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Review Article

Endoscopic Techniques in Fetal Surgery

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Fetal endoscopic surgery (FETENDO) involves many techniques that allow surgical procedures to be performed inside the uterus without an hysterotomy. The impetus for developing these minimal access techniques for fetal surgery is the unusual occurrence with an open hysterotomy of preterm labor, premature rupture of membranes, and maternal complications resulting from tocolytic therapy. The unique requirements of this approach necessitated a modification of existing endoscopic techniques, the development of novel fetoscopic instruments, and the inclusion of a wide variety of specialists. Technical expertise in the field and a natural evolution of techniques have given rise to innovative repairs previously not envisioned. Severe congenital diaphragmatic hernia, diseases of monochorionic twins, and obstructive uropathy have already been successfully treated using fetoscopic surgical techniques. Fetoscopic correction of many other non-life threatening anomalies continues to evolve. The future of fetoscopic surgical intervention depends on the continual evolution of novel approaches to disease, the elucidation of the pathophysiology and treatment of other fetal disorders, and a better understanding of treatment of complications of such intervention.

Key Words: Fetus, fetal surgery, fetoscopy, minimal access surgery, endoscopy

INTRODUCTION

The development of fetal surgery has led to promising therapeutic options for a number of congenital disorders including, but not limited to, congenital diaphragmatic hernia, fetal obstructive uropathy, and diseases of monochorionic twins (Table 1). This has been the product of multiple factors: better understanding of the pathophysiology of fetal disorders, technical advances in instrumentation, and improvements in prenatal diagnostic acumen, intraoperative anesthesia, and tocolysis. Despite the increasing application of fetal surgery in the treatment of congenital anomalies, surgical manipulation of the uterus and fetus is associated with significant maternal morbidity including preterm labor, chorioamniotic membrane separation, and rupture of membranes.

In an attempt to reduce these postoperative complications, minimal access fetoscopic techniques have been developed. Based on two hypotheses: (1) operating on the fetus when it is in its normal physiological environment will improve postoperative outcomes and (2) exposing the uterus to a smaller incision will reduce maternal complications-fetsocopy is believed to reduce morbidity in fetal interventions and allow the application of procedures not previously envisioned. While a decade ago, virtually no procedures were performed fetoscopically, fetoscopic or fetoscopically-assisted techniques are now employed in 75% of fetal surgical cases performed at the University of California, San Francisco (UCSF). The broader application of fetoscopy to nonlethal prenatal conditions depends on an improvement in existing fetoscopic techniques, a reduction in maternal morbidity, and continued research examining innovative approaches to treat congenital anomalies.

FETOSCOPY VERSUS OPEN HYSTEROTOMY

The impetus for developing minimal access techniques for fetal surgery was the unusually

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Table 1. Malformations that May Benefit from Fetoscopic Treatment before Birth

Life threatening Defects	Fetoscopic Treatment
CDH	Tracheal clipping Balloon tracheal occlusion
Urinary tract obstruction	Fetoscopic vesicostomy Laser ablation urethral valves Laser SP vesicostomy
TTTS	Fetoscopic laser ablation Amnioreduction
TRAP/Discordant anomalies	Umbilical cord ligation Umbilical cord division RFA
CCAM	RFA Laser ablation
SCT	RFA Fetoscopic vascular occlusion
Amniotic bands	Fetoscopic division
Pleural effusion	Thoracoamniotic shunt
CHAOS	Fetoscopic tracheostomy
Complete heart block	Percutaneous pacemaker
Pulmonary-aortic obstruction	Fetoscopic valvuloplasty
Non-Lethal Defects	
Myelomeningocele	Fetoscopic coverage
Cleft lip/palate	Fetoscopic repair
Stem cell defects	Fetal stem cell transplant

CDH; Congenital diaphragmatic hernia, TTTS; Twin twin transfusion syndrome, TRAP; Twin reversed arterial perfusion, CCAM; Congenital cystic adenomatoid malformation, SCT; Sacrococcygeal teratoma, CHAOS; Congenital high airway obstruction syndrome, SP; Suprapubic, RFA; Radio-frequency ablation.

high occurrence of preterm labor (PTL), premature rupture of membranes (PROM), and alterations in fetal homeostasis during an open hysterotomy.[1] In an attempt to reduce the incidence of these complications, a minimal access approach was developed that utilized endoscopic techniques in fetal surgery (FETENDO).[2] Numerous obstacles were faced in the development of these techniques requiring experimentation in animal models, innovation, and a coordinated effort by numerous investigators (Table 2).

By avoiding a maternal hysterotomy, fetoscopy is believed to keep the fetus within its physiologic environment, avoid the requirement for a large uterine incision, and reduce uterine trauma and associated PTL.[3] The evidence regarding the benefits of fetoscopic surgery to date has been inconclusive. A study by Nakayama et al. reported that in 27 pregnant rhesus monkeys, there was a significant increase in preterm labor and delivery in animals that underwent an hysterotomy when compared to those that underwent minimal uterine trauma (minimal trauma included electrode placement, amniocentesis, and maternal laparotomy). Moreover, a strong correlation between the degree of uterine manipulation and uterine contractile response was found.[4] A more recent study by van der Wildt et al. directly investigated the myometrial activity in pregnant rhesus monkeys following endoscopic access. Fetuses surviving greater than twenty-four hours postoperatively showed no evidence of uterine contractions.[5] In contrast to this study, Luks et al. studied 10 pregnant ewes and found that neither

