

ANESTHESIA FOR FETAL PROCEDURES & SURGERY

Essay

*Submitted for Partial fulfillment of Master Degree
In Anesthesiology*

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2010

❧Acknowledgement❧

*First of all, all gratitude is due to **Allah** for blessing this work until it has reached its end, as a part of his generous help throughout my life.*

*I would like to express my deepest gratitude to **Prof. Dr. Zakaria Abd El Aziz Moustafa**, Professor of Anesthesiology and Intensive Care, Faculty of Medicine- Ain Shams University, for his close supervision, his science advice and for the great effort he has done throughout the whole work.*

*Also, it is my great pleasure to express my deepest gratitude to **Dr. Ahmed Mohamed Shafik Hamed**, Assistant Professor of Anesthesiology and Intensive Care, Faculty of Medicine- Ain Shams University, for the effort and time she spent.*

*Also, I would like to express my deep gratitude to **Dr. Rami Mounir Wahba Gobran**, Lecture of Anesthesiology and Intensive Care, Faculty of Medicine- Ain Shams University, for giving me the great support and encouragement throughout the whole work.*

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❧Abbreviations❧

°C	: Degree celsius
µg	: Microgram
3-D	: Three dimensional
B-2	: Beta 2
BP	: Blood pressure
BPD	: Broncho-pulmonary dysplasia
cAMP	: Cyclic adenosine monophosphate
CCAM	: Congenital cystic adenomatoid malformation
CDH	: Congenital diaphragmatic hernia
cGMP	: Cyclic guanosine monophosphate
CHAOS	: Congenital high airway obstruction syndrome
CM	: Centimeter
CNS	: Central nervous system
CO₂	: Carbon dioxide
COX₂	: Cyclooxygenase 2
CVR	: CCAM volume ratio
Dis	: Diseases
DNA	: Deoxy ribonucleic acid
ECG	: Electro-cardiograph
ECMO	: Extra corporeal membrane oxygenation
EDRF	: Endothelium-derived relaxing factor
EX	: Example
EXIT	: The ex utero intrapartum treatment

❧Abbreviations (Cont.)❧

F/M	: Fetal/ maternal
FETENDO	: Fetal endoscopy
FETO	: Fetoscopic Endoluminal Tracheal Occlusion
FFN	: Fetal fibronectin
Fig	: Figure
FRC	: Functional residual capacity
G	: Gauge
g	: Gram
GA	: Gestational age
Hrs	: Hours
HSC	: Hemopoietic stem cell
IM	: Intramuscular
IQ	: Intelligence quotient
IUFD	: Intrauterine fetal demise
IUGR	: Intra-uterine growth retardation
IV	: Intravenous
kD	: Kilodalton
Kg	: Kilogram
LHR	: Lung to head ratio
LMP	: Last menstrual period
LUTO	: Lower urinary tract obstruction
MAC	: Minimum alveolar concentration
mEq/L	: Mill equivalent per liter

❧Abbreviations (Cont.)❧

Mg	: Milligram
MHz	: Millihertz
Min	: Minute
ml	: Milliliter
MM	: Millimeter
MMC	: Myelomeningocele
mmHg	: Millimeter mercury
MRI	: Magnetic resonance imaging
N2O	: Nitrous oxide
Nd: YAG	: Neodymium YAG laser fiber
NO	: Nitric oxide
NSAIDs	: Non steroidal anti-inflammatory agents
OOPS	: Operations on placental support
P50	: O ₂ tension at o ₂ saturation 50%
PH	: Logarithm of hydrogen ion
pKa	: Ionic dissociation constant
PO₂	: Oxygen tension
PPROM	: Preterm premature rupture of the membranes
PROM	: Premature rupture of membranes
PTL	: Preterm labor
PTLs	: Preterm labors
RDS	: Respiratory Distress Syndrome

❧Abbreviations (Cont.)❧

RH	: Rhesus
SCT	: Sacrococcygeal teratoma
SIDS	: Sudden infant death syndrome
TO	: Tracheal occlusion
TOP	: Termination of pregnancy
TRAP	: Twin reversed arterial perfusion
TTTS	: Twin-twin transfusion syndrome
UAP	: Uterine artery pressure
UBF	: Uterine blood flow
UCSF	: University of California, San Francisco
US	: Ultrasound
UVP	: Uterine venous pressure
Vs	: Versus

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INTRODUCTION

Fetal therapy is a new branch of medicine, developing quickly now, that deals with diseases and congenital anomalies diagnosing and therapy in an unborn child in utero. Nowadays, fetus has become a fully-privileged patient for medical and surgical therapies. Fetal therapy is a fascinating and dynamically developing field of medicine which has practically gone beyond the limits of a medical experiment. Progress in perinatology, medical technique and pharmacology and in study on human genome raise optimism and allow believing that in close future fetal therapy will be broadly accepted as a routine therapeutic method (*Syweński et al., 2008*).

Fetal surgical techniques using animal models were first developed at the University of California, San Francisco in 1980 by Dr. Michael R. Harrison and his research colleagues. In 1981, the first human open fetal surgery in the world was performed at University of California, San Francisco under the direction of Dr. Michael Harrison (*Kristine et al., 2005*).

