INTRAUTERINE FETAL SURGERY – WHERE DO WE STAND

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Prologue

Intra-uterine fetal surgery is relatively new and a costly procedure. It requires a large, collaborative team in which each member is aware of their co-worker's role. Though considered a unique speciality, intra-uterine fetal surgery evolved alongside advances in ultrasonography, the establishment of fetal medicine, and the increased acceptance of fetoscopy for diagnosis and therapy in desperate situations.

As a surgeon, my perspective is consistently shaped by a desire to dispel misconceptions and alleviate apprehension about surgical procedures prevalent among the general public. Although my own specialty is cardiothoracic surgery, my clinical experience has repeatedly shown me how profoundly outcomes can depend on the timing of intervention. For instance, when a neonate with a congenital diaphragmatic hernia is brought to a pediatric cardiac or thoracic surgeon after birth, definitive correction may come too late — the lungs may already have lost their capacity to expand due to prolonged compression from herniated abdominal contents. Had such a condition been corrected in utero through fetal surgery, the prognosis could be markedly improved.

Similar considerations apply to other anomalies, such as posterior urethral valves, where obstructed urinary flow can produce back-pressure, bilateral hydronephrosis, and irreversible renal damage, even though a relatively simple prenatal drainage procedure could preserve kidney function. Encounters like these have compelled me to look beyond the traditional boundaries of my specialty and to appreciate the transformative potential of fetal intervention.

In this endeavor, I have gained invaluable insight into the rapidly evolving field of fetal medicine. Until recently, it was almost unimaginable that the fetus could be regarded as a patient and that surgical procedures could be performed while it remained within the mother's womb. In this article, I describe the evolution of that concept and outline procedures currently in practice. In a sense, the fetus undergoes birth twice — the first time when it is temporarily brought out of the intrauterine environment for corrective intervention, and the second at the time of definitive Cesarean delivery. After the initial procedure, it is returned to a carefully recreated intrauterine milieu, allowing continued growth, development, and organogenesis until term.

The "Crazy Idea" and The Evolution Of Fetal Surgery

The concept of fetal surgery comes from first identifying the details of a fetus, diagnosing the anomaly by a detailed ultrasound examination, then evaluating whether it is a surgically correctable condition and whether the surgery needs to be done while still in the mother's womb, and if not done, it can compromise the fetal well-being or even survival [6]. For example, in a twin pregnancy, if one of the twins is acardiac (has not developed a heart of its own)

and thrives on the heart and circulation of the other healthy twin, then the healthy twin's heart has to work twofold and will soon go into failure. This demands an immediate severance of the vascular connections between the twins to ensure the healthy twin's survival. Likewise, if there is an amniotic band that is cutting through one of the limbs of the fetus, and if severed, it can save that limb, then it should be tried during the intrauterine life.

Intrauterine fetal surgery is fraught with risks and requires strong conviction, determination, and an optimistic outlook for positive results. The hospital unit where such procedures are performed must have a sound financial back-up. This challenging specialty operates within a wide spectrum in which advanced ultrasound, Seldinger techniques, fetoscopic laser for adhesiolysis, band dissolution, and vascular ablation, etc., are all necessary skills. Where a uterine incision is needed, the best results are with life-threatening neural canal defects with skin loss, complex meningomyelocoels, sacrococcygeal teratomas, and similar defects. These pictures became viral on the internet in the '90s. Though these had a fair share of criticism, modern medicine saw the spread and recognition of the new intrauterine fetal surgery as a new specialty.

Figures 1 and 2 depict images that gained widespread attention on the internet during the 1990s. Despite receiving some criticism, these images played a significant role in the recognition and establishment of intrauterine fetal surgery as a distinct medical specialty.

Fetal surgery is also called in-utero prenatal surgery or fetal intervention and helps in the:

1. Early identification of congenital defects incompatible with meaningful postnatal life.
2. Preplanning and modification of the post-natal life by the

Figure 1: Fetal hand spontaneously emerges from the uterine incision and holding the surgoen's finger. Image Credit: [1].

Figure 2: Enlarged view of the fetal hand. This surgery was performed at Vanderbilt Hospital, and findings from the landmark seven-year National Institutes of Health-funded Management of Myelomeningocele Study (MOMS) show that fetal surgery for spina bifida — the most common central nervous system birth defect — provides clear benefits for infants. The image featured appeared in Vanderbilt Hospital's published newsletter.

parents.

3. Termination of and discontinuation of such incompatible pregnancies within legal time.
4. Improvement of the quality of life of all concerned.