Table 2. ObstaCles to be Overcome in Successful Minimal Access Fetal Surgery

Problem	Solution
Poor visualization in turbid amniotic fluid	Pump driven fluid exchanger replaces amniotic fluid with saline while operating
Tenting and separation of chorioamniotic membranes with trocar insertion	Specially designed diamond tipped needle that precisely cuts membranes on entry
Fetal hypothermia with fluid exchange	Exchanged fluid kept at physiologic temperature
Lack of fetal monitoring	Ultrasonographic monitoring
Lack of fetal analgesia	Intramuscular fetal needle puncture with an analgesic
Anterior placental location	Elevation of uterus for anterior placenta with fundic or posterior uterine entry
Mobile fetus	Fetal suture fixation techniques, ultrasound directed trocar entry with knowledge of fetal position
Uterine wall compliance	Effective tocolysis
Cramped intraamniotic operating space	Modify operative techniques and accessories to design single port procedures, ultrasound guidance of operating instruments
Uterine bleeding during trocar insertion	Radially expanding access devices outwardly compress uterine vessels as well as secure the trocar in place

hysterotomy nor endoscopy changed the rate, pattern, or amplitude of the myometrial contractions. However, the authors found that an hysterotomy resulted in a significant reduction in uterine blood flow and uteroplacental oxygen delivery (decreased to 73% of the initial value).[6]

Despite conflicting information in the literature, the experience in human subjects has indicated that there are, in fact, benefits of fetoscopic techniques. The maintenance of fetal homeostasis, decreased use of tocolytics, decreased maternal complications due to tocolytics, and decreased maternal stay are all improvements noted in fetoscopic procedures compared to open procedures.[7]

THE OPERATING ROOM

For fetal cases, the involved personnel consist of a well-orchestrated, multidisciplinary team of professionals, including perinatologists, neonatologists, radiologists, sonologists, pediatric surgeons, resident/fellow assistants, and anesthesiologists, as well as trained nurses, scrub and audiovisual technicians, and a supportive operative administration who are critical in addressing equipment issues. Experience suggests that, for all the personnel involved, there is a steep learning curve associated with FETENDO. Therefore, early supervision is essential as are training courses designed to introduce and provide instruction for the specialized instruments used.

The operating room set-up is the product of years of work and is an essential part of performing fetoscopy successfully. The mother is placed in a modified lithotomy position with her knees low enough to allow one of the surgeons to work between the abducted legs while the assistants are positioned on either side along with the sonologist and perinatologist (Fig. 1). Her right side is slightly elevated with a bump under the hip to prevent vena caval obstruction from the gravid uterus. The monitors (one for the fetoscopic image, and one for the ultrasound image) are side-by-side at the head of the table so that they face the operating team. This set-up is important as the large number of personnel, instruments, and accessories can lead to excessive clutter. This, in turn, can result in problems with

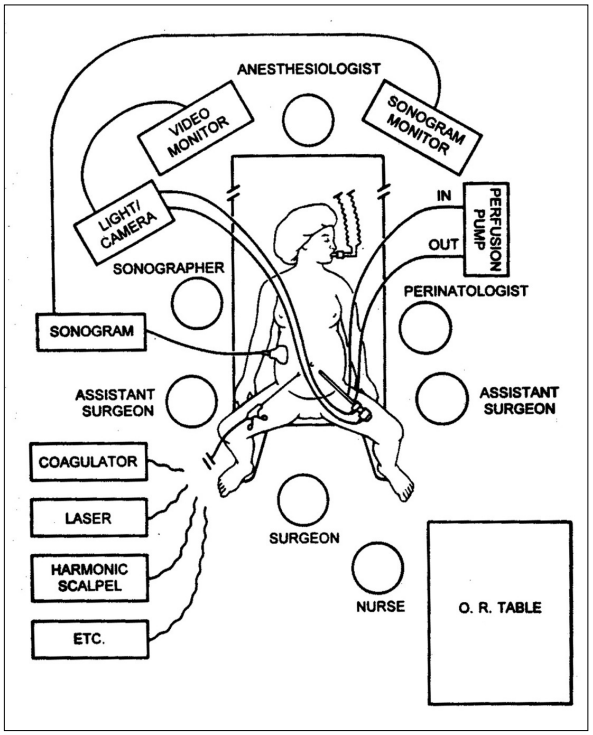

Fig. 1. The operating room setup for fetoscopic surgery. Note the two monitors at the head of the table: one for the fetoscopic picture and the other for the real-time ultrasound image.

the provision of space, access to equipment, and visualization.

ANESTHESIA AND TOCOLYTIC THERAPY

Adequate maternal and fetal anesthesia are critical components of fetoscopic surgery. Work in the 1980s established an effective tocolytic and anesthetic regimen while working with monkeys.[8] These experiments found that perioperative blocking of prostaglandin synthesis, intraoperative relaxation of the uterus with fluothane (an halogenated vapor), and, when needed, post-operative inhibition with β-sympathomimetics were effective in improving fetal survival. Today, an halogenated vapor agent is coupled with regional anesthesia via an epidural catheter. It is delivered in 100% oxygen with muscle relaxants to provide unconsciousness, amnesia, and analgesia for the mother, as well as for fetal and maternal immobility and uterine relaxation for the surgeon. Preoperatively, an indomethacin suppository is given. Intraoperatively, intravenous magnesium sulfate and nitroglycerin are administered as needed to achieve further uterine relaxation. The fetus is relaxed with intramuscular Pancuronium® and Fentanyl® as studies have shown that the fetus is responsive to surgical intervention with an elevation in corticosteroids and acute phase reactants.[9,10] Antibiotics include maternal administration of Cefazolin and amniotic fluid irrigation with Vancomycin.

