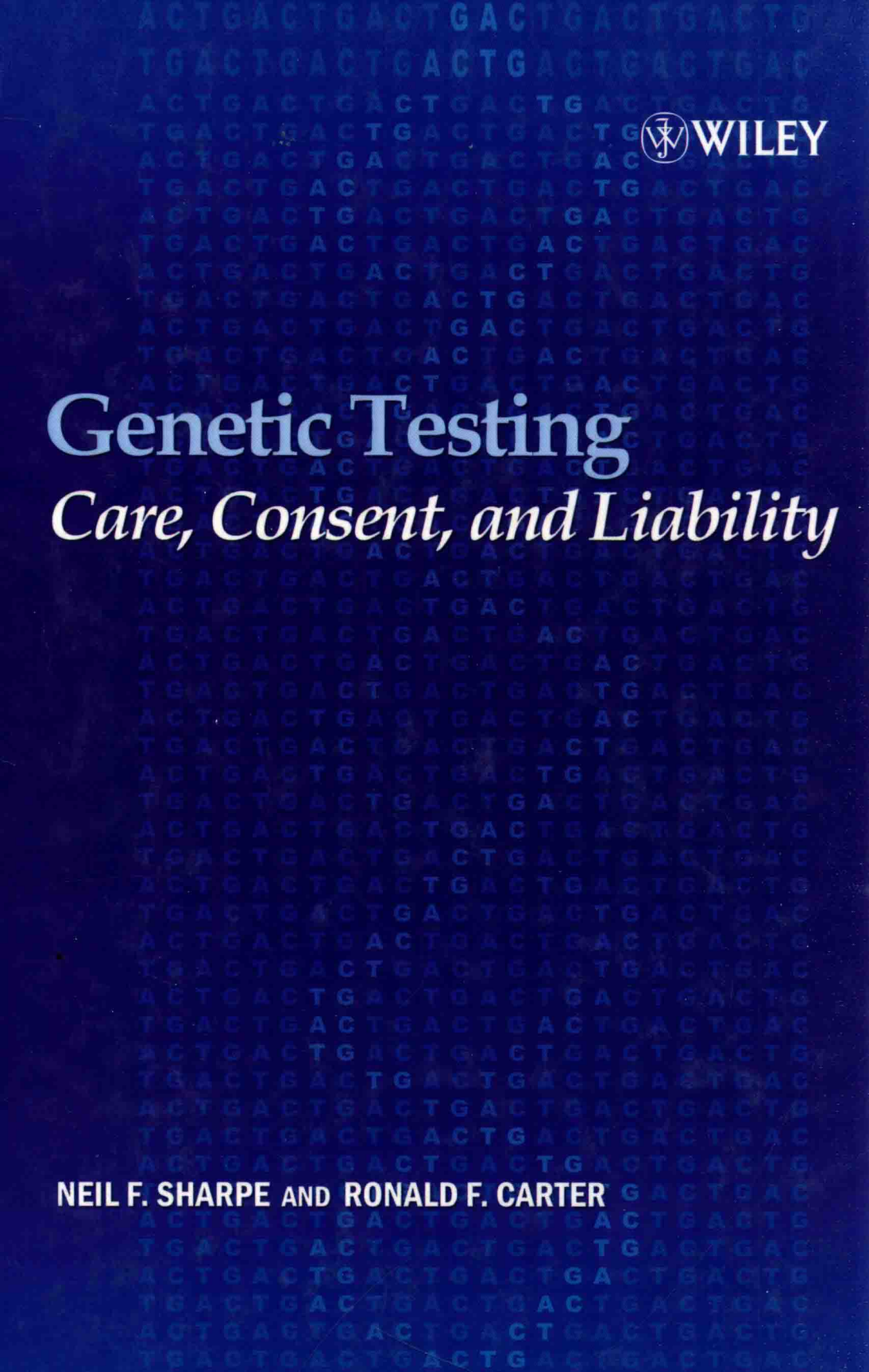
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Genetic Testing
Care, Consent, and Liability
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Genetic Testing

Care, Consent, and Liability

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Genetic Testing

Dedication

This book is dedicated to my wife, Honey, who in the face of a chronic, debilitating disease, always has displayed an indefatigable attitude and inexhaustible courage, laughter, love, and joy.

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Neil F. Sharpe

Dedication

To my wife Ludy, and our children Veronica, Timothy, Emily, and Stephanie: for their patience and understanding in the face of many hours at work on this book.

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To all the scientific contributors to this book, for their willing cooperation and effort in submitting excellent papers, and for their advice and expertise in the preparation of the book as a whole.

Ron Carter

Here, as in all other cases, we must set down the appearances, and first working through the puzzles, in this way go on to show, if possible, the truth of all deeply held beliefs about these experiences, and, if this is not possible, the truth of the greatest number and the most authoritative.

Aristotle
Nicomachean Ethics

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Foreword
Advances in Genetics Reach the Clinic: Challenges for Health Care Providers and Patients

Our understanding of genetic mechanisms of disease has improved so rapidly in recent years that concepts and applications to medicine have moved well beyond the knowledge base of most health care providers and their patients. From the discovery of the correct number of human chromosomes in 1956 [Tjio and Levan, 1956] to the complete sequencing of the human genome in 2003, technical advances in the analysis and manipulation of DNA have rapidly permitted an increasingly accurate understanding of the effects of genetic sequence variations on the human condition.