Fetal surgery is evolving rapidly in the field of mainly ex-utero intrapartum treatment procedures, where new indications are found and new anesthetic techniques are developed, enabling the use of locoregional anesthesia. Further development of anesthetic techniques focuses on minimizing the risks for the mother and preserving the normal neurodevelopment of the fetus. Open fetal surgery remains a major invasive procedure for mother and fetus both, requiring general anesthesia with adequate invasive monitoring. Minimal invasive fetal procedures can be performed with local anesthesia alone or, for the more complex fetoscopic

procedures, with a neuraxial locoregional technique. Fetal anesthesia and analgesia can then be provided by different routes. Ex-utero intrapartum treatment procedures are open fetal procedures, but they can be performed with locoregional anesthesia, when uterine relaxation can be achieved without volatile anesthetics with the use of intravenous nitroglycerin (***De Buck et al., 2008***).

Most prenatal surgeries are high risk and may be considered experimental. The greatest risk is that the placenta will be nicked during surgery, causing blood hemorrhaging, uterine contractions, and birth of a premature infant who may not survive. Preterm labor is the most common complication of prenatal surgery. Fetoscopic surgeries are less dangerous and traumatic than open fetal surgery and reduce the risk of premature labor. Subsequent children of a mother who has undergone prenatal surgery usually are delivered by cesarean section because of uterine scarring (***Hedrick et al., 2003***).

The fetus reacts to nociceptive stimulations through different motor, autonomic, vegetative, hormonal, and metabolic changes relatively early in the gestation period. With respect to the fact that the modulatory system does not yet exist, the first reactions are purely reflexive and without connection to the type of stimulus. While the fetal nervous system is able to react through protective reflexes to potentially harmful stimuli, there is no accurate evidence concerning pain sensations in this early period. Cortical processes occur only after thalamocortical connections and pathways have been completed at the 26th gestational week (***Rokyta, 2008***).

Anesthesia for fetal surgery involves two patients, the mother and the fetus. Thus maternal-fetal safety should be taken

into consideration. Maternal management includes uterine relaxation, prevention of premature labor, pre, intra and postoperative tocolytic agents and postoperative analgesia, in addition to those related to inherent pregnancy changes. Fetal management includes anesthesia, immobility and prevention of fetal asphyxia (*Schwarz et al., 2003*).

AIM OF THE WORK

The aim of the review is to present the possibilities of anesthesia for fetal therapy now at hand, to delineate general tendencies of further development and to highlight dangers and controversies.

HISTORICAL BACKGROUND

The Ancient Fetal Medicine:

In attempting to explain how the fetus was related to the child, Aristotle, a Greek philosopher and scientist, thought that a miniature man in the father's sperm grew into a baby in the mother's womb. Hippocrates, a Greek physician regarded as the father of medicine, came to the "brilliantly intuitive" conclusion that the fetus urinates in utero and that amniotic fluid is largely composed of fetal urine. Andreas Vesalius, the father of modern anatomy, made the first "truly analytic" observations on the living mammalian fetus. He pointed out that the fetus attempts to breathe when exposed to air. He also noted that the fetal arteries in the umbilical cord pulsate regularly until fetal breathing begins (*Harrison, 1982*).

The experimental fetal surgery:

It was not until the 19th century that experimental animal preparations were used to make physiologic observations on the living mammalian fetus. Bichat in 1803 was the first to study fetal movement. Zunt in 1877 and later Preyer in 1885, studied intact fetal guinea pigs suspended in warm saline and noted that once a fetus had been allowed to breathe, it could not be returned to its mother and survive (*Harrison et al., 2001*).

In 1918, Mayer removed fetal guinea pigs from the uterus and placed them in the abdominal cavity. Some of these fetuses survived for several days. In 1925, Bors reported the first successful fetal surgery procedure. He amputated the limbs of guinea pig fetuses through a small uterine incision. The incision was closed and viable fetuses were eventually delivered.

Hooker and Nicholas in (1930) developed a technique for spinal cord section and other investigators developed techniques

for the ablation of critical fetal endocrine organs. In (1939) **Tobin** performed fetal adrenalectomy

In (1949) **Foote and Foote** explored decapitation as a means of studying the influence of the pituitary on subsequent fetal development. The need for long-term experimentation led to the use of larger experimental animals. Sheep were probably the most widely used animals, because they were relatively cheap and had a high incidence of twinning. The other major reason for using sheep was that it has a relatively quiescent ovine. The sheep uterine wall, even during pregnancy, is very thin and nowhere near as muscular or vascular as the primate uterus.

Between the late 1950s and the early 1960s, the emphasis of physiologic experimentation shifted from acute and ablative experiments to chronic experiments, using variety of long-term catheterization techniques. Maloney studied the functional development of the respiratory system in a fetal lamb model (**Maloney, 1983**).

Jackson and his colleagues in (1963) were able to correct coarctation of the aorta. In (1966) **Holder and Aschraft** attempted to create experimental biliary atresia.

De Lorimier's group in (1969) developed a model for studying the diaphragmatic hernia in the fetal lamb and **between (1970) and (1973) Beck** developed models for studying obstructive uropathy in sheep. **Kent and his colleagues** in (1972) studied the physiology of the circulation in lamb with diaphragmatic hernia. The use of primates as a model for fetal surgery has been relatively restricted. Primates are expensive and the pregnancies are more difficult to maintain. However, many models for fetal surgery have been developed exclusively for primates.

In (1969) **Chez and Hutchinson** conducted experiments observing renal function in a variety of monkey models these were relatively short term catheterization studies. In (1969) **Parshall**