INTRAOPERATIVE SONOGRAPHY AND MONITORING

One general limiting problem for fetal surgery is the lack of intravenous access to the fetus in the perioperative and postoperative period. In the absence of this system, other noninvasive means of monitoring have been studied. Transcutaneous pulse oximetry appears to be the most promising, as desaturation is an indicator of acute fetal distress.[11] While commonly used in open fetal procedures, this modality has only had experimental success in fetoscopic procedures.[12] As a result, alternative means of monitoring have been used. Ultrasound has provided a simple means of obtaining information regarding the fetus' well being. Periodic sonography serves as a monitoring device during the operation by determining the fetal heart rate, contractility, and maternal amniotic fluid volume. The operating room set-up is ideal for this as it allows easy viewing of two real-time images of the womb: the endoscopic image and the sonographic image (described earlier).

In addition to monitoring, the sonogram guides trocar insertion sites by mapping the position of the placenta and fetus and directing the trocar to the site of operation within the womb. Other functions that are aided by ultrasound include finding the location of intertwin membranes and arteriovenous connections (for twin surgery) and guiding instruments to the trachea (for congenital diaphragmatic hernia), umbilical cord (radio-frequency ablation or harmonic scalpel cord division for acardiac/acephalic or discordant twins),[13] or tumor (radio-frequency ablation device to ablate tumors).[14]

WORKING MEDIUM

Establishing a working environment within the uterus is critical to the success of FETENDO. This environment must be created without altering the maternal or fetal homeostasis while at the same time providing a visible operative field. Unlike postnatal abdominal and thoracic endoscopy that utilize a gas medium to create a visual field, a fluid medium appears to be ideal for the fetus. Studies investigating the use of carbon dioxide in fetoscopy have found that carbon dioxide results in severe fetal hypercapnia and acidosis.[15-17] In addition to the physiological perturbations a gas media can cause in fetoscopy, a gas media would also make the use of ultrasonography more difficult.[18] Studies have also shown that a liquid medium may allow for a wider range of safe intrauterine working pressures than a gas medium, allowing for the preservation of umbilical blood flow and fetal arterial oxygen saturation.[19] Experiments investigating the maternal uptake of this intrauterine fluid in animals have shown no significant fluid shift to the maternal compartment.[20]

Regardless of what specific fluid medium is chosen, one major problem in fetoscopy has been operating in very turbid amniotic fluid often worsened by procedural bleeding. For these reasons, a device was designed that would constantly exchange isothermic fluid around the endoscope, maintaining a physiologic amniotic and fetal temperature (Fig. 2). Fluid exchange, using isotonic Ringer's lactate, averages 100 to 200 ml/minute. In addition to providing good visualization and normothermia, the perfusate under pressure can often assist in difficult cases by preventing the collapse of the oropharynx (see CDH below) and dispelling bleeding.

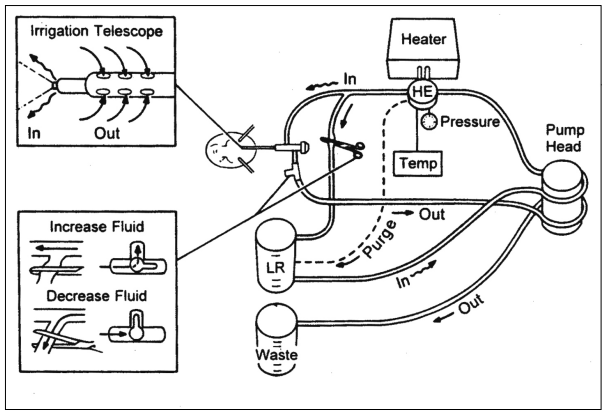

Fig. 2. The high-flow irrigating system consists of an extracorporeal pump and a heat exchanger that continuously circulates warmed lactated Ringer's solution via a sheath through which the fetoscope is placed (inset).

EQUIPMENT

Endoscopes

Instrumentation in endoscopic fetal surgery has rapidly developed from its inception with large multiport 10 mm trocars. Currently, interventions may be performed with fetoscopes as small as one millimeter. Seldom is more than one port required, as the complex equipment now in use has the capability to visualize, perfuse, and instrument simultaneously. Endoscopes have a variety of lengths and angles from which to view with offset eyepieces that allow instruments to be passed more easily. Commonly, multipurpose endoscopes are 18 cm in length, 1.2 to 3.5 mm in size, and 0 to 30 degrees in angulation. These allow access to all areas of the amniotic cavity with optimal visualization. The small caliber of the fetoscopes often allows them to be inserted percutaneously traversing the abdomen and uterus. Depending on the location of the placenta and fetus, a minilaparotomy may be necessary to gain access to safe parts of the uterus. Flexible curved fiberoscopes passed via flexible cannulas can accommodate the anterior placentas.[21] Despite the small size of these instruments, they have maintained good resolution. Concern over fetal retinal injury due to bright light exposure has been excluded.[22]

Trocars

Recently, a change has been made from balloon-based trocars to a radially expanding access system (InnerDyne, Inc. Salt Lake City, Utah, USA). The amniotic cavity is entered using a diamond cut needle within the sheath of the device, rather than the veress needle. This minimizes membrane tenting and separation. The sheath is expanded to accommodate 2, 3, or 5 mm instruments and is

secured with a medium sized suture. The expandable design helps control uterine bleeding by outward pressure (Fig. 3).

