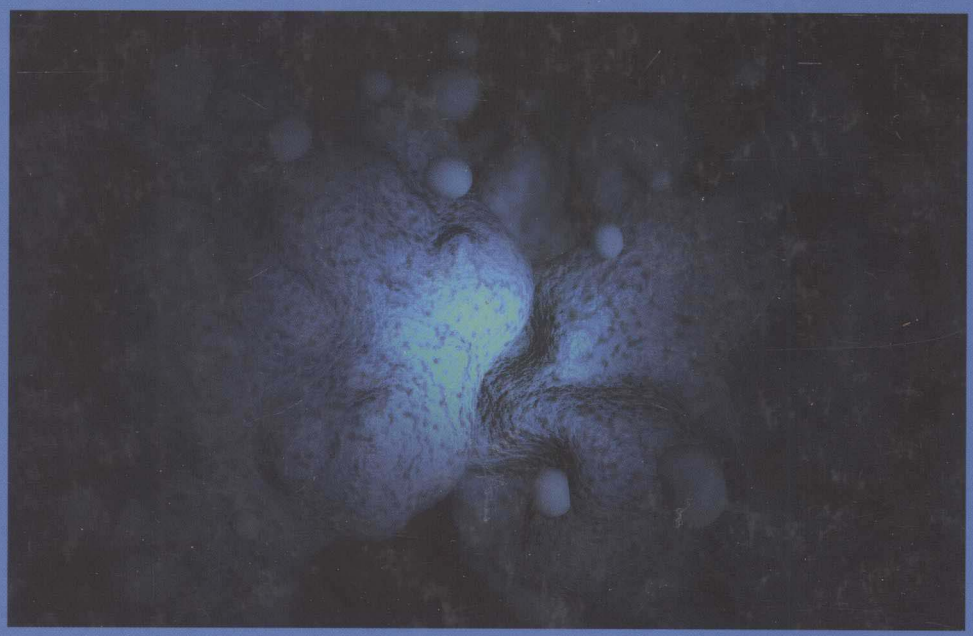
Contemporary Hematology

ALLOGENEIC STEM CELL TRANSPLANTATION

Second Edition

Edited by

Hillard M. Lazarus
Mary J. Laughlin



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Allogeneic Stem Cell Transplantation

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Dr. Hillard M. Lazarus dedicated his contributions to his wife Joan and his sons Adam and Jeffrey for their unwavering encouragement and support.

Preface

Allogeneic hematopoietic stem cell (HSC) transplantation has undergone fast-paced changes after our original publication of *Allogeneic Stem Cell Transplantation: Clinical Research and Practice*, first published more than 5 years ago. In this second edition, the editors have focused on topics relevant to evolving knowledge in the field in order to better guide clinicians in decision-making and management of their patients, as well as help lead laboratory investigators in new directions emanating from clinical observations. Some of the most respected clinicians and scientists in this discipline have responded in this second edition by providing state-of-the-art discussions addressing these topics.

Important advances have been recognized in HLA disparity between HSC donor and recipient triggers for T-cell and NK-cell allorecognition; such may induce the graft-versus-host disease (GVHD) and graft-versus-leukemia (GVL) effects and may cause an engraftment failure. This text covers the scope of human genomic variation, the methods of HLA typing, and interpretation of high-resolution HLA results. Durable GVL responses may be the result of the elimination of leukemia stem cells or the establishment of a durable immune control on their progeny.

Alternative sources of donor HSC continue to be used for transplantation at an increased frequency and include HLA-matched unrelated donor and umbilical cord blood; overall patient outcome has improved steadily using these diverse stem cell sources. The administration of reduced-intensity as well as non-myeloablative conditioning has also brought forth new concepts in the management of hematologic malignancies, thought to be of emerging importance in patients with lower grade malignant disorders such as chronic lymphocytic leukemia, multiple myeloma, and low-grade non-Hodgkin lymphoma. The elderly or those with comorbid conditions who have acute leukemia in complete remission also may benefit by using this lower-intensity therapy. The reduced toxicity of these novel conditioning regimens has also raised new possibilities in the application of allogeneic HSC transplantation for patients with non-malignant hematologic disorders such as sickle cell anemia and selected solid tumors such as renal cell carcinoma.

Allogeneic SCT remains the only available curative therapy for hematologic malignancies and some inborn errors such as beta-thalassemia. Its application, however, may result in significant morbidity and mortality, predominantly as a consequence of opportunistic infections and GVHD. While differences in HLA between donor and recipient make a crucial contribution to the alloreactivity

driving the donor-mediated GVL response, the cytokine milieu both promotes and regulates the allogeneic response after transplantation. As such, genetic studies correlating donor, host, or the combination of cytokine polymorphisms with disease outcomes have provided useful insight into disease pathogenesis, often confirming effects that have been determined in pre-clinical studies. It is now clear that the polymorphic expression of key cytokines (particularly tumor necrosis factor and interleukin 10) has a demonstrable effect on disease outcome and overall transplant-related mortality.

Many challenges in allogeneic SCT remain and include the risk of graft failure, recurrent disease, acute GVHD, opportunistic infections and long-term sequelae such as chronic GVHD, increased risk of second malignancies, endocrinopathies, and iron overload. The editors hope that this new information, well summarized by the authors in this text, will be of significant benefit to clinicians and researchers in allogeneic HSC transplantation. We envision that the generation of further knowledge and clinical studies to be of ultimate benefit to our patients.

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