A 'crazy idea' taxed Dr. Michael Harrison while observing the renowned pediatric surgeon, Hardy Hendren, performing a flawless congenital diaphragmatic repair sometime after birth. Unfortunately, the baby died early, and Michael Harrison thought that further in-utero lung development was necessary for survival, and he hypothesized intra-uterine feto-placental intervention in high-risk selected situations. This was in Boston, Massachusetts. Harrison's opinion was met with skepticism and disbelief at that time. Harrison realized he would have to perform and prove to everyone that his idea was worth the risk. In his own unit at the University of California (UCSF) Hospital, he successfully performed the first surgery on an intra-uterine fetus — a suprapubic cystostomy for the relief of hydronephrosis. The offending space-occupying lesion was surgically removed in the post-natal period.

Experience taught obstetricians that the developing fetus within the mother's body, together with the mother, has certain special needs. Regular and periodic visits to the obstetrician help identify problems during the prenatal period and plan a management strategy for detected defects. The goal is not only for the welfare of the pregnant mother but also to ensure early detection of gestational impairment of blood sugar, pregnancy-related hypertension, and imminent seizure disorders, intrauterine growth anomalies, cervical incompetence threatening a pregnancy, preempting early labor, etc. Repeat and frequent miscarriages and a blighted ovum at the embryo stage often suggest severe congenital anomalies not compatible with life. Non-invasive investi-

Figure 3: Ultrasound image of an intrauterine pregnancy. Image Source: [2].

gations, especially obstetric ultrasound, improved exponentially in the intervening period and were incorporated into antenatal check-ups to help identify feto-maternal problems early and institute measures accordingly. Ian Donald introduced ultrasound in the late '50s and early '60s, enabling obstetricians to visualize intrauterine fetal activity and other abnormalities.

The minimum number of antenatal visits and the timing of the required investigations are protocolized, and WHO guidelines are universally accessible online. Nevertheless, a prenatal visit to an obstetrician is situation-dependent and individualized.

Fetal ultrasound improved by leaps and bounds, courtesy of Kypros Nicolaides, and accurate localization of intrauterine fetal structures became possible. Obstetricians also came to understand that during pregnancy, the hormonal milieu in the mother's body is changed, and most of the drugs have unwanted effects while organogenesis is in progress. Selective drugs can be used only in exceptional circumstances, and most are used for maternal causes - only a few cross the fetoplacental barrier to affect fetal organogenesis. Fetal medicine is an all-encompassing obstetric

specialty in which a detailed ultrasound is performed after clinical examination and counseling. Routine haematological examinations are done at the same time. The primary aims are the well-being of both the mother and the child inside the womb, early detection of fetal structural anomalies, and early identification of genetic and chromosomal abnormalities. The majority of subjects incompatible with a meaningful post-natal life abort spontaneously. Elective termination is planned for fetuses having serious defects, but they can continue growing inside the uterus.

Hobbins and Mahoney introduced fetal endoscopy — fetoscopy in 1974, triggering a dream in the medical fraternity. Fetal surgery began modestly, with diagnostic and therapeutic fetoscopy at the forefront. In 1961, Sir William Liley (New Zealand) did the first percutaneous fetal transfusion, and in 1964, Asensio and Adamsons (Puerto Rico) reported success in direct access to fetal circulation by open hysterotomy. The ’70s saw parallel exponential developments in obstetric ultrasound and in both diagnostic and therapeutic fetoscopy. A combination of uterine ultrasound and therapeutic fetoscopy allowed percutaneous access and approach to the fetus, placenta, and umbilical cord. Percutaneous relief from rhesus incompatibility in bad cases before birth became the first reality.

Lysis of bands entrapping fetal structures in the amniotic band syndrome and the delivery of targeted laser beams in twin-to-twin transfusion syndrome (TTTS) or the twin reversed arterial perfusion syndrome (TRAP) ensured healthy pregnancy outcomes. These complications are common in monochorionic twins.

Michael Harrison is unequivocally regarded as the father of intrauterine fetal surgery because of his belief, dedication, and giving a final form to his "crazy idea" from 1981 onwards. He led from the front. He was instrumental in the innovations and the continued evolution of a specialty that challenged the skills of

