Fetal Surgical Intervention for Congenital Anomalies

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Grand Rounds
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Objectives

- Brief history of fetal intervention
- What is fetal surgical intervention?
  - Who
  - Where
  - How
  - Why
- What anomalies are amenable to fetal surgery?
- What is my role as the obstetrician?
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History

• 1870s/1880s:
  • Zuntz and Preyer observed intact fetal guinea pigs suspended in warm saline
    • Fetus must be surrounded by warm salt solution
    • Once separated and allowed to breathe, cannot return to mother and survive

• 1920s:
  • First successful in utero manipulation
  • First successful delivery after in utero manipulation

• 1930s-1940s: experimental fetal observation
  • purse-string sutures to minimize LOF

• 1950s: disruption
  • Removal of rabbit testes affects sexual development
  • Interrupting puppies’ mesenteric blood supply caused intestinal atresia
History

- 1960s-1970s: simulation of anomalies
  - Coarctation of aorta (puppies)
  - Congenital diaphragmatic hernia (lamb)
  - Congenital hydronephrosis (rabbit, lamb)
  - Congenital heart disease (lamb)
  - Difficult to study in primates d/t uterine contractility and preterm labor
  - Pathophysiology and consequences of abnormal development able to be observed and predicted
  - Barriers to human studies: imaging and fetal monitoring

- Concomitant Non-Surgical Fetal Interventions
  - Rh-related hydrops successfully treated with in utero transfusion in 1960s
  - Neonatal RDS successfully prevented with ANCS in 1972
History

- 1970s:
  - Ultrasound – non-radioactive (no harmful effects to mother/fetus!)
    - Visualization of normal/abnormal fetal anatomy
    - Live-moving pictures
    - Guided procedures – amniocentesis, needle aspiration
  - Awareness of normal/abnormal development and physiology
    - Counseling, prognostication, management plans
    - Field of Fetal Medicine was established
At this juncture,

- Neonates born with uncorrectable undetected anomaly
- Fetuses detected with anomalies before birth
  → fetuses might require intervention prior to birth

Poor/guarded/lethal prognosis

- Termination
- Expectant management – high likelihood IUFD
- Early delivery – esp if threat to fetus/mother
- Intervention in utero? – risk to mother, outcome for fetus unknown

1980s: University of California at San Francisco

- Identification of few anomalies with simple anatomic defect preventing normal development
  - Congenital hydronephrosis, diaphragmatic hernia, obstructive hydrocephalus
- Normal development in utero could be restored in animal model
- Lamb model helpful in diagnosis/treatment
  - Uterus not prone to premature contractility
  - Surgery on over 500 fetal Rhesus monkeys at UC-Davis
History

- 1982: (UCSF) fetoscopic placement of double-ended pigtail shunt for obstructive uropathy 2/2 posterior urethral valves

- 1982: (UCSF) open hysterotomy/vesicostomy for obstructive uropathy

- 1982: (Denver) catheter shunt for hydrocephalus

- Collaboration among providers/investigators around the world to share info, discuss treatment and techniques, form ethical guidelines, and standards of care
  - International Fetal Medicine and Surgery Society (IFMSS)
  - North American Fetal Therapy Network (NAFTNet)

- Since then, >500 fetal interventions w/o maternal mortality

- Recent developments w/intervention for NON life-threatening conditions
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Multidisciplinary Team

- Pediatric Surgeons
  - Fetal Surgery
  - Urology
  - Neurosurgery
  - Otolaryngology
  - Plastic Surgery
- Obstetricians
  - Maternal-Fetal Medicine
  - Reproductive Genetics
- Anesthesiologists
- Fetal Radiologists
- Sonographers
- MRI Technicians
- Geneticists
  - Genetic Counselors
- Neonatologists
  - Perinatal APRNs
- Nurse Coordinators
- Lactation Support
- Psychosocial Services
Fetal Treatment Centers

• Academic medical centers
  • Often within research study protocols
  • Vary in interventions provided

• NAFTNet Members

• Others outside of NAFTNet
  • Children’s Mercy Hospital, Kansas City, MO
  • Maternal Fetal Care Health Center, HCA Midwest Health, Overland Park, KS
NAFTNet Fetal Treatment Centers