Accessories

Accessories are very important adjuncts in fetal procedures allowing for the operative intervention to be performed. Along with ultrasound and the perfusion pump, which have been discussed, other accessories include a radio-frequency ablation device (RFA), tracheal clips and balloon occluders, thoracoamniotic and vesicoamniotic shunts, an harmonic scalpel, and a neodynium-yttrium aluminum garnet (Nd-YAG) laser.

FETAL POSITIONING

Operating on the fetus in its fluid environment is one of the most difficult aspects of fetoscopic surgery. Manipulating the fetus with trocars while maintaining endoscopic visualization of the operative field is a challenging task for any endoscopic procedure, further complicated by the ease at which the fetus can move in the amniotic cavity. Fixation techniques have been devised for certain procedures to maintain the fetus in an accessible position. The most experience with this has been garnered with tracheal clipping for congenital diaphragmatic hernia. Here, a transuterine suture is placed under sonographic guidance through the center of the fetal chin and returned out of the uterus. The suture is subsequently fixed to the operating table so as to maintain upward tension on the chin. In addition, a sonographically placed transuterine T-bar is used to stabilize the trachea and help guide the surgeon to the anatomic midline, thus preventing potential injury to adjacent nerves and blood vessels.[23]

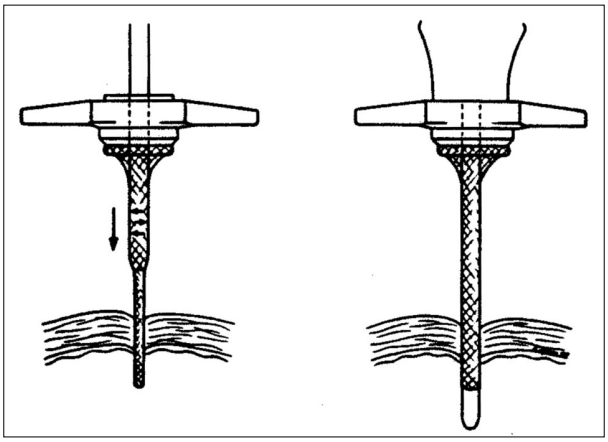

Fig. 3. A 5-mm cannula/obturator is used for radial expansion of the sheath. The mechanism stabilizes the access system, controls myometrial bleeding by virtue of its outward expansion, and keeps the membranes from separating and tearing.

Access to the fetus is determined partly by the position of the fetus and the placenta. In the case of a posterior placenta, access to the uterus is achieved percutaneously and in cases of an anterior placenta, a low abdominal incision is required to expose the uterus and gain access to the fetus. Once the placenta has been mapped, careful planning can optimize the fetal position and ease of intervention by means of version, trocar placement, and adjustments in the amniotic fluid volume. The placental position has not to date prevented access to the fetus.

DISORDERS AMENABLE TO FETOSCOPIC PROCEDURES

The timing of fetal surgery depends on the malformation being treated and the pathophysiologic course encompassing that disorder. Commonly, accurate early diagnosis and the fragility of the fetal tissue are limiting factors at less than 18 weeks' gestation. After 30 weeks' gestation, manipulations on the uterus are associated with a high risk of PROM and PTL. It is then more reasonable to deliver the fetus and treat the malformation with postnatal care.

CONGENITAL DIAPHRAGMATIC HERNIA (CDH)

CDH is a simple anatomical defect, where abdominal viscera herniate into the thorax through a posterolateral opening in the diaphragm. Despite advances in neonatal critical care, CDH still has an overall mortality of 50% resulting primarily from pulmonary hypertension and hypoplasia, as well as appreciable long-term morbidity.[24] The clinical spectrum of CDH ranges

from minimally affected infants who do well with neonatal care to severely affected infants who die despite all interventions. Identification of this latter group has been made possible through the sonographic identification of liver herniation into the hemithorax and measurement of the lung-to- head ratios.[25-27] Attempts to improve the outcome of this group have led to decades of experimentation and technical innovation into prenatal methods of treating CDH. The initial experience with open fetal surgical diaphragmatic repair was fraught with high mortality and prompted alternative approaches designed to reverse lung hypoplasia.[28] After extensive animal research,[3,29] fetuses undergoing fetoscopic tracheal occlusion were found to have increased lung growth and improved outcomes as compared to those that underwent an open tracheal occlusion procedure or had received standard postnatal care.[7]

The techniques to occlude the fetal trachea have evolved rapidly. The first and older approach involves the application of externally placed titanium clips. Three to four 5 mm trocars are used to dissect the trachea, aided by fetal and tracheal fixation (Fig. 4). Following the identification of the recurrent laryngeal nerves, two clips are applied to completely occlude the trachea.[30] The second and more recent approach involves the placement of an intratracheal balloon.[31] The fetoscope is used to enter the amniotic cavity using a single 5 mm radially expanding trocar. Once inside, fetal landmarks and ultrasound are used to guide the surgeon to the fetal mouth. With gentle pressure and hydrodissection the mouth is opened, the hypopharynx exposed, and the trachea cannulated with the fetoscope. Following adequate visualization of the carina, a detachable occlusive balloon is threaded through the endoscope and deployed 2 cm proximal to the carina (Fig. 5).

