Fetal Therapy: Scientific Basis and Critical Appraisal of Clinical Benefits

Edited by

Mark D. Kilby
Professor of Fetal Medicine, School of Clinical and Experimental Medicine, College of Medical & Dental Services, University of Birmingham, and Fetal Medicine Centre, Birmingham Women’s Foundation Trust, Edgbaston, Birmingham, UK

Dick Oepkes
Professor of Obstetrics and Fetal Therapy, Leiden University Medical Center, Leiden, the Netherlands

Anthony Johnson
Professor of Maternal-Fetal Medicine, The University of Texas Health Science Center, Houston, TX, USA
To those patients and families who entrust us with their most precious possession, their developing child and those that have been our teachers and mentors over the years. A special thank you to each of our families for their support, tolerance and understanding.

Mark Kilby, Anthony Johnston and Dick Oepkes.
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Contributors

Abdullah Al Ibrahim, MD
National Reference Centre for the Management of Complicated Monochorionic Pregnancies; Department of Obstetrics and Fetal Medicine, Paris Descartes University, Assistance Publique-Hôpitaux de Paris, Hôpital Necker-Enfants-Malades, Paris, France

Cheryl Albuquerque, MD
Department of Obstetrics and Gynecology, Santa Clara Valley Medical Center, San Jose, CA, USA

Margot M. Bartelings, MD, PhD
Department of Anatomy & Embryology and Cardiology, Leiden University Medical Center, Leiden, The Netherlands

Marie H. Beall, MD
Department of Obstetrics and Gynecology, David Geffen School of Medicine at UCLA, Los Angeles, CA, USA

Guillaume Benoist, MD
Department of Obstetrics and Fetal Medicine, Paris Descartes University, Assistance Publique-Hôpitaux de Paris, Hôpital Necker-Enfants-Malades, Paris, France

Tara Bharucha, MB BChir, MA, MRCP
Echocardiography Laboratory, Labatt Family Heart Centre, Hospital for Sick Children, Toronto, ON, Canada

Nico A. Blom, MD, PhD
Department of Pediatric Cardiology Amsterdam-Leiden, Leiden University Medical Center, Academical Medical Center Amsterdam, Leiden, The Netherlands

Paul Brady
Centre for Medical Genetics, University Hospitals Leuven, Leuven, Belgium

Janet Brennand, MD, FRCOG
The Ian Donald Fetal Medicine Unit, The Southern General Hospital, Glasgow, UK

Alan Cameron, MD, FRCOG
The Ian Donald Fetal Medicine Unit, The Southern General Hospital, Glasgow, UK

Julene S. Carvalho, MD, PhD, FRCPCCH
Fetal and Paediatric Cardiologist, Royal Brompton Hospital and St. George's Hospital; Reader in Fetal Cardiology, St. George's Hospital, University of London, London, UK

Daniel Challis, MBBS, FRANZCOG, CMFM, DDU
Royal Hospital for Women, Randwick, NSW, Australia

Gihad E. Chalouhi, MD
National Reference Centre for the Management of Complicated Monochorionic Pregnancies; Department of Obstetrics and Fetal Medicine, Paris Descartes University, Assistance Publique-Hôpitaux de Paris, Hôpital Necker-Enfants-Malades, Paris, France

Frank A. Chervenak, MD
Department of Obstetrics and Gynecology, Weill Medical College of Cornell University, New York, NY, USA

Robert L. Chevalier, MD
Department of Pediatrics, University of Virginia, Charlottesville, VA, USA

Filip Claus
Division of Medical Imaging, University Hospitals Leuven, Leuven, Belgium

Sarah Clements, FRANZCOG, DDU
Royal Hospital for Women, Randwick, NSW, Australia

Timothy M. Crombleholme, MD
Ponzio Family Chair and Professor of Surgery, Obstetrics and Gynecology, and Pediatrics, University of Colorado School of Medicine; Division of Pediatric General, Thoracic and Fetal Surgery, Colorado Institute for Maternal Fetal Health, Children's Hospital Colorado, Aurora, CO, USA

Anna L. David, PhD, MRCOG
Department of Maternal and Fetal Medicine, Institute of Women's Health, University College London, London, UK