- University of Michigan Health System, Ann Arbor, MI
- University of Maryland, Baltimore, MD
- Johns Hopkins Center for Fetal Therapy, Baltimore, MD
- Brigham and Women’s Hospital, Boston, MA
- Advanced Fetal Care Center, Children’s Hospital, Boston, MA
- University of North Carolina, Chapel Hill, NC
- Advocate Children’s Hospital–Center for Fetal Care, Chicago, IL
- Cincinnati Fetal Center, Cincinnati, OH
- Wexner Medical Center (Ohio State), Columbus, OH
- Southwestern Medical Center, Dallas TX
- Colorado Fetal Care Center, Denver, CO
- Wayne State University, Detroit MI
- Texas Children’s Fetal Center, Houston, TX
- UT Health Science Center at Houston and Children’s Memorial Hermann Hospital, Houston, TX
- Children’s Hospital of Wisconsin Fetal Concerns Center, Milwaukee WI
- Minneapolis-Midwest Fetal Care Center, Minneapolis, MN
- Montreal Fetal Treatment Program, Montreal, QC
- CHU Sainte-Justine Research Center, Montreal, QC
- Vanderbilt University Medical Center, Nashville, TN
- Yale Fetal Care Center, New Haven, CT
- Columbia University, New York, NY
- Weill-Cornell University/New York Hospital, New York, NY
- Children’s Hospital of Philadelphia (CHOP), Philadelphia, PA
- Magee-Women’s Hospital of UPMC, Pittsburgh, PA
- Fetal Treatment Program of New England, Providence, RI
- Mayo Clinic, Rochester, MN
- University of Rochester, Rochester, NY
- University of California, Davis, Sacramento, CA
- University of California, San Francisco (UCSF), San Francisco, CA
- Evergreen Hospital, Seattle, WA
- Lucile Packard Children’s Hospital, Stanford, CA
- The Fetal Care Center (WashU), St. Louis, MO
- St. Louis Fetal Care Institute (Cardinal Glennon), St. Louis, MO
- University of Toronto, Toronto, ON
- Mount Sinai Hospital, Toronto, ON
- Hospital for Sick Children, Toronto, ON
- University of British Columbia-BC Women’s, Vancouver, BC
Fetal Surgery Principles

- Candidates
  - Healthy maternal surgical candidate
    - No health benefit, but all the risk
    - No fetal intervention without maternal informed consent
  - Correctable fetal anomaly/malformation
    - Clear benefit to the fetus
    - Beneficence vs. autonomy/non-maleficence

- Risks/Morbidities
  - Preterm labor/birth
  - Hemorrhage (mother or fetus)
  - Death (mother or fetus)
  - Injury to surrounding structures (mother or fetus)
  - Anesthesia complications
  - PPROM
  - Chorioamniotic separation
  - Chorioamnionitis
  - Placental abruption
  - Future infertility
  - Uterine rupture (current and future)
  - Mandatory cesarean section
Approaches:
Ex Utero Intrapartum Treatment (EXIT) Procedure

• Purpose: controlled delivery to allow for fetal intervention and establishment of airway prior to cord clamping/cutting

• Indications: severe airway obstruction or likelihood of cardiopulmonary insufficiency at birth
  • Cervical masses, congenital lung malformations (CLM), congenital high airway obstruction (CHAOS), pulmonary agenesis, transition to ECMO

• Process
  • General anesthesia (fetal anesthesia, uterine relaxation)
    • Maintenance of placental circulation
    • Dorsal supine leftward tilt
  • Pfannenstiel incision, customized hysterotomy based on placenta
  • Partial delivery of fetus, placement of monitors
  • Fetal airway establishment +/- surgical intervention
  • Delivery
  • Transition to postnatal care, completion of cesarean section

• Safety
  • UCSF 1993-2003, 52 EXITs, 51 live births, 52% alive long term
  • CHOP 1996-2002, 31 EXITs, one fetal death
  • Increased risk of postop wound infection, no difference in hospital stay
The EXIT procedure

The baby's head and shoulders are extracted while the rest of the body is still in the womb and the umbilical blood circulation is intact. A breathing tube is inserted into the baby's windpipe.
EXIT Procedure
Approaches: Open Fetal Surgery

- **Purpose:** surgical intervention on fetus while maintaining placental perfusion, with the goal of continuing intrauterine gestation as long as possible postoperatively.

- **Indications:** neural tube defects (e.g., myelomeningocele), congenital cystic adenomatoid malformation (CCAM), congenital heart disease, pulmonary sequestration, sacrococcygeal teratoma.

