

Preface

Sickle cell disease (SCD) was first described in the USA over 100 years ago [1]. Nearly six decades ago, SCD became known as the first molecular disease after Linus Pauling described the different electrophoretic movements of hemoglobin A compared to hemoglobin S [2]. In the 1970s, research funding for SCD significantly increased, and findings from those research studies allowed SCD to move from a nearly universally fatal disease of childhood to a chronic illness [3]. Today, there are nearly 100,000 children and adults in the USA alone with SCD and millions more worldwide [4]. Although hydroxyurea and blood transfusion therapy decrease many SCD-associated complications, they are often underutilized in developing countries and neither cure the disease. Patients with SCD experience multisystem complications including recurrent and painful vaso-occlusive crises, acute chest syndrome, stroke, splenic sequestration, and pulmonary hypertension. As a result, organ damage begins at a young age and is progressive, contributing to an average life expectancy of SCD patients that is half that of the general population [5, 6]. Even though life expectancy of patients has improved in the last several decades in the developed world, very high childhood mortality rates (50–90%) exist in underdeveloped countries of Africa and India where the vast majority of SCD patients are globally. SCD remains a highly morbid disease that causes chronic and progressive physical damage, as well as poorer overall quality of life for affected children and adults worldwide.

Currently, the only available cure for SCD is hematopoietic stem cell transplant (HSCT). Successful transplants in children with SCD additionally result in organ damage reversal or stabilization of CNS vasculopathy. When a matched sibling donor is available for SCD patients, HSCT has excellent overall survival (93%, 95% confidence interval 91.1–94.6%) and good event free survival (91%, 95% confidence interval 89.6–93.3%) [7]. HSCT, however, is still vastly underutilized, even for those with donors; in fact, just over 1000 transplants for SCD patients have been documented in the literature[7]. Since SCD affects nearly 100,000 children and adults in the USA alone, and millions more worldwide, considerably less than 1% of people effected by SCD have been cured. Causes for the low numbers of HSCT performed for SCD patients are multifactorial and

include concern about toxicities from conditioning regimens or graft-versus-host disease, lack of provider or family awareness of HSCT as a curative option for SCD, and, most importantly, lack of an available suitable donor. This has led to the field investigating less toxic conditioning regimens (reduced intensity), novel graft manipulation techniques and medications to prevent graft-versus-host disease, and donor options other than matched siblings referred to as alternative donors. While outcomes with alternative donor transplants still need to be optimized, encouraging progress with unrelated bone marrow, umbilical cord blood, and most recently half-HLA-matched (haploidentical) parents and siblings has led to the majority of patients having a transplant donor option. Probably the most exciting advance in the HSCT for the SCD field in the last decade has been the ability to transplant adults with SCD using very low intensity conditioning and HLA-matched donors [8, 9]. The success rate of approximately 88% with no graft-versus-host disease is remarkable especially in a patient group that for many decades were considered too sick to proceed to transplant. Although the concept that gene therapy may ameliorate human genetic diseases emerged in the 1970s, this field of medical research experienced many obstacles over the last three and a half decades which prolonged the translation of this genetic technology into clinical medicine. However, along with these obstacles came broadened knowledge of safe gene delivery and editing systems which carved the path to making the concept of gene therapy to alleviate human diseases such as SCD a reality. Gene therapy trials in SCD are now underway, and very preliminary results show promise [10]. Unlike HSCT, gene therapy offers the potential of curative therapy to virtually all people affected by SCD.

This book aims to provide a comprehensive, state-of-the art review of HSCT for SCD and serves as a valuable resource for clinicians and researchers with an interest in SCD as well as HSCT. The book reviews new data about risk prediction for severe SCD; presents unique challenges of HSCT for patients with SCD; profiles the supportive care guidelines for SCD patients who are undergoing HSCT; highlights our current understanding of the best transfusion support for SCD patients prior to, during, and after HSCT; and provides new perspectives about the ethics of HSCT for pediatric patients with SCD. Several landmark phase III trials that utilized matched unrelated and haploidentical donors for HSCT in SCD patients have been placed in context with respect to current management.

We hope that this book will serve as a useful resource for physicians and researchers interested in this challenging, yet exciting, curative therapy for SCD. We thank the authors who contributed chapters to this book. We dedicate this book to our spouses, children, parents, and other family members who have supported us throughout our careers. We also thank our mentors who inspired us to continue working to improve the care of children with SCD and their families: Drs. Naomi Luban, Jeffery L. Miller, Derek Persons, and Naynesh Kamani. We also dedicate this book to our patients who live with this debilitating disease and inspire our work with their strength, resilience, and fighting spirits.

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