Philip De Koninck
Division of Woman and Child, Department of Reproduction, Development and Regeneration, University Hospitals Leuven, Leuven, Belgium; Investigators of the TOTAL trial, Eurostec Programme, Leuven, Barcelona and London, Europe
### List of contributors

<table>
<thead>
<tr>
<th>Name</th>
<th>Institution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jan Deprest, MD, PhD</td>
<td>Division of Woman and Child, Department of Reproduction, University Hospitals Leuven, Leuven, Belgium; Investigators of the TOTAL trial, Eurostec Programme, Leuven, Barcelona and London, Europe</td>
</tr>
<tr>
<td>Roland Devlieger, MD, PhD</td>
<td>Division of Woman and Child, Department of Reproduction, Development and Regeneration, University Hospitals Leuven, Leuven, Belgium</td>
</tr>
<tr>
<td>Sascha Drewlo, PhD</td>
<td>Department of Obstetrics &amp; Gynaecology, Maternal-Fetal Medicine Division, Mount Sinai Hospital, University of Toronto, ON, Canada</td>
</tr>
<tr>
<td>Alexander Engels</td>
<td>Division of Woman and Child, Department of Reproduction, Development and Regeneration, University Hospitals Leuven, Leuven, Belgium</td>
</tr>
<tr>
<td>Mohammed Essaoui, MD</td>
<td>National Reference Centre for the Management of Complicated Monochorionic Pregnancies; Department of Obstetrics and Fetal Medicine, Paris Descartes University, Assistance Publique-Hôpitaux de Paris, Hôpital Necker-Enfants-Malades, Paris, France</td>
</tr>
<tr>
<td>Diana L. Farmer, MD, FAAP, FACS, FRCS</td>
<td>Professor and Chief, Pediatric Surgery, Vice Chair, Department of Surgery; Surgeon-in-Chief, UCSF Benioff Children's Hospital, San Francisco, CA, USA</td>
</tr>
<tr>
<td>Dario O. Fauza, MD, PhD</td>
<td>Associate, Department of Surgery, Children's Hospital Boston; Associate Professor of Surgery, Harvard Medical School, Boston, MA, USA</td>
</tr>
<tr>
<td>Caroline E. Fox, MBChB, MRCOG</td>
<td>Fetal Medical Centre, Birmingham Women's Foundation Trust, School of Clinical and Experimental Medicine, University of Birmingham, Edgbaston, Birmingham, UK</td>
</tr>
<tr>
<td>Jon Frampton, BA, PhD</td>
<td>Professor of Stem Cell Biology, College of Medical &amp; Dental Sciences, University of Birmingham, Edgbaston, Birmingham, UK</td>
</tr>
<tr>
<td>Philippa Francis-West, BA, PhD</td>
<td>Professor in Cell and Developmental Biology, Department of Craniofacial Development and Stem Cell Biology, King's College London, London, UK</td>
</tr>
<tr>
<td>Adriana C. Gittenberger-de Groot, PhD</td>
<td>Department of Cardiology, Leiden University Medical Center, Leiden, The Netherlands</td>
</tr>
<tr>
<td>Philip L. Glick, MD, MBA, FACS, FAAP, FRCS (Eng)</td>
<td>Division of Pediatric Surgery, University of Buffalo, Buffalo, NY, USA</td>
</tr>
<tr>
<td>Cecilia Götherström, PhD</td>
<td>Kardinska Institutet, Department of Clinical Sciences, Intervention and Technology Division of Obstetrics and Gynaecology; Karolinska University Hospital, Stockholm, Sweden</td>
</tr>
<tr>
<td>Kirsten Grabowska, MD FRCSC</td>
<td>MFM Fellow, Department of Obstetrics and Gynecology, University of Calgary, Alberta, Canada</td>
</tr>
<tr>
<td>Eduard Gratacos, MD</td>
<td>Hospital Clinic-Idibaps, University of Barcelona and CIBER-ER, Barcelona, Spain; Investigators of the TOTAL trial, Eurostec Programme, Leuven, Barcelona and London, Europe</td>
