The Practical Guide to the Genetic Family History

Second Edition

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Division of Medical Genetics
University of Washington School of Medicine

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Wiley-Blackwell is an imprint of John Wiley & Sons, formed by the merger of Wiley's global Scientific, Technical, and Medical business with Blackwell Publishing.

Published by John Wiley & Sons, Inc., Hoboken, New Jersey.
Published simultaneously in Canada.

Library of Congress Cataloging-in-Publication Data:

Bennett, Robin L., MS, CGC.
The practical guide to the genetic family history / Robin Bennett. – 2nd ed.
p. cm.
Includes bibliographical references and index.
ISBN 978-0-470-04072-0 (pbk. : alk. paper)
1. Genetic counseling. 2. Medical history taking. 3. Genealogy. I. Title.
[DNLM: 1. Medical History Taking. 2. Pedigree. 3. Genetic Counseling–methods. QZ 50 B4722p 2010]
RB155.7.B46 2010
616′.042–dc22 2009054241

Printed in the United States of America

10 9 8 7 6 5 4 3 2 1

"I've learned that people will forget what you said, people will forget what you did, but people will never forget how you made them feel."
Maya Angelou

Dedicated to my family–Scott, Maggie and Paul, Colin, Evan, and Maren, Kristin and D. Paul, and auntie Jo; my teacher–Mr. Tougaw; and my friends–Leslie and Nancy.

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Foreword

The publication of the second edition of Robin Bennett's *The Practical Guide to the Genetic Family History* is an exciting event. This book initially appeared in 1999 with comprehensive coverage of all aspects of the genetic family history and its clinical utility for medical genetics. Bennett is a highly experienced genetic counselor with a deep knowledge of clinical genetics who has worked in the field for 25 years, during a time when medical genetics and its applications have continued growing. From early emphasis on pediatric diseases, medical genetics is now becoming increasingly important for other areas of adult medicine, such as oncology and cardiology. With these developments, our new knowledge of genomics is beginning to be useful in medicine.

The new edition covers practically all conditions encountered by genetic counselors and medical geneticists for diagnosis, reproductive choices, and genetic counseling. Comprehensive listing of diagnostic clues from the family history and patients is particularly useful. The book also deals with many topics requiring genetic knowledge, such as for assisted reproduction in both male and female infertility. The important role of genetic tests by biochemical and molecular methods and their use in patients and family members at genetic risk is covered. There is an extensive chapter about cancer genetics and its practical applications. Many tables allow access to extensive information in an easy manner. Topics such as the current status of adoption provide aid about how to deal with adoptive parents and adoption agencies. Recent developments emphasizing the use of family history by organizations such as the Surgeon General's Office, the Centers for Disease Control and Prevention, and National Institutes for Health reflect current standardization of family histories, an area in which the author's interest and experience has played an important role over the years.

The book is unique not only in accurately and comprehensively covering the medical and genetic aspects of hereditary disease but also in dealing with the many psychological, social, and ethical problems that often arise in such cases. As a medical geneticist who has worked with the author for 25 years, I have admired her approach to patients and their families over a wide range of clinical problems. The new edition of *The Practical Guide to the Genetic Family History* is full of "clinical pearls" for dealing with practical problems posed by patients, their families, and referring health professionals. Bennett provides many insights for dealing sympathetically with the realities and the uncertainties of imperfect knowledge that are often encountered in this area. Specific experiences with patients are often cited to illustrate such problems.

The book is highly recommended for the training of genetic counselors and for MD trainees in medical genetics as well as other professionals such as nurses, social workers, and physician assistants who work with patients who have been diagnosed with a genetic disease. *The Practical Guide to the Genetic Family History* will serve as a most useful reference for all health professionals needing up-to-date advice for practical genetic information.

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March 2009

Preface

If there is genetically determined manifest destiny to become a genetic counselor, perhaps mine was set by my maternal great-great-grandfather, Henry Harbaugh who in 1856 wrote in the annals of the Harbaugh family history:[1] "To cherish the memory of our ancestors is a plain dictate of piety. Only those who care not for their destiny, can be careless as to their origin." Although I am not as pious as those Harbaugh and Eyeler ancestors whose descendants still worship in the hollows of mortar that they laid in the hills of the Harbaugh Valley of west-central Maryland, I do have conviction that a medical-family history continues to grow as an essential tool in the armamentarium of clinical diagnosis and client centered care.

