Handbook of Pediatric Autopsy Pathology
Handbook of Pediatric Autopsy Pathology

Enid Gilbert-Barness,
AO, MBBS, MD, FRCPA, FRCPath, DSci(hc), MD(hc)
Professor of Pathology and Laboratory Medicine,
Pediatrics and Obstetrics and Gynecology,
University of South Florida School of Medicine and Tampa General Hospital,
Tampa, Florida

Diane E. Debich-Spicer, BS
Tampa General Hospital, Tampa, FL

Foreword by
John M. Opitz,
MD, MD(hc), DSci(hc), MD(hc)
Professor, Pediatrics (Medical Genetics), Human Genetics, Obstetrics and Gynecology,
and Pathology, University of Utah Medical School, Salt Lake City, UT

HUMANA PRESS * TOTOWA, NEW JERSEY
Handbooks.

Gilbert-Barness, Enid, 1927--
p. ; cm.
Includes bibliographical references and index.
ISBN 1-58829-224-X (alk. paper)
1. Pediatric pathology--Handbooks, manuals, etc. 2. Autopsy--Handbooks, manuals, etc. 3. Fetal death--Handbooks, manuals, etc. 4. Perinatal death--Handbooks, manuals, etc.
RJ49.G535 2004
618.92007--dc22
2004003496
Dedicated to the memory of John L. Emery, whose legacy will continue to inspire those whose lives he touched.

The signature of John Emery.
Foreword

It is a profoundly gratifying and joyous occasion to welcome and recommend Gilbert-Barness and Debich-Spicer’s *Handbook of Pediatric Autopsy Pathology*, the distillation of a professional lifetime of experience, practice, and discovery by one of the world’s most distinguished pediatric pathologists (ably assisted by her coworker D. Debich-Spicer).

For over a third of a century I have been privileged to collaborate closely, at first as fellow faculty member in Madison, subsequently in a long-distance consultative relationship (Helena to Madison, and finally Salt Lake City to Tampa) with one of the most tireless and devoted experts in constitutional, pediatric, developmental, and genetic pathology. Initially it was for me, as apprentice, to learn from this peerless teacher, the practical aspects of studying dead fetuses and infants for inferences of pathogenesis and cause, with the aim to attain diagnosis and a deeper understanding of the underlying biology of the condition.

This was an apprenticeship which arose, long ago, out of a combined NIH Medical Genetics Research Center Grant at the University of Wisconsin in which we studied together, whenever possible, the infants and children before death, and after death with all of our trainees, involving coworkers in anatomy, genetics, embryology, and pathology.

An apprenticeship moreover that motivated me to continue the vitally (meant literally) important study of dead embryos, fetuses, and infants in Montana, part of a region (including Idaho, Montana, Wyoming, North and South Dakota, and Nevada) without a single pediatric pathologist. This regional fetal genetic pathology program could not have functioned without the almost daily advice and input of Dr. Gilbert-Barness and her coworkers.

In recognition of her role as one of the most highly regarded pathology teachers in the world, the University of Wisconsin created the distinguished Enid Gilbert-Barness Lectureship before her departure to the University of South Florida. She has been President of the Society of Pediatric Pathology, the International Pediatric Pathology Association and of several related organizations, has taught on every continent (except Antarctica), was a founder of the International Workshops of Fetal Genetic Pathology, is the editor of the two volume Potter’s *Pathology of the Fetus and Infant* (under revision) with its companion Atlas, and the author (with D. Debich-Spicer) of *Embryo and Fetal Pathology* (2004), and with her husband, Lewis A. Barness, author of *Metabolic Diseases: Foundations of Clinical Management, Genetics, and Pathology*, vol. 2 (2000), and *Clinical Use of Pediatric Diagnostic Tests* (2003).

