Fetal Therapy: Scientific Basis and Critical Appraisal of Clinical Benefits

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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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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 preganacy 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.

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