The path of my destiny was farther laid by my maternal grandmother, Marjorie Warvelle Harbaugh, who stoked my mind with the art, poems, and images of my ancestors intertwined in elaborate genealogical trees. Her genealogical stories are what I remember best—the guillotined French revolutionary hero Jacques Pierre Brissot de Warville; Leonard Harbaugh, an engineer of the locks of the Potomac canals who was a confidant of George Washington; tales of ancestors voyaging from Denmark, Germany, England, and Ireland during times of persecution and famine; and her artistic sister, Florence, who died in a tuberculosis sanitarium shortly before her marriage. I recall the haunting emotion relayed when she spoke of her brother, Gerald, whom she describes in her memoirs as "the greatest burden of love to his mother as her imbecile son, her only son and greatly wished for child" who at 13 months was "tragically dropped down the stairs" and then never developed normally. The fragments of Gerald's existence are documented with his silver engraved cup in my china cabinet, the half-page of my grandmother's memoirs, and only one picture

[1]Henry Harbaugh, Annals of the Harbaugh Family in America from 1736 to 1856. Chambersburg, PA, 1856.

out of thousands of family images: Without question, the photograph of Gerald is of a boy who has Down syndrome (a condition that was just beginning to be recognized in the medical literature a few years after his birth). His short life of 14 years influenced my family for three-quarters of a century.

During my 25-year career as a genetic counselor I have drawn an estimated 20,000 pedigrees from family interviews. The stories documented are beyond a set of neatly drawn symbols. The structure of a medical-family history goes farther than simply assisting the clinician in medical diagnosis; a pedigree can help the clinician identify genetic testing strategies, identify patterns of inheritance, calculate risk of disease, make decisions on medical management and surveillance, develop patient rapport, and serve as a template for patient education. The medical-family history also harbors the stories of a family's beliefs on wellness and disease causality, their tragedies and their dreams. My goal in this book is to provide not only the science of pedigrees but the sensitive approach that must also accompany the gathering and recording of this information.

The Practical Guide to the Genetic Family History provides clinicians not only with the hows of taking a medical-family history and recording a pedigree but also the whys. The utility of taking a family history is reviewed in Chapter 1. In Chapter 2, a brief review of genetics is provided in the context of recognizing patterns of inheritance from a family pedigree and for providing genetic risk assessment and counseling. Standard pedigree nomenclature and the approach to recording a medical-family history are reviewed in Chapter 3. Chapter 4 is similar to a Cliff's Notes version of a basic overview of the directed questions to ask when recording a medical-family history for a specific medical indication (e.g., renal disease, hearing loss, mental illness). This section is greatly expanded on from the first edition. Of course, not every medical system is covered. My choice of disease categories is based on the general categories of disease for which I have had the most inquiries.

Over the past 10 years, cancer genetics has been one of the greatest fields of expansion in medicine and genetics, therefore Chapter 5 is solely devoted to this topic. Medical-family history plays a critical role in identifying families who can benefit from genetic testing and for providing cancer risk assessment so that high-risk families can be offered earlier and more intensive surveillance for cancer.

Pedigree analysis requires that the health facts recorded on individuals be accurate. This requires obtaining medical records on relatives. Although this can be time-consuming, it is often necessary. Chapter 6 details how to assist a patient in obtaining medical records, including death certificates. There is also information about how patients can research their own medical-family history and learn to record their own medical pedigree. It is helpful to the clinician if a patient has done the footwork in obtaining medical-family history information in advance of an appointment.

Adoption and assisted-reproductive technologies using gamete donation provide challenges in taking a medical-family history (see Chapters 7 and 8, respectively). The chapters that focus as these topics have been expanded on from the first edition. There is a growing movement to release closed adoption records and original birth certificates, and for openness in the release of health information about birth parents

and gamete donors. A model medical-family history form to be used for adoption is detailed in Appendix 4; it can easily be adapted for use by programs providing assisted-reproductive technology services.

Genetic information carries unique personal, family, and social consequences. If a potential genetic disorder is identified through pedigree analysis, the patient and family members can benefit from referral to a board-certified genetic counselor, a medical geneticist, or genetic nurse specialist. Information on how to find a genetic specialist and what to expect from a genetic consultation is given in Chapter 9.

With the use of electronic health records, there are ethical issues to consider in recording a pedigree; these are detailed in Chapter 10. Researchers and individuals who are considering publishing a pedigree will find valuable information regarding issues to consider when involved in a family study or using a pedigree in publication.

Throughout the book I use clinical examples to illustrate certain themes. The case scenarios and pedigrees are based on hypothetical families. The names, family relationships, and psychosocial issues are fictitious, although the clinical information is often based on facts drawn from several families I have seen in my practice. The genogram of the fictional character Harry Potter (Figure 1.4) is interpreted from the series of four books by J. K. Rowling. The ecomap of soccer legend David Beckham (Figure 1.5), and the pedigrees of the Darwin-Wedgwood family (Figure 3.11) and of actress Elizabeth Taylor's immediate family (Figure 3.6) were drawn from information available in the public domain. I am grateful to the creative energy and genetic experience of Leslie Ciarleglio for the illustrations of the Potter genogram and the Beckham ecomap.

