15. MINIMALLY INVASIVE FETAL THERAPY

Stephen R. Carr, M.D.
Francois I. Luks, M.D.

HISTORICAL PERSPECTIVE

- **First reported fetal treatment 1967**
  - Liley: percutaneous fetal blood transfusion for rhesus disease.
  - Initially blind procedures – ultrasound guidance introduced later
- **Widespread application of ultrasound-guided techniques**
  - Diagnostic procedures: amniocentesis, chorionic villous sampling, skin biopsy (see chapter 5)
  - Therapeutic techniques: drainage of amniotic fluid (amnioreduction), pleural effusion, bladder obstruction
- **Development of endoscopic techniques**
  - Spin-off of laparoscopic surgery (early 1990’s)
  - Less invasive than open fetal surgery (comparable to needle techniques?)
  - Often combination of endoscopy, needle technique, ultrasound
  - Requires high level of expertise, tertiary center
  - Example: severe twin-to-twin transfusion syndrome (see chapter 14)

TYPES OF FETAL INTERVENTION

Non-invasive intervention
- **Transplacental therapy**
  - No direct violation of amniotic cavity
  - Administer medication to mother to affect fetus
  - Examples: Maternal digoxin to treat fetal supraventricular tachycardia or acardiac twin-associated hydrops of the normal twin
- **Minimally invasive intervention**
  - Requires entering the gravid uterus – needle, incision
  - More aggressive form of fetal treatment
  - Significant risks: infection (wound, chorioamnionitis), bleeding (uterus, fetus), tear/rupture of amniotic or chorionic membrane, premature labor, chronic amniotic leak (and oligohydramnios)
  - Significant risk of fetal death – depends on invasive nature and severity of disease
  - Needle techniques vs. endoscopic fetal surgery
  - Single vs. multiple ports

**INDICATIONS FOR MINIMALLY INVASIVE FETAL INTERVENTION**

Very few fetal anomalies meet above criteria (see rationale). Several are described in more detail elsewhere in the syllabus.

- **Aqueductal stenosis (isolated hydrocephalus)**
  - Isolated obstruction of CSF flow at level of aqueduct (4th ventricle)
  - Leads to isolated hydrocephalus
  - Originally treated with (percutaneous) ventriculoamniotic shunt
  - Complications: bleeding, dislodgement (fetus pulls catheter out)
  - Neurological outcome: paradoxically worse than untreated group (untreated hydrocephalus often leads to fetal demise; with shunt, fetus survives with neurological deficit)
  - Now abandoned

- **Bilateral urinary tract obstruction (see chapter 8)**
  - Rationale: bladder outlet obstruction (mostly males, posterior urethral valves) leads to 1) hydrenephrosis, renal damage, and 2) oligohydramnios, pulmonary hypoplasia, neonatal death from respiratory failure. Treatment aims at restoring urine flow
  - Treatment options:
    - vesicoamniotic shunt (double pigtail catheter): often dislodged
    - endoscopic cystostomy: reported, but rarely if ever performed today
    - fetal cystoscopy: although described (destruction of urethral valves by laser via cystoscope), not yet acceptably safe and effective
  - Difficulties: Only justified if kidney function preserved (i.e., urine production); in reality, difficult to predict renal function (urine electrolytes, β2-microglobulin, ultrasound criteria). Even if successful (i.e., amniotic fluid restored), chronic renal failure (and transplantation) often unavoidable
- **Congenital lung cyst and pleural effusions**
  - Uni- or bilateral pleural effusions:
    - If part of systemic manifestation (i.e., hydrops)
      - Treat underlying condition first
      - May represent poor prognosis
    - If isolated or idiopathic: risk of pulmonary compression and pulmonary hypoplasia
    - Placement of pleuro-amniotic shunt (double-pigtail catheter) well described
    - Risks: dislodgement, rupture of membranes, injury to intrathoracic organs
  - Large congenital lung cysts/masses (see chapter 7): CCAM, sequestration, Bronchogenic cyst
  - Most lesions asymptomatic
  - May enlarge rapidly in second trimester
    - If very large: lung compression (pulmonary hypoplasia), mediastinal shift (hydrops)
    - Most lesions (80-85%) regress early in third trimester
    - Fetal intervention *only* if impending hydrops
      - If mostly cystic (single large cyst): percutaneous drainage
      - If mostly solid or microcystic: Open fetal surgery and resection (see chapter 16)
  - Experimental techniques: radiofrequency ablation

- **Other indications for fetal surgery**
  - Cardiac anomalies (see chapter on fetal cardiology) (see chapter 10):
    - In general, fetal heart surgery not possible (animal models exist)
    - Hypoplastic left heart syndrome (HLHS): may be caused by aortic valve stenosis in early gestation
    - Balloon valvuloplasty in utero “prevents” development of HLHS?
    - Early results mixed, but promising
  - Twin-to-twin transfusion syndrome (see chapter 14):
    - Most commonly performed fetal surgical procedure today (> 2,000 cases worldwide)
    - Aim: obliteration (laser) of communicating vessels between two twins, in monochorionic gestation (single placenta)
    - Eurofoetus randomized controlled study (150 patients): proven survival advantage over other forms of treatment (amnioreduction)
- Congenital diaphragmatic hernia (see chapters 7 and 16):
  - Experimental evidence that in utero tracheal occlusion causes accelerated lung growth. Clinical application of this principle is feasible, but experimental.
  - Fetal tracheoscopy/tracheal balloon: Elegant, minimally invasive technique, but results mixed at best. Results currently worse than with postnatal treatment (including ECMO).
  - European trial of in utero tracheal occlusion, followed by release of occlusion, is ongoing – with promising early results

**TECHNICAL ASPECTS OF FETAL INTERVENTION**

**Ultrasound-guided techniques**
- Single needle approach: amniocentesis, fetal bladder puncture, chorionic villous sampling, in utero blood transfusion
  - Local anesthesia
  - Complication rate (bleeding, chorioamnionitis, membrane tear, fetal trauma) relatively low
  - Post-procedure uterine contractions: usually short-lived, do not progress to labor
  - Uterus more irritable in third trimester
- Advanced procedures: shunts (vesicoamniotic, pleuroamniotic, ventriculoamniotic)
  - Complication rate higher – risk of premature labor
- “Surgical” techniques: sporadic reports (ultrasound-guided umbilical cord occlusion for acardiac twin)

**Minimally invasive (endoscopic) fetal surgery**
- Spin-off from laparoscopic surgery meets spin-off from open fetal surgery (see chapter 16)
- Specialized instruments, uterine access (atraumatic penetration of myometrium, membranes)
- Working medium: fluid (saline, Ringers) preferable to gas (CO₂)
- Percutaneous or via mini-laparotomy; epidural or general anesthesia
- Laboratory and clinical evidence that endoscopic surgery (“FetEndo”) is less traumatic than open fetal surgery: fewer postoperative contractions, no mandatory C-section
- Complications increase with increasing number and diameter of trocars/instruments