Recently, Dr. Gilbert-Barness (with a group of enthusiastic editorial coworkers) undertook the editorship of the journal *Fetal and Pediatric Pathology*, a journal which recognizes the important contributions to the study and biology of fetal and pediatric death by many other specialists, including embryologists, developmental biologists, and geneticists, experts in maternal-fetal medicine, metabolic diseases, peri- and neonatology, and clinical geneticists.

The present book is an intensely practical, profusely illustrated, and most useful treatise, published at a propitious time in history, e.g., the formation of the International College of Fetal Genetic Pathology and the initiation of the NICHD-sponsored and -supported multicenter study of the causes of stillbirth for both of which this book can serve as a guide for minimal standards in the practice of the causal analysis of fetal and infant death. In reading this book, I had the vivid experience of having revisited the grove of Akademe with my mentor in recognizing so many of the patients Dr. Gilbert-Barness and I have studied together.

Medicine arose out of the study of pathology, one of the most important foundations of biomedicine. And western pathology arose out of observations of malformations preserved in folklore and the notes of early surgeons (e.g., Pare, John Hunter) and physician/naturalists (e.g., Aldrovandi), but was not established as a legitimate medical specialty per se until Giovanni Battista Morgagni (1682–1771), a student of Valsalva and Professor of Pathological Anatomy at Padova for 56 years. His three-volume treatise *De sedibus et causis morborum per anatomam indagatis*
(1779), is no less erudite than the present book, but in over 1500 pages has not a single illustration in it. François Xavier Bichat (1771–1802), a gifted observer, founded histological pathology through his careful study of tissues or “membranes” in disease. Matthew Baillie (1761–1823), nephew of John Hunter and physician of George III, published his wonderful *Morbid Anatomy* with many excellent engravings, that of pulmonary emphysema illustrating the lungs of Dr. Samuel Johnson. Carl (von) Rokitansky (1804–1878), a Czech, was Professor of Pathology at Vienna for 30 years, and like our present authors, performed thousands of autopsies, and from this experience published a much-admired, clear, multivolume compendium on pathology that remained the standard for decades. Of his four sons, he said that the two who were physicians healed (heilen), the two who were musicians howled (heulen). Rudolf (von) Virchow (1821–1902) initially Professor of Pathology in Würzburg, then in Berlin, was the founder of Cellular Pathology, founder and for decades editor of the Archiv für pathologische Anatomie (“Virchows Archiv...”), who is additionally renowned as an anthropologist and an advocate for democracy and social justice with the courage to stand up against Bismarck in Parliament.

Subsequent developments in infections, genetics, and molecular biology have transformed the face of pathology, but never the guiding sentiment of this book: Mantui vivas docueran: Let the dead teach the living. *Handbook of Pediatric Autopsy Pathology* stands as a worthy successor to those of the immortal giants mentioned above, who began, while they continue, to enrich our knowledge of life and death and have set highest standards for its study. This is one of those dozen or so books on the first shelf right over my head at my desk where I can reach it at all times without looking, altogether indispensable for the study and practice of developmental pathology.

*John M. Opitz,*

*MD, MD(hc), DSci(hc), MD(hc)*
Preface

The Handbook of Pediatric Autopsy Pathology has been compiled to fill a current void in the armamentarium for the pathologist performing the pediatric autopsy. The pediatric autopsy must be approached with great care in technique and dissection; malformations may be easily overlooked by the uninitiated. Of major importance in pediatric autopsy pathology is the need for accurate diagnosis in order to provide genetic counseling and the implication of possible recurrence in future pregnancies.

Although adult autopsies have declined in recent years, the importance and demand for pediatric autopsies has accelerated. There have been extensive developments in the pediatric field that enhance the importance of the autopsy, so that at the present time, the autopsy has probably greater importance within the field of the fetal and perinatal pathologist than at any other age. These features largely relate to congenital malformations and genetic counseling. The detailed description of all abnormalities in both fetuses, stillborn, and older children is of paramount importance supplemented by cytogenetic studies, metabolic evaluation, and DNA and other analyses.