Only a few years ago, medical genetic researchers used to struggle to catalog thousands of syndromes based upon clinical presentations and tireless examinations of families and their histories [see McKusick, 1990, for discussion]; a minority of diagnoses could be confirmed by testing, and useful treatment was not possible for even half of all genetic conditions. Now, thousands of genes have been cloned, diagnostic tests are available for over 1000 different genetic diseases, accurate predictions for clinical outcome and recurrence risks are commonly available for many syndromes, therapies with molecular levels of specificity of action are becoming available, and the complex interactions of environmental and genetic components of common adult disorders are increasingly clear.

What was once a quiet little corner of medicine has transformed into a cornerstone of all medical care. The "new genetics" is a focus of vigorous research and high technological competition, the cause of both uneasiness and expectation for patients, a bountiful source of ethical, legal, and social dilemmas, and a minefield of unknowns for many health care practitioners. In the United States, the societal impacts of these issues were extensively reviewed twice within the past 15 years [Andrews et al., 1994; Holtzman et al., 1997]. More recently, a uniquely comprehensive and authoritative

inquiry commissioned by the Australian government has issued a landmark report, *Essentially Yours* [Australian Law Reform Commission, 2003] that is discussed in more detail in Appendix 1 by Professor D. Weisbrot. The office of the Surgeon General of the United States also engaged public interest recently by launching "Family History Day" on Thanksgiving 2004 [www.surgeongeneral.gov]. The Surgeon General's initiative has encouraged families to discuss and document their medical family histories, and the website can be used to construct pedigrees easily and accurately.

The scope of practice for genetics is extending into all medical disciplines, and with less than 90 out of 104,000 residency slots in the United States (0.085 percent of the total) allocated for medical geneticists, there are not nearly enough medical geneticists for the work that needs to be done. Accordingly, other health care professionals must invoke genetics into their level of care. Genetics is quickly moving into the mainstream, propelling advances in prenatal screening, newborn screening, neonatology, pediatrics, oncology, behavioral medicine, and adult medicine. Everything from infertility to psychiatry is being recast in pathogenetic principles founded on genetic paradigms, and nowhere is this more evident than in our understanding of the complex, multifactorial diseases that commonly affect adults: cardiovascular disease, neurodegenerative conditions, and cancer.

The combination of epidemiology, information technology, and large-scale molecular diagnostics has permitted increasingly accurate descriptions of the interactions of environmental and genetic variables affecting morbidity and mortality, and these advances, in turn, are informing a beckoning era of better clinical management through the related developments of pharmacogenomics and proteomics. Even while it remains to be seen how much of this technology we can afford to provide in health care systems around the world, we all look forward to the potential of new diagnostic and therapeutic techniques already demonstrated in such sentinel examples as imatinib (in the treatment of chronic myelogenous leukemia) and diagnostic microarrays (e.g., for developmental genetics and the prognostic evaluation of breast cancer).

Even though many promising advances have yet to make it to the clinic, the sheer rapidity of advances in medical genetics makes it very difficult for nongeneticist health care providers to keep up. Increasingly, genetics is more and more a part of medical care for all health care professionals, yet surveys have repeatedly shown that many health care providers are aware that they have very little knowledge of even basic genetic principles. "Should I be looking for a genetic component of this disease?" "What is the most recent understanding for the disease?" "How much of this is relevant to practice?" "How to know when to refer?" "Where to get testing, and what do the results mean?" "Who else in a family is at risk?" "What about ethical and legal issues, patient privacy, access to genetic information?" "Where do I find the answers?"

This book is intended to be a source of answers for medical students, residents, and nongeneticist health care providers. In keeping with current pedagogical trends away from knowledge-based curricula ("Flexnerian" medical education) and toward competency-based approaches [Carraccio et al., 2002], we have not attempted to compile a definitive knowledge base for teaching medical genetics. We assume that the knowledge base for medical genetics will continue to evolve rapidly.

Rather, we are presenting concepts, issues, and professional skills that will illustrate to the reader how to continue to provide better care for patients with genetic diseases. The information is intended to be quickly accessible at two levels: important concepts and sources of details. Thus, topics have generally been compiled in a format that frequently includes:

- Introductions of topics
- Illustrative case scenarios
- Core concepts
- Resources for self-directed learning
- Detailed, practical discussions written by experts in the field
- Sources of professionally reviewed, consistently updated information

This book contains practical information for health care professionals of all types who need to provide counseling about genetic tests. Numerous common clinical scenarios are discussed with concise and accurate descriptions of essential information, accompanied by further discussion and evolving reference resources for those who wish to delve into further detail. We have provided an overview of both medical and legal perspectives on many issues, and, in addition, we refer extensively to other sources of accurate information throughout this book.

We emphasize that this book is *not* intended to suggest practice guidelines or appropriate standards of care; our purpose is only to provide an accessible resource that presents principles, concepts, and illustrated discussions in an accessible clinical context as an aid to the consideration of genetics in medicine.

It is timely that the American Academy of Family Physicians chose genetics for the 2005 "Annual Clinical Focus" (www.aafp.org/acfgenomics.xml). Professional organizations are responding to the need to provide continuing education in this area, and excellent materials for continuing education in medical genetics are becoming available from a wide variety of sources (e.g., the Foundation for Medical Practice Education, www.fmpe.org/index.asp). The authors of this book hope that health care professionals will also find this format useful in approaching unfamiliar clinical territory in medical genetics.

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