</tr>
<tr>
<td>Fabienne L. Gray, MD</td>
<td>Research Fellow, Department of Surgery, Children's Hospital Boston, Boston, MA, USA</td>
</tr>
<tr>
<td>Lucy R. Green, BSc, PhD</td>
<td>Institute of Developmental Sciences, University of Southampton, Southampton General Hospital, Southampton, UK</td>
</tr>
<tr>
<td>Takushi Hanita, MD</td>
<td>Department of Anatomy and Developmental Biology, School of Biomedical Sciences, Monash University, Clayton, VIC, Australia</td>
</tr>
<tr>
<td>Mark A. Hanson, MA, DPhil, CertEd, FRCOG</td>
<td>British Heart Foundation Professor; Director, Institute of Developmental Sciences, University of Southampton, Southampton General Hospital, Southampton, UK</td>
</tr>
<tr>
<td>Richard Harding, PhD, DSc</td>
<td>Professional Fellow, School of Biomedical Sciences, Monash University, Clayton, VIC, Australia</td>
</tr>
<tr>
<td>Ariane Huynens, MSc</td>
<td>Institute for Medical Immunology, Université Libre de Bruxelles, Belgium</td>
</tr>
<tr>
<td>François Jacquemard</td>
<td>Department of Obstetrics and Fetal Medicine, Paris Descartes University, Assistance Publique-Hôpitaux de Paris, Hôpital Necker-Enfants-Malades, Paris, France</td>
</tr>
<tr>
<td>Edgar Jaeggi, MD, FRCP</td>
<td>Professor of Pediatrics and Head of Fetal Echocardiography, Labatt Family Heart Centre, Hospital for Sick Children, Toronto, ON, Canada</td>
</tr>
<tr>
<td>Anthony Johnson, DO</td>
<td>Professor of Maternal-Fetal Medicine, The University of Texas Health Science Center, Houston, TX, USA</td>
</tr>
<tr>
<td>Mark P. Johnson, MD</td>
<td>Professor, Departments of Surgery, Obstetrics &amp; Gynecology and Pediatrics, University of Pennsylvania School of Medicine and the Children's Hospital of Philadelphia, Philadelphia, PA, USA</td>
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<td>Name</td>
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<tr>
<td>Monique R. M. Jongbloed, MD, PhD</td>
<td>Department of Anatomy &amp; Embryology and Cardiology, Leiden University Medical Center, Leiden, the Netherlands</td>
</tr>
<tr>
<td>Sarah Keating, MD</td>
<td>Department of Obstetrics &amp; Gynaecology, Maternal-Fetal Medicine Division, and Department of Pathology &amp; Laboratory Medicine, Mount Sinai Hospital, University of Toronto, ON, Canada</td>
</tr>
<tr>
<td>Debra Kennedy, MBBS, FRCAP</td>
<td>Mothersafe Program, Royal Hospital for Women, Randwick, NSW, Australia</td>
</tr>
<tr>
<td>Sundeep G. Keswani, MD</td>
<td>Assistant Professor of Surgery, Pediatrics, and Obstetrics and Gynecology, Fetal Care Center of Cincinnati, Division of Pediatric General, Thoracic and Fetal Surgery, Cincinnati Children's Hospital Medical Center, University of Cincinnati College of Medicine, Cincinnati, OH, USA</td>
</tr>
<tr>
<td>Nahla Khalek, MD</td>
<td>Assistant Professor of Clinical Obstetrics &amp; Gynecology, Department of Surgery, University of Pennsylvania School of Medicine and the Children's Hospital of Philadelphia, Philadelphia, PA, USA</td>
</tr>
<tr>
<td>Mark D. Kilby, MBBS, DSc, MD, FRCOG</td>
<td>Professor of Fetal Medicine; School of Clinical and Experimental Medicine, College of Medical &amp; Dental Sciences, University of Birmingham, and Fetal Medicine Centre, Birmingham Women's Foundation Trust, Edgbaston, Birmingham, UK</td>
</tr>
<tr>