The effect of any environmental or nutritional hazard is most obvious when related to periods of growth, and the fetus and the newborn are such periods in human development. Thus, any new environmental hazard and the effects of environmental agents and drugs including chemicals such as lead or radioactive materials, alcohol, or intrauterine infection, can and are best assessed by sampling specific tissues and organs from fetuses, stillborns, and newborn infants at autopsy examination.

The careful performance of perinatal autopsies followed by dissemination of the findings to parents, clinicians, and public health organizations is important in the reduction of perinatal mortality and morbidity. Every pathologist should have a working knowledge of the pediatric autopsy.

The careful performance of neonatal autopsies both adds to our basic understanding of neonatal diseases and is an excellent monitor of the results of treatment.

The development of perinatology, prenatal diagnosis of birth defects, and genetic counseling requires accuracy of prenatal diagnostic techniques, including ultrasonography and correlation of clinical data with the results of carefully performed fetal autopsies. Parents and clinicians depend on accurate autopsy diagnoses for intelligent family planning.

The autopsy examination is the foundation upon which a complete perinatal autopsy is built. In addition to the performance of a skilled autopsy biopsy, other ancillary studies and techniques are necessary to address the vital issues of accurate diagnosis. The Handbook of Pediatric Autopsy Pathology thoroughly addresses these issues including microbiologic, cytogenetic, X-ray, and special studies such as enzyme and DNA analysis in metabolic diseases. This handbook also addresses the examination of the embryo in spontaneous abortions. The approach outlined is simple enough to be used routinely by the general pathologist with conventional facilities.

Part I and the Introduction provide a general description of the techniques used in the pediatric autopsy as well as general aspects of the autopsy including the death certificate, cause and manner of death, obtaining permissions from the family, and examination of the placenta. Part II includes hydrops, chromosomal defects, and congenital abnormalities, with a discussion of major malformations. Disorders of each of the organ systems and metabolic diseases are discussed in Part III, including the autopsy on metabolic disorders. Part IV includes sudden infant death, the medicolegal and forensic autopsies, special procedures, infection control, and biological hazards at the autopsy. At the end of each chapter is an appendix that includes standard reference tables.

This book is not intended to be an exhaustive treatise on pediatric pathology, but rather a guide to the actual performance of the pediatric autopsy as well as to the recognition and interpretation of pathologic findings.

The Handbook of Pediatric Autopsy Pathology provides the prosector with a valuable source of information for conducting a meaningful and comprehensive autopsy. Thus, it should also be useful for general pathologists, as well as for specialist pediatric pathologists.
The Handbook of Pediatric Autopsy Pathology is dedicated with great pride to Professor John L. Emery who was the master of pediatric pathology and whose techniques in performing an autopsy have been acclaimed worldwide. He, in fact, recognized the need for a pediatric pathology autopsy manual and initiated the writing of this book before his untimely death and before it could become a reality. Not only was he a pediatric pathologist par excellence, but a poet and an accomplished artist. Some of his sketches have been included in this volume.

Enid Gilbert-Barness,
AO, MBBS, MD, DSci(hc), MD(hc)

Diane Debich-Spicer, BS
### Contents

- Dedication ...................................................................................................................... v
- Foreword ........................................................................................................................ vii
- Preface ........................................................................................................................... ix
- Color Plates .................................................................................................................. xiii
- Companion CD (Inside Back Cover) ........................................................................... xiv

#### PART I: GENERAL PRINCIPLES

1. General Principles ......................................................................................................... 3

#### PART II: TECHNIQUES

2. Pediatric Autopsy: *Fetus, Newborn, and Child* ................................................................ 7
3. Examination of the Human Embryo .................................................................................. 75
4. The Placenta .................................................................................................................... 117

#### PART III: DEVELOPMENTAL DISORDERS

5. Hydrops ......................................................................................................................... 145
6. Chromosomal Defects .................................................................................................... 151
7. Congenital Abnormalities .............................................................................................. 165