This volume is meant to be a handy reference using a pedigree as a primary tool for making a genetic risk assessment and counseling. Any healthcare provider, including physicians, nurses, medical social workers, and physicians assistants, will benefit from learning this approach to pedigree analysis. To find more information about a specific condition, you will need to turn to one of the many excellent references on genetic disorders, many of which are noted in the references in each chapter. Appendix 5 lists several of the online resources to query for more information about genetic disorders, their inheritance patterns and genetic testing. Appendix 7 is a source for the gene names and symbols associated with most of the disorders mentioned in this book along with the pattern of inheritance.

The pedigree as a tool of practice in health risk assessment and counseling has been available for a century, but the science of the pedigree has really just begun, first with the clarification of standard pedigree nomenclature from the National Society of Genetic Counselor's Task Force and their recommendations published in 1995 and then from national and international efforts of developing tools for decision analysis of pedigree data, such as the efforts of the U.S. Surgeon General's Office, the Centers for Disease Control and Prevention, and the National Institutes of Health State of the Science Conference in 2009. The second edition of the *Practical Guide to the Genetic Family History* continues to expand on earlier work and provide suggestions for future areas of research.

While preparing this edition, I had the privilege of traveling to Saudi Arabia and meeting with genetic counselors and geneticists. I was humbled in recognizing how biased the literature on clinical genetics, family history, and genetic counseling is toward a Western approach to health, disease, and family values. Although I hope that this edition of the *Practical Guide to the Genetic Family History* will reach a worldwide audience, I recognize that my approach is clearly colored from the perspective of a woman of northern European ancestry providing genetic counseling services in the United States. I look forward to hearing from colleagues and families from around the world about different approaches to taking and recording a family history that are more effective from their perspectives.

The foundation of my work lies with my colleagues on the National Society of Genetic Counselors Pedigree Standardization Work Group: Robert Resta, Kathryn Steinhaus French, and Debra Lochner Doyle, and with the assistance of the original task force members who also included Stefanie Uhrich and Corrine O'Sullivan Smith. I am particularly indebted to Robert Resta for his thoughtful edits of my work and his historical perspectives on family history.

I appreciate all I have learned from the opportunity of chairing the Family History Work Group of the National Coalition of Health Professional Education in Genetics (NCHPEG), particularly Joseph McInerney, Chantelle Wolport, Eugene Rich, Maren Scheuner, Siobhan Dolan, and Michael Rackover. I continue to bathe in the primordial soup of genetics with my colleagues at the University of Washington Medical Center, who always support my work including Dr. Arno Motulsky, Dr. Peter Byers, Dr. Virginia Sybert, Dr. Gail Jarvik, Dr. Wylie Burke, Dr. Marshall Horwitz, Dr. Elizabeth Swisher, Dr. Wendy Raskind, and of course my genetic counseling co-workers: Corrie Smith, Mercy Laurino, and Debbie Olson. I was fortunate to have the critical reviews of Heather Hampel, Sara Wyrick, Stephanie Jellison, and Kathleen Delp.

The staff at John Wiley & Sons, including Ian Collins, Kristen Parrish, and Thom Moore, have been generous in their patience and guidance.

I am blessed by a large and close family who continuously inspires me—particularly my sister, Kristin; and brother, Paul (thanks for reminding me to dance the Lucky); my father, Paul; and my cousins Lizz and Tom—and by the support of my husband's family, particularly his sisters Dona, Shelley, and Dale. At the top of my family tree of gratitude are my children, Colin, Evan, and Maren; my aunt Jo, who keeps me plum in family history art quilts; my mother, Maggie, who steers my rudder; and of course, my husband, Scott MacDonald, who is always by my side.

My Mercer Island High School biology teacher, Bill Tougaw, remains the person to whom I dedicate my career and this work. Charles Rice, my uncle and a psychology professor at Kenyon College, provided me with career guidance during my college years.

A pedigree is a map that can help predict disease, but it is not destiny. Knowledge of family history can be used to change the course of family medical history. The families I have worked with continue to impress me with their strength, and they leave imprints on my life. As my gift to them I will end with a long forgotten poem of my maternal grandfather, Marion Dwight Harbaugh, whose life as a geologist

was also devoted to maps (and he has left the legacy of geology to his son and grandson):

The Grand Canyon

In a glamorous land on the top of the world
Where the sky is an endless blue
A wedge of heaven has driven deep
And split the earth in two,
And torn its face in a jagged wound
All splotched and stained with blood
That long since poured from its riven veins
In a surging ghastly flood.

I stood one day and gazed in awe
At that gaping, beautiful gash
That stretches from dawn to the setting sun
Like the trail of a dragging lash;
And I looked for miles to its deepest depths
To behold with wondering eyes
The sinuous edge of that mighty wedge
That still presses down from the skies.

Then I trembled to think of the fearful powers
That buffet the world and me,
And I pitied the earth that since its birth
Has suffered so patiently;
But then I began to understand
How a life is shaped and steeled,
And made both rugged and beautiful
By the scars where its wounds have healed.

—Marion Dwight Harbaugh (1934)