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# Hemoglobin and Its Diseases

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# Hemoglobin and Its Diseases

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A subject collection from *Cold Spring Harbor Perspectives in Medicine*

EDITED BY

David J. Weatherall

*Weatherall Institute of Molecular Medicine*

Alan N. Schechter

*National Institutes of Health*

David G. Nathan

*Dana-Farber Cancer Institute*



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## Hemoglobin and Its Diseases

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*Front cover artwork:* The image shows the phenomenon of red cell rosetting. This is how normal red cells aggregate around malaria parasite-infected cells and are a marker of the severity of malaria. It is significantly diminished in  $\alpha$ -thalassemic red cells that are infected. Image supplied by D.J.P. Ferguson, Oxford University.

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## Preface

THE INHERITED DISORDERS OF HEMOGLOBIN are by far the commonest Mendelian diseases. It is estimated that between 300,000 and 400,000 babies are born with these conditions each year. They were the first genetic diseases to be characterized at the molecular level; hence, early work in this field led to the era of molecular medicine.

It is a surprising fact that, although work on the inherited disorders of hemoglobin opened up the whole field of human molecular genetics between 1950 and 1970, more recently it has become sidetracked from the mainstream of human genetics. Indeed, there has been a steady decline in its place in the literature of human genetics over the last 40 years. This is particularly surprising because the human hemoglobin field has disclosed many hundreds of the different mutations that are associated with monogenic disease, taught us more about the genetic basis for the phenotypic heterogeneity of inherited diseases than any other condition, and has provided increasing insight into the evolutionary and population biology of these conditions.

Why have the hemoglobin disorders drifted away from the mainstream of human molecular genetics over recent years? Although it is not absolutely clear why this has happened it probably reflects the way in which human genetics in general, and medical genetics in particular, have evolved over the last half-century. Medical genetics only became a clinical specialty in a few key centers in the United States and Europe in the 1950s and 1960s, and it was natural that they should focus on chromosomal conditions and monogenic diseases, which were common in their particular populations. Although there were increasing numbers of immigrant communities in these regions in which inherited hemoglobin disorders were not uncommon, they tended to be seen in hematology rather than genetics centers. In this way the two fields gradually drifted apart. This tendency is unfortunate because the remarkable technical developments in genomics have so much to offer each field.

The inherited disorders of hemoglobin occur at their highest frequency in the developing countries of the tropical belt, although they are being also seen with increasing frequency in emigrants from this region to the richer countries. As the poorer countries go through an epidemiological transition characterized by improved hygiene, nutrition, and public health facilities and better medical care in general, babies with hemoglobin disorders who would have died in the first few years of life are now surviving to present for diagnosis and treatment. This phenomenon occurred in many Mediterranean populations after World War II and will undoubtedly increase the global burden of hemoglobin disorders in many developing countries in the future. For example, it has been estimated recently that if early deaths due to sickle cell anemia are controlled in sub-Saharan Africa, the population of patients with this disorder could reach five to six million in the foreseeable future.

For these reasons, in this book we have attempted to give a broad coverage of the hemoglobin disorders, ranging from their basic biology and molecular pathology, through their clinical manifestations and management, to the various aspects of their population biology and the reasons for their high and increasing frequency. As well as being of value to workers in the hemoglobin field, we hope that this broad view will also be of interest to workers in medical genetics in general because of the many lessons that have been learned from the study of the abnormal hemoglobins, which are relevant to other monogenic diseases and, at least to some extent, to polygenic disease as well.

We acknowledge the great help that we have had from our colleagues who have given a great deal of time to produce their individual chapters. We are also grateful to the considerable help that we

Preface

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DAVID J. WEATHERALL  
ALAN N. SCHECHTER  
DAVID G. NATHAN