#### PART IV: ORGAN SYSTEMS AND METABOLIC DISORDERS

8. Cardiovascular System .................................................................................................. 191
9. Respiratory System ....................................................................................................... 251
10. Gastrointestinal System .............................................................................................. 271
11. Liver, Gallbladder, Biliary Tract, and Pancreas ............................................................ 291
12. Renal System ................................................................................................................ 301
13. Male and Female Genitourinary Systems .................................................................. 337
14. Central Nervous System .............................................................................................. 347
15. Thymus, Spleen, Lymph Nodes, and Immunodeficiency ............................................. 371
16. Skeletal System ............................................................................................................ 379
17. Eye and Adnexa Sectioning ......................................................................................... 405
18. Metabolic Diseases ....................................................................................................... 415

#### PART V: SPECIAL CONSIDERATIONS

19. Sudden Infant Death .................................................................................................... 451
20. Pediatric Forensic Pathology ....................................................................................... 471
21. Special Procedures ..................................................................................................... 499
22. Infection Control and Biological Hazards in the Autopsy ........................................... 513

Index .................................................................................................................................. 519
Color Plates

Color Plates 1–16 appear as an insert following page 370.

**PLATE 1** Features of embryonic development. (See Figs. 5, 6B, 7, 8A, 9A, 10A, 10C, 11A, and 13C, Chapter 3.)

**PLATE 2** Lymphaticovenous connection in normal embryo and its lack in cystic hygroma. (See Fig. 8, Chapter 5.)

**PLATE 3** Cleared and fixed specimen of lung after gelatin impregnation showing arteriovenous malformation in familial hemorrhagic telangiectasia. (See Fig. 24, Chapter 9.)

**PLATE 4** Illustration of venous sinuses of brain showing vein of Galen. (See Fig. 19, Chapter 14.)

**PLATE 5** Radial aplasia demonstrated by staining with Alizarin red. (See Fig. 1, Chapter 16.)

**PLATE 6** Galactosemia. Microscopic section of liver showing pseudoglandular pattern of hepatocytes and cholestasis. Similar changes are seen in tyrosinemia and hereditary fructose intolerance. (See Fig. 1, Chapter 18.)

**PLATE 7** Metabolic enzyme defects in the glycogen storage diseases. (See Fig. 2, Chapter 18.)

**PLATE 8** Tongue with marked hypertrophy in an infant with glycogen storage disease type 2. (See Fig. 4, Chapter 18.)

**PLATE 9** Metachromatic reaction of urine on filter paper (left) compared with normal urine (right). (See Fig. 14B, Chapter 18.)

**PLATE 10** Gangliosidosis type 2—Tay–Sachs disease (hexosaminidase A deficiency). Cherry red spot of the retina. (See Fig. 15, Chapter 18.)

**PLATE 11** Metabolism of carnitine. (See Fig. 23, Chapter 18.)

**PLATE 12** Oxalosis. Oxalate crystals in bone marrow with a sunburst appearance. (See Fig. 27, Chapter 18.)

**PLATE 13** Wilson disease. Kayser–Fleischer ring of cornea. (See Fig. 29, Chapter 18.)

**PLATE 14** Microscopic appearance of extramedullary hematopoiesis in the liver. (See Fig. 3, Chapter 19.)

**PLATE 15** Shaken baby syndrome: retinal hemorrhage and massive hemorrhage into the globe of the eye. (See Fig. 13, Chapter 20.)

**PLATE 16** A patulous anus and fissures around the anus in sexual abuse. (See Fig. 21, Chapter 20.)

Additional color images may be found on the Companion CD.
Companion CD

Color versions of selected illustrations—more than 400 figures—may be found on the Companion CD attached to the inside back cover. The image files are organized in folders by chapter number and are viewable in most Web browsers. The number following "f" at the end of the file name identifies the corresponding figure in the text. The CD is compatible with both Mac and PC operating systems.