Preface

The universe is full of magical things patiently waiting for our wits to grow sharper.

– Eden Phillpotts

It took a lot of blood, sweat and tears to get to where we are today, but we have just begun. Today we begin in earnest the work of making sure that the world we leave our children is just a little bit better than the one we inhabit today.

–Barack Obama

Without doubt, we are living in the most exciting of times in the history of clinical medicine especially in the realm of cancer research and treatment. The rate at which scientific progress has occurred and is being translated into improved medical diagnostics and therapeutics is breathtaking. Our improved understanding of basic molecular biology and genetics has presented cancer researchers and clinicians with a staggering array of therapeutic targets and novel therapeutic modalities. At this moment in time, we can only stand in awe at what the future almost certainly holds in store for future victims of this often devastating disease. However, as important as promising new and often novel cancer therapies have been, progress in our ability to effectively and safely support patients through cancer treatment has been equally exciting and groundbreaking often built as well upon the foundation laid by advances in molecular biology and genetics.

Among the barriers to the optimal delivery of systemic cancer therapies, hematologic toxicity arising from the myelosuppressive effects of most cytotoxic cancer treatments remains the lead cause of treatment-related complications including neutropenia, anemia, and thrombocytopenia. Such "cytopenias" result in frequent, serious, and potentially life-threatening complications including a wide range of bacterial, fungal, and parasitic infections, hemorrhagic complications as well as clinically significant fatigue. In addition, the risk or occurrence of such complications also often result in limitations to the full delivery of effective and potentially curative systemic chemotherapy while, at the same time, compromise quality of life and increase costs associated with the care of cancer patients. Many of the most exciting novel and targeted cancer therapies are, in fact, most effective when

combined with traditional cytotoxic and myelosuppressive chemotherapy. Likewise, complications of cancer treatment are often exacerbated by our multidisciplinary and combined modality efforts to improve long-term survival and cure among cancer patients.

Supportive care efforts including the appropriate and timely use of empiric broad-spectrum antibiotics in patients with fever and neutropenia and selective blood transfusions in patients with severe anemia and thrombocytopenia greatly improved early efforts to deliver antineoplastic chemotherapy. However, improved understanding of hematopoiesis and the factors that control the proliferation and morphologic and functional differentiation of hematopoietic lineages has provided insights and opportunities for reducing the complications associated with myelosuppression and other disorders resulting in neutropenia, anemia, or thrombocytopenia. This improved understanding coupled with outstanding advances in recombinant DNA technology has resulted in the development and clinical validation of a number of hematopoietic growth factors.

Hematopoietic Growth Factors in Oncology represents the latest in a series of texts in the Cancer Treatment and Research series edited by Dr. Steven T. Rosen. This volume brings under a single cover a discussion of the early discoveries, extensive preclinical and clinical investigation, and the validation of these efforts through the successful clinical extension of these discoveries into clinical hematology and oncology practice improving the treatment and quality of life of countless patients. As Editors, we have been extremely fortunate to have engaged in this project some of the world's leading investigators and authorities on both the science and the clinical application of the hematopoietic growth factors. We want to extend our very sincere thanks to this outstanding representation of investigators who have assisted us in assembling this comprehensive repository of information on the development and clinical application of these agents.

The text begins with an outstanding review of the biologic, physiologic, and pharmacologic underpinnings of the discoveries, laboratory studies, and early preclinical and clinical development of the hematopoietic growth factors from some of the actual pioneers in these fundamental studies. While the anticipation around development of early-acting hematopoietic growth factors has not been fully realized, developments in granulocyte colony-stimulating factors, the erythropoietic-stimulating agents, and the thrombopoietin factors have in many ways exceeded the expectations of many. The next three parts in this book then highlight the further clinical development and application of the three major categories of the hematopoietic growth factors, by individuals involved in both the pivotal studies and extended clinical trials that have further defined the efficacy and safety of these agents. Current recommendations for clinical application of the hematopoietic growth factors based on practice guidelines from major professional organizations are presented along with the evidence synthesis available on both efficacy and safety. While we are constantly made aware of the need to balance efficacy and safety, the emergence of the erythroid-stimulating agents, the myeloid growth factors as well as the new thrombopoietic agents have had a great impact on the supportive care of patients with cancer.

In the final part of this volume, a number of very important special considerations regarding the use of the hematopoietic growth factors are discussed including their often controversial role in management of patients with acute leukemia and the myelodysplastic syndromes, their efficacy and toxicity in older cancer patients, and the cost and cost-effectiveness of these agents in the prevention and treatment of hematologic complications exemplified by the use of G-CSF for the prevention of febrile neutropenia in patients receiving cancer chemotherapy. The authors emphasize that any comprehensive evaluation of benefits, harms and costs must consider not only the immediate reduction in risk of neutropenic complications in patients receiving cancer chemotherapy but also the potential long-term effects on disease control and survival when treatment intensity is sustained or enhanced with the adjunctive use of the myeloid growth factors.

In total, this represents the most comprehensive compilation available of preclinical and clinical experience related to the development, validation, and clinical application of the hematopoietic growth factors. The editors share the perspective of the individual authors that no aspect of cancer care deserves more attention as well as further clinical research than the treatment and prevention of life-threatening complications of cancer treatment. We recognize and share the excitement and anticipation of all hematologists and oncologists arising from the multitude of diagnostic and therapeutic breakthroughs of the past two decades. At the same time, we also recognize the importance of the many supportive care efforts enabling the optimal management of patients including the optimal delivery of modern cancer therapy while improving the quality of life of patients with cancer and other blood disorders throughout the course of their illness. Optimal clinical outcomes for each patient in the most complete sense remains the primary goal of all hematologists and oncologists as it is for other healthcare providers. The availability of advanced supportive care measures including the hematopoietic growth factors utilized in a rational, effective, and cost-effective fashion will further enhance these goals and bring us closer to that ultimate goal of optimal patient care.

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http://www.springer.com/978-1-4419-7072-5

Hematopoietic Growth Factors in Oncology
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2011, XV, 433 p., Hardcover
ISBN: 978-1-4419-7072-5