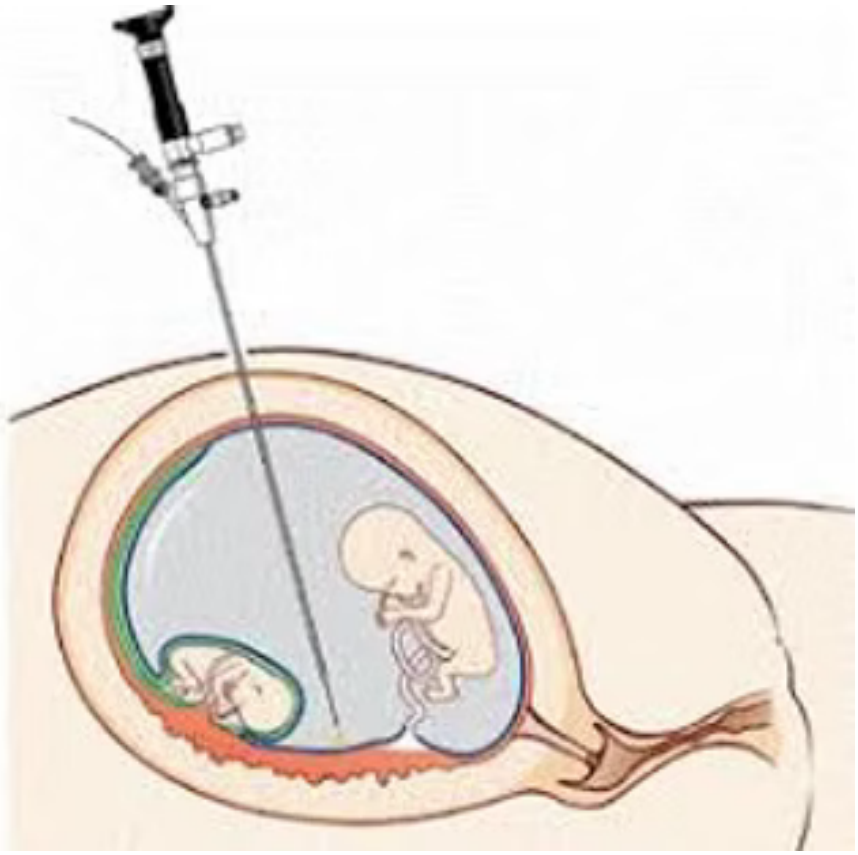

Figure 4: Fetoscope inside the uterus. Image Credit [3].

several surgeons. The premature death of a congenital diaphragmatic hernia (CDH) in the postnatal period gave him the"crazy idea" which taxed him, and it was a long way before a final form with acceptable mortality was realized.

The idea of prenatal uterine intervention has certain benefits, viz, prevention of irreversible organ damage if pregnancy is allowed to continue when the unborn baby is affected with congenital diaphragmatic hernia (CDH), obstructive uropathy, or hydrocephalus. and some neural canal defects. Fetoscopic laser ablation of certain vessels in twin-to-twin transfusion syndrome (TTTS), blood transfusion in severe fetal anaemia, and early management of rhesus incompatibility can ensure a healthy postnatal life and prevent unnecessary perinatal morbidity and mortality. Understanding the pathophysiology of hydrops fetalis and its correction, drainage of pleural collections to improve lung de-

velopment in the expanded state, and fetal endoscopic procedures help ensure early recognition and management. Some conditions call for a hysterotomy – the uterine opening and the fetal position within the uterus have to be planned and tailored for maximal exposure facing the operators. A hysterotomy. Partial or total extraction of the fetus is sometimes required, depending upon the nature of the surgery needed.

Fetal surgery in the mother's womb is still evolving and has a wide spectrum. After withstanding countless religious, social, cultural, and ethnic criticisms and objections, gradual innovations by daring clinicians allowed a quantum increase in the ambit of fetal surgery.

With time, more procedures were added to its ambit.

Procedural Possibilities

The recent day options include:

- Fetoscopic major fetal vascular and cord needle access.
- Therapeutic fetoscopic tracheal occlusion with external clips.
- Endoluminal tracheal occlusion (FETO) for severe congenital diaphragmatic hernia (CDH).
- Fetal vesicoamniotic shunt (VAS) and fetal cystoscopy for bladder obstruction.
- Open fetal surgery for sacrococcygeal teratoma (or SCT, a tumour on the tailbone of the fetus) resection.
- Open fetal surgery to remove a congenital cystic adenomatoid malformation (CCAM) of the lung.
- Fetoscopic laser ablation for twin-twin transfusion syndrome (TTTS) and twin anaemia-polycythemia sequence (TAPS), con-

ditions in which twins have problems with blood flow.