The clip procedure has been abandoned, as the tracheal balloon procedure requires fewer ports, causes less tracheal damage, and can be performed more quickly.[31] Removal of the clips or balloon is performed at birth while the fetus is on placental support during the EXIT (Ex Utero Intrapartum Treatment) procedure.[32] Outcomes are pending but retrospective results have shown

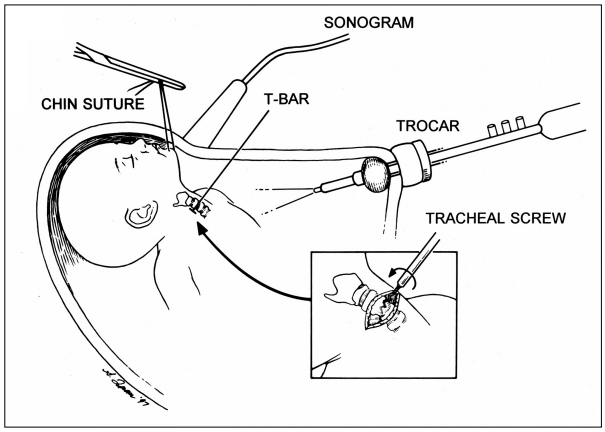

Fig. 4. Method for occluding the trachea with clips. Under sonographic guidance, the fetus' neck is exposed and the head stabilized by placing a temporary transuterine chin suture. Using ultrasound, a T-fastener and suture are placed in the fetal trachea to aid in locating the midline fetal neck. After anterior tracheal dissection, a tracheal "screw" can be placed in the anterior tracheal wall to facilitate safe posterolateral dissection, if necessary.

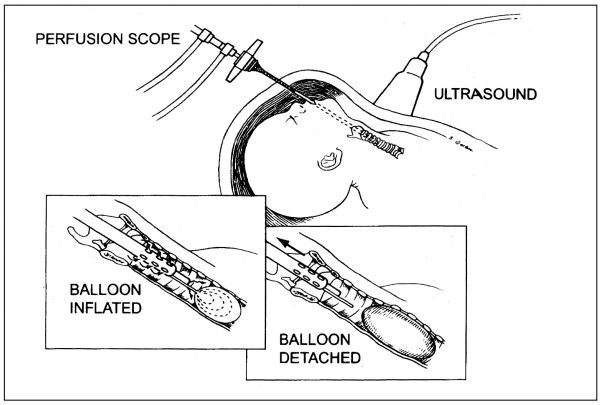

Fig. 5. Method for occluding the trachea with a balloon. Using sonographic and endoscopic guidance, the fetal trachea is cannulated with the telescope. After inflation, the balloon is detached 2 cm proximally to the carina (inset).

a dramatic reduction in mortality with fetoscopic tracheal occlusion compared to standard postnatal care.[7] Today, minimal access prenatal intervention is being compared to standard postnatal care for severe cases of CDH in a National Institutes of Health funded randomized control trial at UCSF.

FETAL OBSTRUCTIVE UROPATHY

Fetal urinary tract abnormalities are the most

frequently diagnosed congenital anomalies.[33] Prenatal intervention is possible for select fetuses with urinary tract obstructions whose renal and pulmonary development is threatened but potentially salvageable. Fetuses are selected for intervention based on three variables: fetal karyotype, detailed sonographic evaluation, and serial urine evaluations to determine the extent of underlying renal damage.[34,35] The aim of prenatal intervention is to bypass or directly treat the obstruction, restoring the amniotic fluid to normal levels. Initial intervention with open vesicoamniotic shunting[36] has largely been supplanted by percutaneously placed shunts. These aim to decompress the obstructed bladder. Although placement of such a shunt appears simple and straightforward, the procedure can be technically difficult and can carry an appreciable complication rate due largely to displacement and obstruction.[37,38]

Minimal access techniques hold a great deal of promise not only because catheters can be placed under direct vision thereby ensuring proper positioning, but also because alternative direct approaches to treatment can be employed. Quintero et al. reported their experience with *in utero* percutaneous cystoscopy for managing fetal lower obstructive uropathy.[39] Endoscopic visualization of the underlying pathology, most commonly the posterior urethral valves, was possible in most cases. In several cases, following identification, the posterior urethral valves were ablated.[40] Although innovative, survival to the neonatal period with these approaches has been uncommon. Moreover, the long-term benefit of vesicoamniotic shunting has not been proven.[41]

DISEASES OF MONOCHORIONIC TWINS

In monochorionic, monozygotic twin pregnancies, a single placenta with two separate umbilical cords supplies oxygen and important nutrients to two fetuses. In 10 to 15% of these pregnancies, the presence of abnormal vascular connections (arterioarterial, venovenous, and arteriovenous) leads to disproportionate or unbalanced flow between the two fetuses; one fetus is required to pump a larger share of the blood while the second receives inadequate flow.[42] This can lead to twin-twin transfusion syndrome (TTTS) and in extreme cases of unbalanced circulation, twin reversed arterial perfusion (TRAP). Because of shared circulation between the co-twins, the *in utero* demise of a non-viable twin can result in neurological damage to the viable fetus, commonly consisting of multicystic leucoencephalomalacia, with a comparable risk of co-twin intrauterine death.[43-46] If intervention can be done at an early enough gestational age, the onset of the debilitating effects associated with these disorders can be prevented.

