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Multi-author Reviews

Developments in sickle cell anemia research, Part II

Introduction

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In this issue we complete the review of sickle cell anemia research. Dr. Brugnara covers the important issue of volume regulation and cation transport in sickle cells. Since the polymerization reaction is highly dependent on initial concentration of deoxyhemoglobin S (as you can read in Dr. Ferrone's contribution) a reduction in red cell volume will favor sickling and an increase in red cell volume will reduce sickling. Dr. Ferrone updates the polymerization reaction of hemoglobin S, highlighting the now visually proven double pathway: homogenous reaction that starts from the formation of small size nuclei, and the heterogenous reaction, that is initiated 'piggy back' to a pre-existing fiber. These pathways predominate under different conditions; they have morphological, rheological and possibly clinical significance. Dr. Croizat reviews the present knowledge on the properties of circulating BFU-E in sickle cell anemia patients, and reports that they vary according to the patients' HbF level: the implication is that patients with more severe anemia (low HbF) have BFU-E properties different from those with high HbF and less anemia.

Although sickle cell anemia is one of the best understood genetic diseases, a specific treatment is not available yet. Dr. Charache reports here the effort to augment HbF (an inhibitor of sickling) using pharmacological means. The results are encouraging in that all patients exhibit an increase in HbF, and in some cases, a considerable increase when treated with hydroxyurea. Is this sufficient to significantly abrogate one of the most incapacitating complications of the disease: painful crises? An ongoing collaborative project will answer this question. Finally, Dr. Perrine reports on her pioneering work in the development of butyrate derivatives as HbF enhancers. Arginine butyrate seems to increase HbF rapidly and without apparent side effects. If these findings are confirmed in further studies, this drug alone, other derivatives, or its combination with other potential agents (hydroxyurea, erythropoietin) might turn out to be the first generation treatment for sickle cell anemia.