- **Process (20-30 weeks):**
  - General anesthesia (fetal anesthesia, uterine relaxation/tocolysis—indomethacin, inhalation)
    - Maintenance of placental circulation
    - Dorsal supine leftward tilt
  - Pfannenstiel incision, stabilize uterus, minimal tension on vessels, classical hysterotomy, specialized stapler
    - Absorbable, hemostatic hysterotomy, fixes membranes to uterine wall
  - Minimal exposure of fetus, care to avoid compression/stretch of umbilical cord
  - Maintenance of amniotic fluid volume continual warm LR infusion +/- abx
  - Surgical intervention, closure
  - Epidural postop analgesia, tocolysis and close monitoring
  - Planned classical cesarean at 36 wga or sooner for maternal/fetal indications

- **Safety**
  - PTL most common complication, average delivery 34 wga, mean 10 weeks postop
  - Non-cardiogenic pulmonary edema in mother due to release of vasoactive agents from myometrial
Open Fetal Surgery
Open Fetal Surgery
Open Fetal Surgery
Approaches: Fetoscopic Surgery

- **Purpose:** minimally invasive surgical intervention on fetus to avoid maternal morbidity associated with a laparotomy, and possibly reduce risk of preterm labor. Similar goals to maintain placental perfusion and continue intrauterine gestation as long as possible postoperatively.

- **Indications:** twin-to-twin transfusion syndrome (TTTS), amniotic band syndrome, congenital diaphragmatic hernia (CDH), myelomeningocele

- **Process (>18 weeks):**
  - General anesthesia (fetal anesthesia, uterine relaxation/tocolysis—indomethacin, inhalation)
    - Maintenance of placental circulation
    - Dorsal supine leftward tilt
  - Ultrasound-guided placenta-avoiding approach, skin incision, transabdominal/transuterine trocar placement
  - 3mm flexible fetoscope with 1mm working channel or 5mm laparoscope
  - Amnio-exchange with warmed crystalloid for adequate visualization
  - Surgical intervention, closure
  - Epidural postop analgesia, tocolysis and close monitoring
  - Planned delivery at 36 wga or sooner for maternal/fetal indications

- **Safety**
  - Less maternal morbidity (length of stay, need for TF, ICU admission)
  - No difference in PPROM or PTL
Fetoscopic Surgery

When Perform?

18 - 20 weeks
Loss rate 2 - 5%

Fetoscopy
- IU surgery
- TTT syndrome
- Ichthyosis

Images A and B
Fetoscopic Surgery

- Fetoscope
- Amniotic sac of donor twin
- Amniotic sac of recipient twin
- Amniotic membrane of recipient twin
- Recipient twin
- Donor twin
- Amniotic membrane of donor twin
- Shared placenta
- Chorionic membrane
- Vein
- Artery
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Myelomeningocele (MMC)

- Spina bifida/open NTD with exposed spinal canal elements
  - Most commonly lumbar/cervical
  - Motor and somatosensory abnormalities corresponding to level of defect
  - Autonomic dysfunction w/ bowel/bladder
  - Arnold Chiari II hindbrain herniation, hydrocephalus, VP shunting

- Prognosis: usually liveborn, healthy, but 30% mortality before adulthood
  - Defect + associated trauma in utero contribute
  - Standard therapy is postnatal repair + rehab

- Fetal Surgery: open or fetoscopic closure
  - Minimize trauma in utero

- Management of Myelomeningocele Study (MOMS) Trial:
  - RCT at CHOP compared outcomes of in utero vs. postnatal repair
  - Outcomes: fetal/neonatal death or need for VP shunt <12 mos, composit of mental development and motor function at 30 mos
  - 68% in utero, 98% postnatal (shunts 48% and 82% respectively)
  - Improvement in cognitive development and motor function and secondary outcomes w/ in utero surgery
    - Risk of preterm delivery (38%) and uterine dehiscence (10%), fetal death (3%)
  - Study discontinued after 158 patients
Myelomeningocele (MMC)

- [https://youtu.be/bLnYzCcTEEA](https://youtu.be/bLnYzCcTEEA)
Congenital Pulmonary Airway Malformations (CPAM)

- Includes
  - Congenital Cystic Adenomatoid Malformation (CCAM)
    - Overgrowth of respiratory bronchioles and formation of cysts
    - Bronchopulmonary Sequestration (BPS)
    - Hybrid lesions

- Prognosis: mostly benign, usually get outpaced by growth of the lung in the third trimester
  - Majority survive to delivery and undergo postnatal therapy
  - With rapid growth can impede venous return or cause high-output heart failure via AV shunting
  - Hydropic findings (polyhydramnios, placentomegaly, edema, fluid accumulations) in 80% if CCAM volume ratio (CVR) >1.6

- Fetal Surgery: thoracoamniotic shunt, open fetal thoracotomy and resection
  - Betamethasone has been shown to shrink CCAM, resolve hydrops, and improve survival in some cases
Congenital Pulmonary Airway Malformations (CPAM)
Sacroccocygeal Teratoma

- Neoplasm
  - Similar to CCAM, can cause high-output heart failure, nonimmune hydrops, and IUFD via vascular shunting
  - Preterm labor, obstructed labor, delivery trauma, tumor rupture, hemorrhage

- Prognosis
  - Dependent on tumor volume to fetal weight ratio
  - TFR > 0.12 associated with 80% incidence of hydrops, 60% mortality

- Fetal Surgery: most common approach is open hysterotomy resection/debulking
  - Cystic lesions may be percutaneously drained
  - RFA/laser coagulation to decrease vascularity
  - EXIT
Congenital Diaphragmatic Hernia (CDH)

- Herniation of abdominal contents into the thorax compresses/impairs lung development, resulting in pulmonary hypoplasia/hypertension.