TWIN TWIN TRANSFUSION SYNDROME (TTTS)

TTTS, the most common of these abnormalities, appearing in 10 to 20% of monochorionic pregnancies,[47] is characterized by unbalanced flow between co-twins resulting in a hydropic recipient twin with cardiac failure and polyhydramnios and a donor pump twin with intrauterine growth retardation and oligohydramnios. Expectant management results in 80-100% mortality.[48]

There are differing views regarding the best treatment strategy to employ in TTTS but options include serial amniocentesis, laser photocoagulation of abnormal vascular connections, or selective termination of the unhealthy twin in severe cases (Fig. 6). Each of these interventions can reverse and even improve the underlying disease process and lead to the survival of one and even both fetuses. Patients have been stratified into risk groups based on presence of fluid in the donor bladder, abnormal Doppler studies, and the presence of hydrops and/or fetal death.[49] Treatment for lower grade disease usually begins with one or more amniocenteses of the recipient sac.[50] For non-responders or those fetuses who present with or develop more severe disease, laser photocoagulation of the abnormal communicating vessels (principally arteriovenous) is performed using a Nd-YAG laser passed via a fiber through an operating endoscope.[51,52] Some investigators elect to coagulate all vessels that cross the intertwin septum,[53] whereas others selectively divide the communicating vessels along the shared meridian intertwin membrane, terming it the "sonographic evaluation, laser-endoscopic coagulation

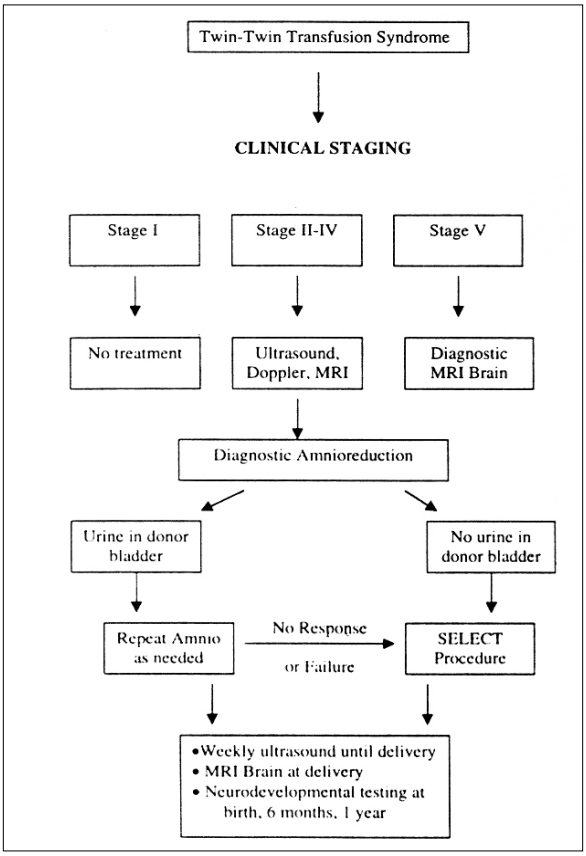

Fig. 6. Algorithm for the management of twin-twin transfusion syndrome. Sonographically evaluated laser endoscopic coagulation for twins (SELECT) is shown. Stages: I, urine in donor bladder; II, no urine in donor bladder; III, abnormal Doppler flow; IV, Hydrops in recipient; V, death of one twin.

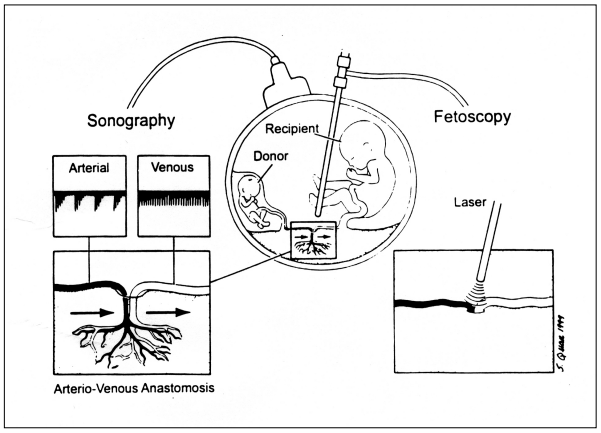

Fig. 7. Schematic representation of the sonographic evaluation, laser-endoscopic coagulation for the twins (SELECT) procedure. A sonographic evaluation demonstrates arterial and venous spectral Doppler flow patterns on either side of the arteriovenous anastomosis. The flow is directed away from the donor twin toward the recipient twin. At fetoscopy, the unpaired feeding artery and draining vein are identified and selectively laser coagulated.

for twins" (SELECT) procedure (Fig. 7).[54-56] This approach may be a more effective alternative than serial amniocentesis as there are more pregnancies with greater than one survivor, fewer intrauterine deaths, and a lower incidence of brain abnormalities.[53] Survival statistics with laser treatment show the survival of at least one twin in 82%.[51] When the disease has progressed so far that one donor twin's life is threatened (hydrops, poor cardiac contractility), the recipient twin can be selectively terminated using a variety of techniques (described later).

TWIN REVERSED ARTERIAL PERFUSION (TRAP)

The incidence of TRAP in monochorionic twin pregnancies is approximately 1 in 35,000 live births.[57] The TRAP physiology develops when there is reversed umbilical blood flow from an advantaged twin to its co-twin, a condition most often present when the co-twin has an acardiac acephalic morphology. The advantaged twin is structurally normal but at risk for developing *in utero* cardiac failure if no intervention occurs. Without intervention, it has been reported that if the ratio of the acardiac twin to the pump twin weight is > 50%, the probability of pump twin death is 64%. If it is greater than 75%, the mortality increases to 90%.[58]

