

Preface

THIS BOOK IS THE RESULT OF CONTRIBUTIONS from a remarkable variety of sources. In addition to the valuable contributions by the section editors and authors, enormous gratitude is extended to those who contributed methods, forms, or tables. These generous submissions attest to the quality of professionals in the field of cellular therapy.

A Word on the Organization of Content

A glossary and a list of abbreviations are included as appendices at the back of the book. These are intended not to be comprehensive for the field of cellular therapy but to cover those terms and abbreviations commonly used in this book. Where there are multiple definitions available for words or terms, we have selected those specific to the subject matter of this book. Appendices related to specific chapter or method content appear with the chapter immediately after the text. For this edition, sample methods are located in a separate section following the descriptive text sections. The methods are intended to serve as general outlines of procedures rather than as step-by-step standard operating procedures. Wherever methods were not submitted by the chapter authors, the appropriate contributors are acknowledged at the end of each chapter text.

Specific company names may be mentioned merely for the convenience of the reader and should not be considered endorsements of specific products or manufacturers.

A Word from the Editor in Chief

The best indicator I can think of when contemplating the growth of the cell therapy field is the time elapsed between the books I have edited on the subject. I first thought of working on a manual of cell (then called “bone marrow”) processing techniques early in my career when I realized there was no place to “look up” how to do any of the procedures I was expected to perform. With the generous help of the true pioneers in the field, I was able to put together the relevant SOPs for operating a processing lab. My directors at Georgetown then encouraged me to put the information I had acquired together and publish it to assist those in other labs with the same needs. That book¹ was published in 1991. It was 18 years before AABB published the first edition of *Cellular Therapy: Principles, Methods, and Regulations*,² an extensively updated version of the first manual. Now, 7 years later, there have been so many advances in cell and tissue processing that another update was due.

When I was first hired to set up and manage a laboratory for cell processing almost 30 years ago, I never anticipated what would be coming along in the future. The cells that we processed came primarily from bone marrow, and investigators were just beginning to examine peripheral blood “stem” cells as another source of hematopoietic cells for therapeutic use. The first successful umbilical cord blood transplant had just recently been performed. Marrow transplantation was an accepted, though high-risk, therapy of last resort for patients with hematologic malignancies and marrow failure—if

the patient wasn't too old and was fortunate enough to have an HLA-identical sibling donor. Although some visionaries may have started tossing around the idea of a registry of HLA-typed unrelated volunteer marrow donors, eventually to become the National Marrow Donor Program (NMDP), not even the most optimistic among them could have imagined that in a short time more than a million people would offer to donate their marrow and, later, mobilized peripheral blood and lymphocytes to strangers. In those days the only option for patients not eligible for an allogeneic transplant was often a dreadful treatment consisting of high-dose radiation or chemotherapy followed by a "transplant" with autologous marrow that had previously been collected and cryopreserved. The cell processing laboratory staff (typically consisting of one technologist working alone) not only processed, tested, and froze the marrow, but was also often expected to assist with the marrow harvest procedure, thawing, and infusion.

Besides the procedures for concentration and cryopreservation of marrow cellular products that were performed in most cell-processing laboratories, investigators were starting to develop the forerunners of many of the "designer" cellular therapy products described in this volume. There were experimental protocols for purging residual cancer cells from autologous marrow and for depleting T-cells from allogeneic grafts. These were extraordinarily labor-intensive procedures that often employed toxic chemicals and pharmacologic agents. Few assays were available for demonstrating the purity or potency of manipulated cellular products. Although these attempts at marrow purification may have reduced the probability of relapse or graft-vs-host disease, the procedures themselves often increased transplant-related morbidity and mortality by delaying immune reconstitution or lengthening the period of marrow aplasia.

The cell-processing laboratories of 1987 were a far cry from the sophisticated facilities in operation today. Any but the most basic procedures were performed in research laboratories at academic medical centers. The clinical cell processing laboratory was usually staffed with a single technologist, who was often shared with another laboratory or the blood bank. There was not (and still is not, as of this writing) a formal training program for techni-

cal staff to learn this specialized work. The technical procedures were learned from more experienced people in other laboratories, with frequent frantic telephone calls to those mentors when something went wrong.

I had the good fortune to spend a short time at the beginning of my cell-processing career in a laboratory at Johns Hopkins that was operated single-handedly by Janice Davis, under Scott Rowley as the medical director. Within a few days I was supposed to be trained to operate a cell-processing laboratory by myself. I was amazed and a little intimidated by Janice's breadth of knowledge and by the variety and diversity of tasks she was able to perform. When I asked her who took over if she got sick, she told me, "I'm very healthy. I hardly ever get sick." And when I asked her for the name of a reference book or manual on cell processing, which I could purchase to keep in my lab, she just laughed. "There is no such book," she replied. That was when the idea took shape to put together the original manual for cell-processing laboratories and the dedicated people who make them work.

Looking back, I realize what an incredible challenge the individuals performing this work have faced and continue to face as novel and increasingly complex cellular therapies move from bench to bedside. The development of tissue- and cell-based therapies for malignancies, regenerative medicine, and autoimmune diseases is occurring at a dizzying pace. Protocols involving selection, expansion, and combination of cells with other materials from a wide variety of sources are developed by basic scientists and often turned over to clinical laboratory scientists for translation and application. Along with developing and mastering complex cell-processing techniques, translational scientists must also develop and validate methods for determining the identity, purity, and potency of these unique and often poorly characterized products. And they must perform these procedures in compliance with regulatory requirements and professional standards that did not exist in 1987.

Although this book cannot possibly address all of the situations one might encounter in this rapidly expanding and unpredictable laboratory specialty, I hope it will provide some help in dealing with issues that may confront the staff of today's cellular therapy facility.

A Word from the Associate Editor

What an honor and privilege it has been to work in such an exciting and rewarding field for over 20 years! The phrase “cellular therapies” has expanded to include an innumerable number of products and therapies, hematopoietic stem cell transplantation has become standard therapy for many diseases, and specialized cells of different types are being developed for a variety of uses. Though movement towards regulatory approval sometimes seems to progress at a glacial pace, the commercialization of some of these products has entered a new era and venture funding in this area is no longer considered a fringe investment.

I entered the field of cell therapy in 1994, after five years in a clinical hematology and transfusion medicine laboratory. It was late enough in the evolution of the field that I was able to learn many procedures from the work of pioneers like Dr. Stephen Noga, Ellen Areman, Janice Davis, Doug Padley, Diane Kadidlo, and several of the other contributors to this project. It was still early enough that peripheral blood stem cells and other treatments that are routine in many cancer centers today were considered experimental, often requiring storage of autologous “back-up” bone marrow collections for use if the cells failed to engraft.

I will echo Ellen’s remarks about the rapid advances of technology as well as the unpredictability and exponential growth potential of our field. I have had the joy and privilege to work with many

passionate, diligent, and motivated physicians, nurses, researchers, and other technologists who patiently taught me things not found in textbooks or journal articles and helped me better understand hematopoietic cells and the people who donate and receive them. It is extraordinary to look back now and recall the number of bright lights in the cell therapy field with whom I have had the honor to interact over the years. I never would have predicted that I would work side-by-side in academic and research facilities as well as in professional organizations with those individuals whose accomplishments I so long admired, as well as brilliant young investigators who have gained my appreciation and respect. The first publication was a great learning experience and this second one has taught me even more. I truly consider it an honor to have worked so closely with Ellen.

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References

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2. Areman EM, Loper K, eds. Cellular therapy: Principles, methods, and regulations. 1st ed. Bethesda, MD: AABB, 2009.