<td>John Kingdom, MD, FRCSc, FRCOG, MRCP</td>
<td>University of Toronto Maternal-Fetal Medicine Division, Program in Development and Fetal Health, Lunenfeld Research Institute; Departments of Obstetrics &amp; Gynaecology, Mount Sinai Hospital, Toronto, ON, Canada</td>
</tr>
<tr>
<td>Tak Yeung Leung, MD, FRCOG</td>
<td>Department of Obstetrics and Gynaecology, The Chinese University of Hong Kong, Prince of Wales Hospital, Shatin, New Territories, Hong Kong, PRC</td>
</tr>
<tr>
<td>Marianne Leruez-Ville, MD</td>
<td>Department of Obstetrics and Fetal Medicine, Paris Descartes University, Assistance Publique-Hôpitaux de Paris, Hôpital Necker-Enfants-Malades, Paris, France</td>
</tr>
<tr>
<td>Nicola A. Lewis, FRCS (Eng), FRCS Paed Surg</td>
<td>Department of Paediatric Surgery, Birmingham Children's Hospital, Birmingham, UK</td>
</tr>
<tr>
<td>Katrine M. Løfberg, MD</td>
<td>Postdoctoral Research Fellow, Division of Pediatric Surgery/ Fetal Treatment Center, University of California San Francisco, CA, USA</td>
</tr>
<tr>
<td>Enrico Lopriore, MD, PhD</td>
<td>Division of Neonatology, Department of Pediatrics, Leiden University Medical Center, Leiden, the Netherlands</td>
</tr>
<tr>
<td>Fergus P. McCarthy, MB BCh MRCPI</td>
<td>Anu Research Centre, Department of Obstetrics &amp; Gynaecology, University College Cork, Cork, Ireland</td>
</tr>
<tr>
<td>Laurence B. McCullough, PhD</td>
<td>Center for Medical Ethics and Health Policy, Baylor College of Medicine, Houston, TX, USA</td>
</tr>
<tr>
<td>Geoffrey A. Machin, MD, PhD</td>
<td>Department of Laboratory Medicine and Pathology, Mackenzie Health Sciences Centre, Edmonton, Alberta, Canada</td>
</tr>
<tr>
<td>Khadija Madani</td>
<td>Department of Obstetrics, Leiden University Medical Center, Leiden, the Netherlands</td>
</tr>
<tr>
<td>Arnaud Marchant, MD, PhD</td>
<td>Institute for Medical Immunology, Université Libre de Bruxelles, Belgium</td>
</tr>
<tr>
<td>Vedanta Mehta, BSc (Hons), MSc, PhD</td>
<td>Department of Maternal and Fetal Medicine, Institute of Women's Health, University College London, London, UK</td>
</tr>
<tr>
<td>Catherine L. Mercer, BA, BM, MRCPCH</td>
<td>Centre for Human Development, Stem Cells and Regeneration, Faculty of Medicine, University of Southampton, UK</td>
</tr>
<tr>
<td>Kenneth J. Moise Jr., MD</td>
<td>Professor of Obstetrics, Gynecology and Reproductive Sciences, Professor of Pediatric Surgery, UT Health – University of Texas Medical School at Houston; Co-Director, the Texas Fetal Center, Children's Memorial Hermann Hospital, Houston, TX, USA</td>
</tr>
<tr>
<td>Ben W. Mol, MD, PhD</td>
<td>Academic Medical Centre, Department of Obstetrics and Gynaecology, Amsterdam, the Netherlands</td>
</tr>
<tr>
<td>R. Katie Morris, PhD, MRCPG</td>
<td>Clinical Lecturer in Fetal Medicine, School of Clinical and Experimental Medicine, University of Birmingham, Birmingham, UK</td>
</tr>
<tr>
<td>Kypros Nicolaides, BSc, MD, FRCOG</td>
<td>Harris Birthright for Fetal Medicine, King's College Hospital, London, UK; Investigators of the TOTAL trial, Eurostec Programme, Leuven, Barcelona and London, Europe</td>
</tr>
<tr>
<td>Dick Oepkes, MD, PhD</td>
<td>Professor of Obstetrics and Fetal Therapy, Department of Obstetrics, Leiden University Medical Center, Leiden, the Netherlands</td>
</tr>
</tbody>
</table>
List of contributors

