

THE UNBORN PATIENT

Prenatal Diagnosis and Treatment

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FOREWORD

Our generation is the first ever to have a reasonably complete outline of the development of a baby from conception. In 1930 the liberation of an ovum from a human ovary was first observed. In 1944 the union of the human sperm and ovum was first seen, through a microscope. In the 1950s the events of the first six days of life were described—those critical early steps in a prodigious journey which sees the single-celled zygote develop into the 30 million million cells of an adult.

Although by the turn of the century John William Ballantyne had established principles of antenatal care that conferred benefits on the fetus as a member of a statistical class, it was not until the 1960s that accurate specific diagnosis and therapy tailored to individual fetal needs became a reality in at least one disorder: Rh hemolytic disease. Since that time, the physical environment, anatomy, and physiology of the fetus, as well as fetal genetics, endocrinology, and biochemistry all have become accessible to observation and study.

Inevitably, with so much new knowledge arriving in a sequence determined largely by chance developments in technology, progress has been uneven. In particular, rapid advances in amniotic fluid analysis, ultrasonic imaging, and fetoscopy have meant that diagnostic procedures have flourished in a therapeutic vacuum. As a consequence, antenatal diagnosis has acquired in the minds of some the sinister image of a "search and destroy" mission.

However, on the positive side, around the world a few score investigators and teams with a positive commitment to fetal survival and welfare are attempting fetal therapy as the logical sequel to fetal diagnosis. This book represents a landmark in this endeavor.

Obviously the field bristles with problems. As in any new area of medicine mistakes are inevitable, for good intentions have never been a guarantee against monumental blunders. Improvements in diagnostic skills, a better understanding of the natural history of some fetal disorders, a wider awareness of fetal tolerance and compliance, critical consideration of serious ethical issues, and long-term surveillance of survivors are urgently needed. Even for some everyday problems that are not peculiar to fetal therapy, notably premature labor and premature rupture of the membranes, our current ignorance is quite majestic.

Since there is no precedent for anything until it is done for the first time, progress and improvement will be inevitable. Already, for a variety of disorders, the physician and the parents are no longer helplessly dependent on what time, luck, and intrauterine life present them with at birth. No longer need the attendants of a pregnant woman always be helpless spectators at the death of a baby. The day on which a child is born, whether it be under Capricorn or Pisces, is not necessarily simply a matter of fate but also can be a matter of whether we can care for the baby more safely and efficiently in the uterus or in the nursery.

Provided we remember that we are merely at the forefront of human knowledge, it is possible that the World Health Organization dream of "health for all by the year 2000" will include the unborn. Some day, for a wider range of fetal illness, we may be able to offer a brighter prospect than the present dismal alternatives of neonatal death, abnormality, or abortion.

A. W. Liley, K.C.M.G., Ph.D., D.Sc. (Hon),
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**Sir William Liley, pioneer in fetal treatment
and eloquent advocate for the fetal patient,
died peacefully in June, 1983. He will be
sorely missed.**

PREFACE

ACKNOWLEDGMENTS

As originally conceived, this book was to be a small project of short gestation. A few years ago this seemed appropriate, because there was little information about fetal management and the field was changing so rapidly that a monograph would have to be frequently updated. But in the last two years the field has exploded and information has accumulated so rapidly that our little mouse has become an elephant with a correspondingly longer gestation. We have reluctantly conceded that our original plan to write a short monograph about our personal experience in developing the Fetal Treatment Program at the University of California, San Francisco, would not do justice to the field. At the same time, we felt that this rapidly changing and exciting field was not ready for a "textbook" with the usual drawbacks of large multi-authored works. With the help of a few carefully selected contributors in special fields, we have written a cohesive book based on our own experience and incorporating the growing experience of other investigators around the world. We have tried to deal with all of the questions (medical, physiological, social, ethical, legal) that may arise when a family seeks help with an abnormal fetus. We recognize that this is a very young book in a very new and rapidly growing field.

As is often the case, the conception of this book was an accident. In this case three individuals with highly different backgrounds—a pediatric surgeon, an obstetrician geneticist, and a sonographer—shared an interest in fetal defects. Five years of constant discussion, speculation, experimentation, and interaction in caring for fetuses and their families led to the development of The Fetal Treatment Program at UCSF and eventually to the gestation of this monograph. The first trimester was taken up with clinical speculation and intense experimental investigation. In the second trimester, the first therapeutic maneuvers were attempted and then refined in human fetuses. With the initial flurry of interest and excitement surrounding the first human fetal cases, the Kroc Foundation agreed to sponsor a meeting that brought together pioneering investigators from around the world and produced the consensus statement on fetal treatment that was published in the *New England Journal of Medicine*. The Kroc Foundation also kindly agreed to underwrite the cost of color plates for this book. The third trimester, involving the actual writing, rewriting, and editing, has proved somewhat painful but has yielded, we hope, a healthy and vigorous issue.

