell anemia). These abnormal hemoglobins exhibit anomalous physical-chemical properties, and clinical manifestations are associated with some of these structural alterations.

In this work, the author describes a new asymptomatic variant of normal human hemoglobin. The trait was found in a Caucasian family living in the southern part of Brazil, and the hemoglobin, called "Porto Alegre," was first detected as an increased amount of A3-like hemoglobin on paper electrophoresis. Studies of the amino acid sequence of this new hemoglobin revealed a substitution of serine by cysteine at position 9 of the beta chain, which yields two extra sulphydryl groups per molecule of hemoglobin. The main characteristic of hemoglobin "Porto Alegre" is its ability to polymerize in vitro, and this property is dependent upon the manner in which the protein is prepared and maintained. Polymerization of the tetrameric hemoglobin molecule is a unique property of this protein and has not been demonstrated with other variants of human hemoglobin. Hemoglobin "Porto Alegre" is a *tetramer* in vivo. However, molecular weights of the polymer, determined by osmotic pression, indicate that it forms a *dodecamer* in vitro. Chemical evidence suggests the dodecamer is formed by a link through the extra sulphydryl groups of the beta chain. No satisfactory explanation has yet been found for this phenomenon. Maintenance of the reduced form of cysteine by a glutathion redutase system is not a promising explanation. Due to the distance between the extra sulphydryl groups and to the steric configuration of the beta chains, the formation of an intramolecular sulphydryl bridge in the tetramer seems unlikely.

Further studies will be needed to clarify the point, especially with respect to the role of normal enzymes and other components of erythrocytes that could maintain reduced sulphydryl groups. An x-ray analysis of the new polymer will be of interest and seems likely to show the postulated contact between beta chains necessary to form the polymer.

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