Ramesha Papanna, MD, MPH
Instructor and Fellow, Division of Maternal-Fetal Medicine, Department of Obstetrics, Gynecology, and Reproductive Sciences, Yale School of Medicine, New Haven, CT, USA

Robert E. Poelmann, PhD
Department of Anatomy & Embryology, Leiden University Medical Center, Leiden, the Netherlands

Jute Richter
Division of Woman and Child, Department of Reproduction, Development and Regeneration, University Hospitals Leuven, Leuven, Belgium; Investigators of the TOTAL trial, Eurostec Programme, Leuven, Barcelona and London, Europe

Michael G. Ross, MD, MPH
Professor of Obstetrics and Gynecology and Public Health, David Geffen School of Medicine at UCLA, Los Angeles, CA, USA

Rodrigo Ruano, MD, PhD
Professor of the Department of Obstetrics and Gynecology, Baylor College of Medicine, Houston, TX, USA

Jack Rychik, MD
Professor of Pediatrics, and Director, Fetal Heart Program, The Children's Hospital of Philadelphia, University of Pennsylvania School of Medicine, Philadelphia, PA, USA

Neil J. Sebire, MBBS, BClinSci, MD, DRCOG, FRCPath
Professor, Department of Paediatric Histopathology, Great Ormond Street Hospital for Children NHS Trust, London, UK

Foula Sozo, PhD
Department of Anatomy and Developmental Biology, School of Biomedical Sciences, Monash University, Clayton, VIC, Australia

Stephen Sik Hung Suen, MBChB, MRCOG
Department of Obstetrics and Gynecology, The Chinese University of Hong Kong, Prince of Wales Hospital, Shatin, New Territories, Hong Kong, PRC

Leslie N. Sutton, MD
Chief, Pediatric Neurosurgery, The Children's Hospital of Philadelphia; Professor of Neurosurgery and Pediatrics, University of Pennsylvania School of Medicine, Philadelphia, PA, USA

Dick Tibboel
Erasmus Pediatric Hospital, Rotterdam, the Netherlands

Danielle R. M. Timmermans, PhD
Department of Public and Occupational Health, EMGO Institute for Health Care Research, VU University Medical Center, Amsterdam, the Netherlands

Jaan Toelen
Division of Woman and Child, Department of Reproduction, Development and Regeneration, University Hospitals Leuven, Leuven, Belgium

Wayne Tworetzky, MD
Director of Fetal Cardiology, Department of Cardiology, Children's Hospital Boston, Harvard Medical School, Boston, MA, USA

Yves Ville, MD, PhD
National Reference Centre for the Management of Complicated Monochorionic Pregnancies; Department of Obstetrics and Fetal Medicine, Paris Descartes University, Assistance Publique-Hôpitaux de Paris, Hôpital Necker-Enfants-Malades, Paris, France

Melissa Walker, MSc
Department of Obstetrics & Gynaecology, Maternal-Fetal Medicine Division, Mount Sinai Hospital, University of Toronto, ON, Canada

Martin A. Weber, MB, BS, MD, FRCPath
Department of Paediatric Pathology, Great Ormond Street Hospital for Children NHS Trust, London, UK

Shari L. Wellen, MD
Instructor of Pediatrics, Division of Cardiology, The Children's Hospital of Philadelphia, University of Pennsylvania School of Medicine, Philadelphia, PA, USA

Magnus Westgren
Department of Clinical Science, Intervention and Technology, Karolinska Institute, Stockholm, Sweden

Louise E. Wilkins-Haug, MD, PhD
Director, Division of Maternal-Fetal Medicine, Department of Obstetrics and Gynecology, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA

David I. Wilson, BA, MBBS, PhD, FRCP
Centre for Human Development, Stem Cells and Regeneration, Faculty of Medicine, University of Southampton, UK

R. Douglas Wilson, MD, MSc, FRCSC, FACOG
Department of Obstetrics and Gynecology, University of Calgary, Calgary, Alberta, Canada

Sana Zakaria, BSc, MSc
Department of Craniofacial Development and Stem Cell Biology, King's College London, London, UK
Foreword

Charles H. Rodeck, MB, BS, BSc, DSc, FRCOG, FRCPath, FMedSci.
Emeritus Professor of Obstetrics and Gynaecology
Institute for Women’s Health
University College London
London, UK

The history of fetal medicine has run a disorderly course, lacking in synchronicity. A landmark date is 1963, when William Liley published the first example of direct fetal therapy, intra-peritoneal blood transfusion for rhesus alloimmunization. This was long before the ultrasound technology that we regard as a sine qua non, and that we take for granted, was available. How much safer and more effective would the procedure have been with ultrasound guidance, at a time when hemolytic disease of the fetus was fairly common. Not long afterwards, rhesus porphylaxis was introduced and the condition became less frequent, just as its treatment with intravascular transfusion improved. It has now become so rare that it is difficult to provide training and to maintain skills.