The therapeutic goal of completely interrupting the vascular communication between the two twins, although simple in concept, is difficult to accomplish. Initial attempts to remove the abnormal fetus from the uterus, termed sectio parva, were unsuccessful.[59] As a result, alternative approaches were explored. The first strategy employed the concept of umbilical cord embolization, most often employing potassium chloride. While this technique was minimally invasive, successful intervention was rare and transplacental passage of the chemical to the co-twin was possible.[46] Newer approaches offering better results have attempted to ligate and/or divide the umbilical cord. A variety of methods have been

employed to accomplish this including the use of an extracorporeal knot,[60] laser obliteration,[61] bipolar coagulation,[62] and ultrasonic transection.[13] The most commonly used methods at our institution employ selective ultrasound guided RFA termination at the umbilical cord insertion (Fig. 8)[63] and the CUT (cord ultrasonic transection) procedure using a 5 mm harmonic scalpel to both coagulate the umbilical vessels and divide the cord completely.[13] The outcomes with cord ligation are much better than cord embolization with failure of embolization in 8 out of 17 published cases and failure of cord ligation in only 2 out of 23 published cases.[64] Considering the perinatal mortality for the normal twin is at least 50% without intervention, fetoscopic therapy has resulted in an increase in survival, which justifies its prophylactic use for treating TRAP.[61]

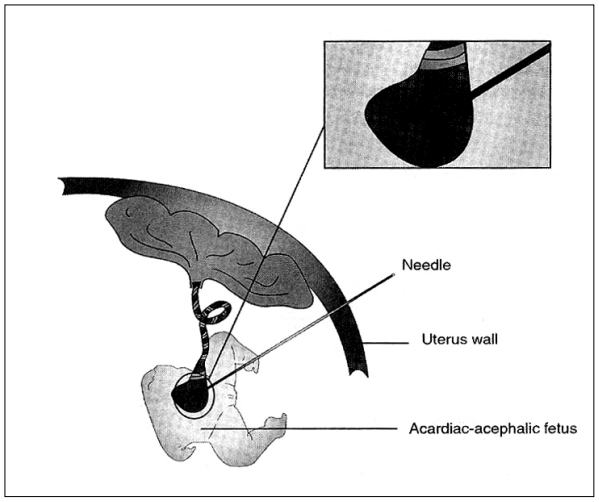

Fig. 8. Technique for radio-frequency ablation (RFA) of an acardiac-acephalic fetus. The RFA needle is introduced into the fetus near the insertion of the umbilical cord (inset).

Monochorionic twins discordant for an anomaly

Monochorionic twins are more likely to suffer from congenital malformations and heart defects.[65] In these cases, one twin's abnormality predicts intrauterine demise. Due to shared placental circulation, the other normal twin is threatened if its co-twin should die. Crombleholme et al. reported a case in which fetoscopic treatment was used to treat such discordant twins.[44] Following ligation of the umbilical cord of the unhealthy twin, the healthy twin went to term and was born neurologically intact with normal subsequent development. In the rare case of a monochorionic, monoamniotic twin gestation discordant for an anomaly, the umbilical cord must be divided after it is ligated to reduce the risk of cord entanglement.[46]

SACROCOCCYGEAL TERATOMA (SCT)

SCT is the most common type of tumor in the fetus and neonate, occurring in 1 out of 40,000 live births.[66] Although most fetuses diagnosed with SCT have an uneventful intrauterine course, a small subset (< 20%) with large tumors develop hydrops from the high-output failure due to the shunting effect of large arteriovenous fistulae at the tumor base, a finding that rapidly leads to fetal demise.[67] In addition, some mothers develop a pre-eclamptic-like "mirror syndrome" that mimics the condition of the fetus.[68] *In utero* therapy may benefit both the fetus and the mother. Options include open exploration and removal of the tumor,[69] minimal access techniques to stop the blood flow to the tumor via an ultrasound guided RFA probe,[14] or fetoscopically guided laser ablation.[70] As such intervention is rare, determining the approach that provides the best outcome has been difficult.[71]

AMNIOTIC BAND SYNDROME

Amniotic bands are a frequent cause of fetal deformities of the limb, craniofacial region, and trunk.[18,72-74] The complications associated with these constrictive bands range from syndactyly to limb amputation.[75] Severe forms of this syndrome, including cases of umbilical cord constriction,[76] are good candidates for early release if this can be accomplished fetoscopically. Less severe forms of this syndrome do not warrant fetoscopic intervention at this time given the potential for fetal and maternal morbidity. Recently, Quintero treated two such cases, dividing the band using scissors via a single port with ultrasound guidance.[77] This restored adequate blood flow distal to the obstruc-

tion, and only mild or minimal limb dysfunction was present at birth.

PLEURAL EFFUSIONS

Percutaneous thoracoamniotic shunting may be effective in relieving lung compression and any coexisting mediastinal shift caused by pleural effusions from thoracic masses or a chylothorax. This may prevent pulmonary hypoplasia, reverse fetal hydrops, and resolve polyhydramnios, thereby reducing the risk of fetal death or preterm delivery.[78] Pooled data from uncontrolled studies shows that shunting is associated with higher survival rates (68%) than thoracocentesis (41%) or conservative management (52%).[79]

FUTURE DIRECTIONS

While intervention for certain diseases such as myelomeningocele, bronchopulmonary sequestration, and congenital cystic adenomatoid malformation has not proven possible to perform successfully fetoscopically, efforts continue to expand the scope of FETENDO to treat other fetal diseases (Table 1).[80,81]

CONGENITAL HIGH AIRWAY OBSTRUCTION SYNDROME (CHAOS)

CHAOS is usually caused by laryngeal atresia and rarely by isolated tracheal stenosis. The constellation of findings include large echogenic lungs, flattened or inverted diaphragms, dilated airways distal to the obstruction, and fetal ascites and/or hydrops.[82] If hydrops does not develop *in utero*, these babies may be treated using the EXIT procedure, which maintains the baby on placental support while an airway is established by orotracheal intubation or tracheostomy.[32] However, for selected fetuses who develop hydrops from lung overdistension caused by increased fluid accumulation, *in utero* fetoscopic tracheostomy could potentially relieve the obstruction and cause resolution of the hydrops.