- Radiofrequency ablation for fetal tumours.
- Bipolar cord coagulation for twin reversed arterial perfusion (or TRAP, which can happen when twins develop unequally) sequence.
- Fetal cardiac intervention.
- Intrauterine blood transfusion.
- Serial amnioinfusions for bilateral renal agenesis and complex renal diseases.
- Spina bifida /myelomeningocele.
- Twin anaemia-polycythemia sequence (TAPS).
- Twin reversed arterial perfusion (TRAP) sequence.
- Twin-twin transfusion syndrome (TTTS).
- Amniotic band syndrome (ABS).
- Bronchopulmonary sequestration of the lung.
- Lower urinary tract obstruction (LUTO).
- Mediastinal teratoma.
- Neck mass that interferes with airflow.
- Sacrococcygeal teratoma (SCT).
- Congenital cystic adenomatoid malformation (CCAM) of the lung.
- Congenital diaphragmatic hernia (CDH).
- Congenital high airway obstruction syndrome (CHAOS).
- Fetal anaemia.
- Repair of spina bifida/meningomyelocele (MOM), Twin-to-twin transfusion syndrome surgery.

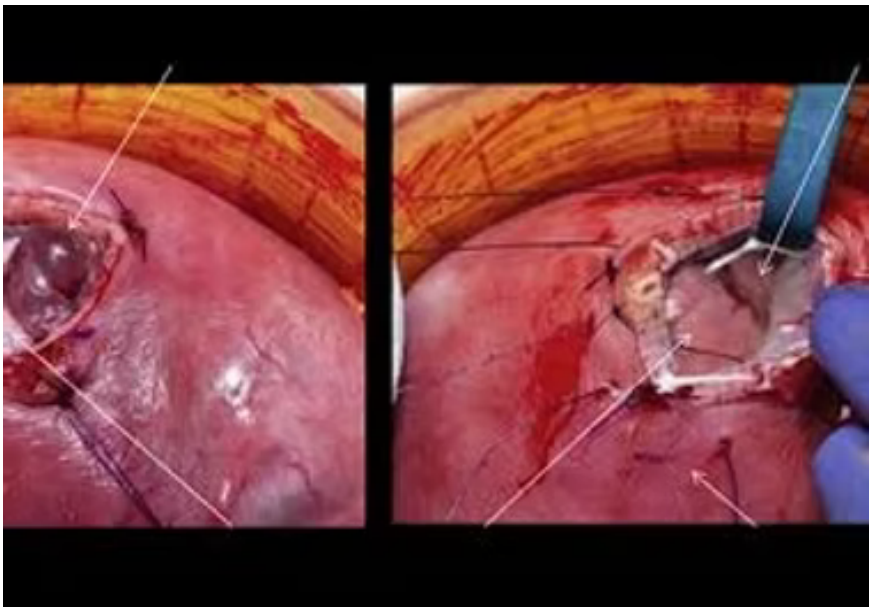

Figure 5: Positioning the fetus and the uterus for a uterine incision in Congenital meningomyelocoel reair. Published in Clinics of Perinatology [4].

- Ex-utero intrapartum treatment (EXIT) surgeries for rare conditions.

Most cases are managed by fetoscopy, laser ablation of errant vessels, and fetoscopic shunt placements. A trans-abdominal approach utilising the modified Seldinger technique makes it a minimally invasive procedure.

CDH repair in intrauterine life is radically different and may not require surgery. The simple application of a tracheal occluder, which may be a fetoscopic external clip or an intratracheal sponge or balloon occluder, helps the developing lung bud to grow normally in the trapped fluid. Therapeutic endoscopic surgery with a fetoscope, also known as 'Fetendo', has obvious advantages.

Intra-Uterine Fetal Surgery By Hysterotomy

Advanced intrauterine ultrasound allowed for an appropriate short hysterotomy, with the lesion accessible and facing the surgeon. Spina bifida and meningomyloceles, considered the most diffi-