Since then, there have been revolutions not only in ultrasound, but also in the laboratory sciences of biochemistry, cell culture, genetics, and molecular biology. These were embraced by fetal medicine, first for diagnosis and then for population screening and prevention of fetal conditions. Overwhelmingly, these are the main pre-occupations of fetal medicine and take place in all hospitals in the context of antenatal care. Fetal therapy has represented a far smaller area of activity (although the love affair of the media for fetal surgery might make one think otherwise!). The reasons for this include the complexity and formidable nature of some of the interventions, the relatively rare indications and opportunities for performing them, and the limited availability of the necessary skills and facilities. The accumulation of knowledge and experience has therefore been slow and rightly has been restricted to highly specialized centers. There is, as yet, no definitive treatment for genetic disease, pre- or postnatally, and the understanding of the molecular basis for malformations is insufficiently advanced to design preventive strategies.

This volume comprehensively surveys the current status of fetal therapy. The words in the title “Scientific Basis and Critical Appraisal” are reflected in the contents, with greater emphasis on scientific methodology, systematic reviews, and randomized controlled trials than in the past. The editors are to be congratulated on the planning and organization of their book and on eliciting outstanding contributions from their authors. They will be essential companions for fetal medicine practitioners and trainees for some years to come.

In an ideal world, every child is a wanted child, and for parents the arrival of a healthy baby is a wonderful event. For those less fortunate, the detection of a fetal abnormality is a massive challenge. The goal of fetal medicine is to help parents decide which is the best option for them, often the least bad option. Parents who willingly continue a pregnancy with an affected fetus, and especially if the pathology has been cured or ameliorated by therapeutic intervention, are a triumph for the practitioners caring for them.
Preface

This textbook is intended to draw together key aspects of the ever-advancing field of fetal therapy and has contributions from specialists in a range of related disciplines. It is directed at postgraduate trainees as well as designated specialists and subspecialists.

Fetal Medicine has continued to advance as a subspecialty over the last twenty years and has embraced methods of fetal assessment and treatment ranging from non-invasive techniques to direct in-utero intervention (including ultrasound directed "needle placement" techniques and direct visualization of the fetus, allowing minimally invasive therapy).

Ever since the widespread introduction and use of ultrasound in obstetrics, clinicians have been able to visualize their second patient, the fetus. This has allowed Fetal Medicine to develop so that increasingly ambitious and intricate interventions can be applied. However, in some areas our understanding of the pathogenesis of fetal disease has lagged behind our ability to intervene and attempt to ameliorate the life-threatening effects of congenital disease.

This volume has chapters from international experts in the field and focuses on aspects of transplacental therapy and both ultrasound and fetoscopic-directed interventions all utilized to treat a range of fetal disease. Case cohort studies provide an increasing body of literature and systematic reviews have allowed critical appraisal of fetal therapy, yet at the beginning of the twenty-first century, there remains a paucity of evidence from randomized controlled trials. Such data would provide an essential contribution directing evidence-based management.

This textbook sub-divides into chapters describing the pathogenesis of disease processes, treatment involving transplacental drug therapy, invasive procedures and fetal surgery. Its aim is to emphasize those treatments which have become established in clinical practice, reviewing the reasons why some therapy has failed to live up to its promise and, where possible, to review the literature systematically. Defining the boundaries of fetal therapy will always be controversial and, of course, its efficacy has to be judged in the light of the potential effects on maternal health. As a generalization, this statement is true, but it is particularly so when considering the use of ever more ambitious fetoscopic techniques. There is an important section on the ethics of in-utero therapy, a rapidly changing and highly important field, which must be considered by specialists intending to practice fetal therapy.

The text is written by authors who are all working at the "cutting edge" of their respective fields. Fetal therapy is complex and the techniques should be delivered in designated centres where the quantity of cases allows the development of a skill base. Audit and research must fuel momentum and progress within this field.

I am personally very grateful to my co-editors, Dr. Dick Oepkes and Dr. Tony Johnson and indeed all contributors to this textbook. I hope that these articles aid education and progress in this fascinating and rewarding medical specialty.

Mark D. Kilby MBBS DSc MD FRCOG.
Birmingham, United Kingdom.
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