- Prognosis: 60-70% survival, but as low as 25% when diagnosed prenatally.
  - Liver herniation, lung-head ratio (LHR) < 1.2 associated with poor prognosis.

- Fetal Surgery
  - Initially open repair of defect – no better outcomes for survival or need of ECMO compared with postnatal repair.
  - When noted that fetuses with congenital high airway obstruction syndrome (CHAOS) developed lung hyperplasia, proposed fetal tracheal obstruction to promote buildup of parenchymal lung fluid.
  - Open hysterotomy with metallic clip, EXIT later (15% survival).
  - Fetoscopic balloon placement for tracheal occlusion, EXIT later (75% survival).
Congenital Diaphragmatic Hernia (CDH)

Liver
Trachea
Compressed lung
Compressed heart
Bowel

FIGURE 10-1 This schematic diagram shows the method of fetoscopic tracheal occlusion. A fetoscope is placed into the fetal mouth, the airway is identified, and a balloon is inserted into the trachea by using both fetoscopic and ultrasonographic visualization.
Twin-Twin Transfusion Syndrome (TTTS)

- Monochorionic (shared) placenta with A-V, V-V, A-A connections and unbalanced flow between two twins
  - Donor – low flow, oligohydramnios, high output heart failure, brain ischemia, small
  - Recipient – fluid overload, polyhydramnios, congestive heart failure, hydrops fetalis, large

- Prognosis: 80-90% mortality for both if untreated

- Fetal Surgery
  - High-volume amnioreduction historically (survival of at least one twin 60%)
  - Fetoscopic laser ablation of vascular connections
    - Offered to Stage II or greater
    - Selective A-V or nonselective
    - 76% single survivor, 36% dual survivors
Twin-Twin Transfusion Syndrome (TTTS)
Twin Reversed Arterial Perfusion (TRAP)

- One normal twin acts as a “pump” for acardiac, acephalic twin via A-A anastomoses
  - Normal twin much like donor twin in TTTS with R/O high output heart failure, hydrops fetalis, 50% mortality

- Fetal Surgery
  - Open hysterotomy/delivery
  - Fetoscopic ligation
  - Bipolar cautery/harmonic scalpel division
  - Thermal/laser coagulation
  - RFA of acardiac/acephalic cord insertion
Twin Reversed Arterial Perfusion (TRAP)
Low Urinary Tract Obstruction (LUTO)

- Bilateral hydronephrosis, keyhole shaped enlarged bladder, megaureters usually on sono
  - Ureteropelvic/ureterovesical junction obstruction
  - Obstructing ureterocele
  - Urethral atresia, posterior urethral valves
  - Consequent oligohydramnios, fatal pulmonary hypoplasia
    - 20-30% ESRD, 45% neurogenic bladder in surviving

- Fetal Surgery
  - Oligohydramnios is absolute indication
  - Vesicoamniotic shunting
  - Open fetal vesicostomy
  - Fetoscopic cystoscopy with ablation of obstruction
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Your Role as the Obstetrician

Largely supportive

- Most referrals to Fetal Care Centers via MFMns
- Unbiased aid in decision-making
  - Options, centers, research
- Counselor of risks/benefits
  - Fetal intervention has implications for your patient’s health
  - “safeguards against limits of voluntariness, ranging from undue influence to coercion”
- Emotional
  - Connection to support services
If you’re interested…

- Amazon Prime Video
  - Twice Born: Stories from the Special Delivery Unit
  - https://www.amazon.com/Twice-Born-Stories-Special-Delivery/dp/B00VHQA3IK

- University of Zurich
  - Video of myelomeningocele repair:
  - https://swissfetus.ch/open-fetal-surgery/spina-bifida/

- Colorado Fetal Care Center
  - 2017 Overview and Outcomes

- Twins and Multiple Births Association
  - Video of fetoscopy/TTTS laser ablation
  - https://www.youtube.com/watch?v=ZWfyLJj_D6Y
References


- NAFTNet

- Cincinnati Fetal Center

- Children’s Hospital of Philadelphia (CHOP)