CLEFT LIP REPAIR

Cleft lip and palate defects are fairly common congenital malformations, occurring in about 1 out of every 700 live births. Conventional treatment of a cleft lip occurs postnatally, a time when the repair is complicated by scar formation. Several animal studies have shown that such repairs can be achieved fetoscopically with minimal or no scarring.[83,84] As prenatal diagnosis can identify fetuses with such palatal malformations as early as 13 weeks' gestation,[84] fetoscopic intervention in humans may be possible in the near future.

CHRONIC FETAL VASCULAR ACCESS

Chronic fetal vascular access improves the ability to monitor the postoperative fetal surgery patient. Successful endoscopic catheterization of placental vessels has been accomplished in a monkey model.[85] Short term cannulation of chorionic plate vessels has been achieved in humans.[86] This may have important implications for treating intrauterine growth retardation, *in utero* hematopoietic stem cell transplantation, and other prenatal cellular interventional therapies.

HEART BLOCKS AND DEFECTS

Animal experimentation may herald a new frontier in fetal surgery with the development of techniques to access the fetal heart and treat complex heart defects. Fetal heart block was initially treated with surgically placed pacemakers but recent work has found corticosteroid injections to be a more effective form of intervention.[87] Defects such as aortic and pulmonic stenosis have been amenable to treatment with fetoscopic techniques in sheep models.[88]

COMPLICATIONS OF ENDOSCOPIC FETAL SURGERY

Despite the initial belief that FETENDO could reduce and even eliminate complications of fetal surgery, the reality of morbidity and mortality

continue to exist.

Bleeding

Hemorrhage has not been a major problem in endoscopic fetal surgery. Careful attention to detail in avoiding the placenta on entering the uterus and the use of radially expanding trocars has dramatically reduced this complication. Minor uterine wall or placental bleeding stops on its own.

Preterm labor (PTL)

PTL has been referred to as the "Achilles heel" of fetal intervention.[89] Although numerous tocolytics are administered and fetoscopic techniques are employed, little progress has been made in preventing PTL which occurs, in some degree, to all mothers undergoing fetal surgery. Current theories regarding the etiology of PTL include rapid changes in uterine volume, infection, hormonal changes, fetomaternal stress, and membrane rupture.[90,91] Animal models used to investigate this problem have been problematic since smaller animals particularly sheep, the most often studied animal, are less prone to PTL.[92] Treatment options include a variety of tocolytics (indomethacin, nitroglycerin, terbutaline, magnesium, (β-sympathomimetics, and nifedipine), none of which provide optimal relief.

Chorioamniotic membrane separation

Separation of the chorioamniotic membranes occurs in as many as 40% of fetal cases.[93] Complete disruption, termed 'shredding', is an early indicator of membrane rupture, and can lead to umbilical cord compromise by amniotic band formation, and is a powerful stimulus for PTL.[94] Ineffective membrane closure techniques may contribute to this problem. While the ideal closure would seal the membranes, prevent amniotic fluid extravasation, and reinforce the myometrium, this closure is not yet available.

Premature Rupture of Membranes (PROM)

Perhaps the greatest problem with fetal surgery is PROM, the most common complication associated with fetoscopy.[95] The cause of the problem is unknown and hypotheses regarding its etiology have led to efforts to minimize uterine trauma during fetal intervention. Despite numerous closure techniques, disrupting the uterine membranes leads to both a functional weakness and an as yet unknown biochemical change that leads to PROM in 6-10% of cases in single port procedures[52] and up to 40-60% in multiple port procedures with longer operating times.[7,96] The significance of this problem is real with perinatal loss rates in fetal surgery as high as 50% in some series,[97] in large part due to sequelae of PROM (PTL, oligohydramnios, premature delivery, chorioamnionitis, and even fetal demise).[53]

The etiology of rupture may be apparent in some cases with ultrasound having demonstrated membrane separation or shredding. In other cases, outside of operative intervention, no explanation is apparent. While innovative techniques to close the membranes using collagen plugs provide some promise,[98,99] observation of the membranes at delivery has often found that the rupture has occurred at a site distant from trocar insertion. Once this diagnosis is made, mothers rarely can carry their fetuses for longer than a few weeks although innovative techniques to seal the ruptured membranes have been attempted.[100,101]

CONCLUSION

Although open fetal surgery has been successful in treating specific fetal diseases, PTL and altered fetal homeostasis resulting from hysterotomy and fetal exposure has limited its broad applications. These limitations have stimulated the development of FETENDO. The experimental and clinical experience suggests a diminution in the severity of postoperative PTL and less impaired fetal homeostasis. Improved outcomes in the areas of life threatening anomalies such as CDH, fetal obstructive uropathy, and diseases of monochorionic twins have been possible through the evolution of techniques that minimize uterine trauma, maintain fetal homeostasis, and allow for an expeditious surgical procedure. Other nonlethal disorders such as heart defects, CHAOS,

and cleft lip may potentially be treated fetoscopically but the fetal and maternal morbidity must be lower to justify *in utero* intervention. In addition, fetal vascular access may allow for better postoperative management of the fetus and provide a means for treating cellular and growth deficiencies. The future of fetoscopic surgical intervention will necessitate progress in clarifying the natural history of fetal disorders, improving diagnostic and imaging techniques, instrument refinements, creation of novel disease specific fetal surgical procedures, and a better understanding of PTL and PROM.

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