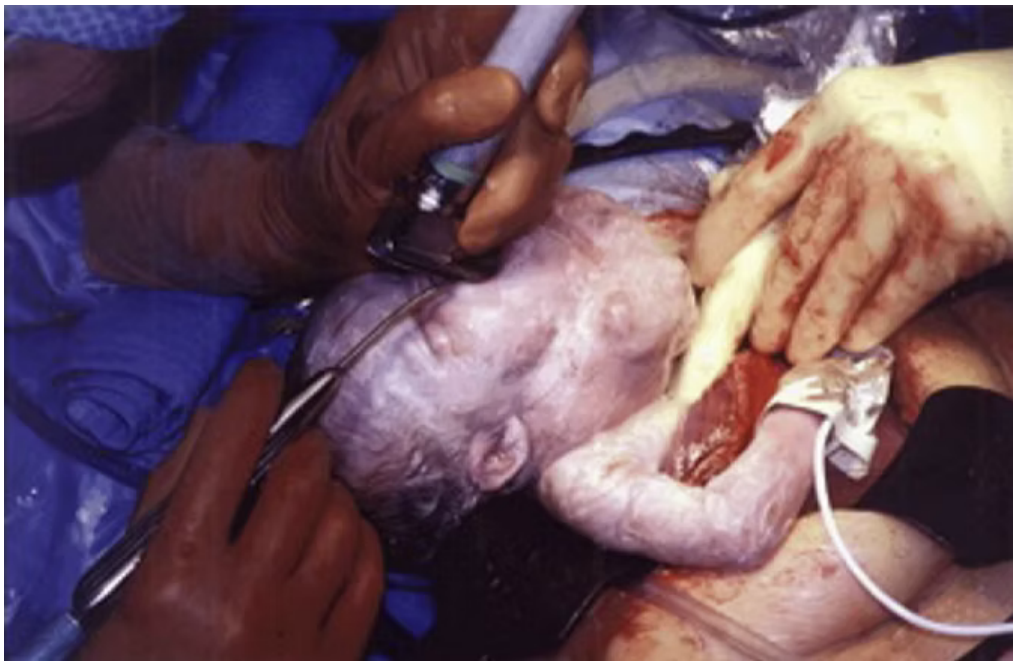

Figure 6: Baby extraction for an EXIT procedure. This photo appeared in 'The Pulse,' a health resource newsletter published by the St. Louis Hospital, Washington University.

cult correctable lesions, are managed thus. Bigger tumours like sacrococcygeal teratomas, some varieties of congenital cystic malformation of the lung, major lung lobar sequestration, mediastinal dermoid, and the congenital high airway obstruction syndrome (CHAOS) require a larger hysterotomy with partial delivery of the fetus, which gets an arterial supply via the intact umbilical cord and undisturbed placenta. Blood loss is minimized by using staplers and a specialised retractor. The partially delivered fetus is returned to the uterine cavity of the mother after the procedure. Continuous amnioinfusion is maintained during the procedure, and the fluid is replenished with isotonic Ringer's or Hartman's solution to make the baby float and cushion the cord just before tying the last uterine closure stitch.

The Exit Procedure

The ex-utero intrapartum (EXIT) surgery needs a word or two. This is a grey area, and the combined skill of an obstetric surgeon, a pediatric surgeon, or a neonatal cardiac surgeon is necessary. Typically, an EXIT procedure is performed when a secondary source of oxygen is required for the survival of the freshly delivered neonate. Lines for extra-corporeal membrane oxygenation may have to be instituted in rare cases. The umbilical cord is clamped, tied, and cut only after the oxygen supply is secured. Separating the membranes and placenta occurs next, and the obstetrician proceeds with uterine and abdominal closure. The neonatal surgeon, meanwhile, does whatever is necessary for the baby.

Pediatric and neonatal cardiac surgeons may prefer early surgical correction in certain congenital cyanotic cardiac defects to limit the ill effects of hypoxic blood and related circulatory changes.

Set-up

Intrauterine fetal surgery is a new subspeciality that was only recognised as unique from 1981 onwards. A large team comprising an obstetrician, a pediatric surgeon, their associates, two anesthesiology teams, nursing personnel, machine operators, and class IV operation theatre assistants and cleaners is the minimum requirement.

A collaborative and coordinated role among the operators is essential for success. The mortality and fetal outcomes vary and are still high (around 6-12%). Direct counselling, confidence in the team, and comprehensive consent are all important. Intrauterine fetal surgery is rare and evolving. Few centres can offer the full gamut. An international Fetal Medicine Foundation (FMF)

Figure 7: A usual set-up of an intra-uterine fetal surgery or an EXIT procedure. Image Credit: [5].

was established by Nicolaides in 1995, and the watchdog bodies publish online yearly medical and surgical procedural guidelines.

Conclusion

Ultrasound localisation, planning, intuition, and innovation are the hallmarks of fetal surgery. Mortality is still high and varies (6-12%). The speciality is practised only in a few centres that can boast of appropriately qualified personnel and appliances. The procedures are costly and only practised in desperate situations. Reporting has been sporadic so far, and though fetal medicine, amniocentesis with amniotic fluid sampling, and chorionic villi biopsy are common, it is heartening to find a few Indian centres joining the bandwagon and offering surgical correction as well. The All India Institute of Medical Sciences (AIIMS), Delhi, Lilavati Hospitals, Bombay, and the Amrita Institute, Kochi are the three centres leading today. Though details are still awaited, the future looks exciting.

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