ACKNOWLEDGMENTS

The Fetal Treatment Program at UCSF evolved through the interaction of professionals in many disciplines who share an interest in the fetus. Many have contributed to the clinical and experimental material presented in this book: pediatric surgeon Alfred de Lorimier; pediatric neurosurgeon Michael Edwards; obstetricians Robert Creasy, Russell Laros, Julian Parer, and Michael Katz; sonographer Peter Callen; anesthesiologist Mark Rosen; and ethicist Albert Jon- sen. Fellows who have contributed mightily and shouldered the responsibility for much of the laboratory and clinical work include Donald Nakayama and Philip Glick in pediatric surgery, Gary Simpson and Allen Hogge in obstetrics and genetics, and Daryl Chinn in sonography. Rita Douglas has arranged sched- ules, kept records, and guided the patients and their families through their many examinations and procedures. Linda London, Barbara Robnett, Kathy Ruvolo, and Tami McDiffit have provided sonographic technical assistance. Ann Levine has been our operating room specialist and Mary Beth Inturrisi our obstetrical nurse specialist. Robin Villa has coordinated the experimental animal work. And in the final analysis, it is the "office" that works through the many changes, revisions, and frustrations inherent in this sort of undertaking. Therefore, thanks go to Florence Dobashi, Rosa Santillana, Patricia Stitch, Grace Black, and very especially to Norma Schlemme, whose untiringly enthusiastic devotion made it all come to pass. Finally, we would like to thank the production staff of Grune & Stratton, whose fine work made publication surprisingly swift and pleasant.

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THE FETUS AS PATIENT: HISTORICAL PERSPECTIVE

The concept that the fetus is a patient, an individual whose maladies are a proper subject for medical treatment as well as scientific observation, is alarmingly modern. It was not until the last half of this century that the prying eye of the ultrasonographer rendered the once opaque womb transparent, letting the light of scientific observation fall on the shy and secretive fetus.

Historically, we approached the fetus with a wonder bordering on mysticism. Enid Bagnold's description captures the awe engendered by a scene no one had actually witnessed:

Hanging head downwards between cliffs of bone was the baby, its arms all but clasped about its neck, its face aslant upon its arms, hair painted upon its skull, closed, secret eyes, a diver poised in albumen, ancient and epic, shot with delicate spasms, as old as a Pharaoh in its tomb.*

Whether this reverence is a reflection of our profound wonder at the "miracle" of differentiation of a fertilized egg into a human infant or a clandestine Darwinian mechanism to ensure survival of the species, it has certainly hindered investigation of fetal pathophysiology and precluded any consideration of fetal therapy. Only in the last few decades have techniques for visualizing, monitoring, measuring, and prodding the fetus begun to alter our perceptions of the living human fetus. Only now are we beginning to view the fetus seriously—medically, legally, and ethically. Now that our perspective is undergoing radical change, it is instructive to trace the medical history of our approach to this, our most reticent patient!

THE FETUS AS SEED AND HOMUNCULUS

Animal husbandry is not complicated unless you think about it. In biblical times, it was enough to describe the phenomenon: someone begat someone who begat someone who, etc. The intricacies of the begetting—the conception and growth of the individual—were matters assigned to the realm of Solomon's wisdom: "And in my mother's womb was fashioned to be flesh in the time of ten months, being compacted in blood, of the seed of man, and the pleasure that came with sleep." (*Wisdom of Solomon* 7:2) There was general recognition that physical characteristics passed from parent to offspring, and this was con-

*From Bagnold E: *The Door of Life*, Ch. 2. New York, William Morrow, 1938.

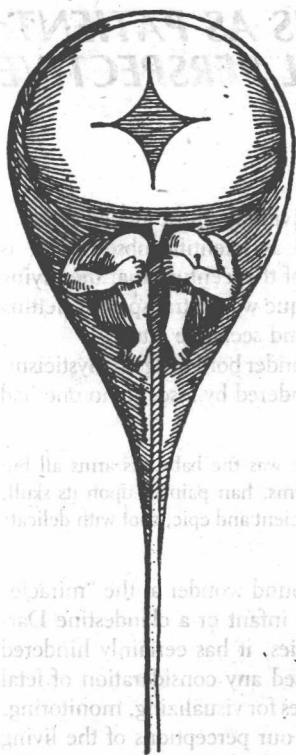


Fig. 1-1. A human spermatozoon is depicted containing a homunculus. (From Hartsoeker: *Essay de dioptrique*, Sect. 88, Paris, 1694. In Meyer AW: *The Rise of Embryology*. Stanford, Stanford University Press, 1939, following p. 78. Reproduced with permission.)

ceptualized as a seed passed from the father to the mother where it grew and later blossomed as a child. Even into the second century, Marcus Aurelius could say, "A man passes seed into a womb and goes away, and anon another cause takes it in hand and works upon it and perfects a babe—what a consummation from what a beginning!" (*Meditations* X:26)

In attempting to explain how the fetus was related to the child, Greek and Roman thinkers conceived the idea of the homunculus—a miniature person living and growing within the mother before birth. This concept undoubtedly evolved from practical experience in animal husbandry and from observation of aborted human and animal fetuses. The fetus was seen to increasingly resemble the child as gestation progressed. In the absence of "modern" biologic information, the homunculus provided a very good explanation for at least the older fetus.

The homunculus, a purely descriptive explanation, was sometimes carried to a wonderfully whimsical extreme. The 18th century writer Laurence Sterne, in *The Life and Opinions of Tristram Shandy, Gentleman*, had his hero soliloquize: