

16. INVASIVE FETAL THERAPY

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HISTORICAL PERSPECTIVE

- ***-First reported fetal treatment 1967***
 - Liley: percutaneous fetal blood transfusion for rhesus disease.
 - First open fetal surgery report (unsuccessful) 1967 (same indication)
- ***Open fetal surgery: (semi)-experimental techniques in only 1-2 centers***
 - Animal experiments (fetal lamb, nonhuman primate) in 1970's and 1980's; diaphragmatic hernia, urinary tract obstruction
 - First human case 1990 (bladder outlet obstruction)
 - Very few indications still acceptable (see below)

INDICATIONS FOR FETAL INTERVENTION

The indications for open fetal surgery are even scarcer than those for minimally invasive therapy (chapter 15). These interventions obviously require the highest form of specialization and multidisciplinary team approach, and most (if not all) are performed within the framework of research or experimental surgery, usually as part of an NIH trial.

The only exception, and a spin-off of open fetal surgery, is the EXIT procedure (see below). This approach to suspected upper airway obstruction at birth allows control of the airway of a fetus/newborn *before* the umbilical cord is clamped. Provided that the required multidisciplinary team is available, this form of treatment is now an accepted (and often the only feasible) mode of delivery for patients with anticipated upper airway obstruction.

- ***Bilateral urinary tract obstruction (see chapter 8)***
 - Indications for in utero urinary tract diversion are fewer than a decade ago. Open vesicostomy is technically feasible, but no better and more invasive than percutaneous techniques (see chapter 15)

- ***Congenital diaphragmatic hernia (see chapter 7)***
 - Pathophysiology: abdominal viscera herniate through posterolateral diaphragm defect (Bochdalek) → lung compression → impaired lung development, pulmonary hypoplasia → neonatal respiratory failure, death
 - Rationale: in utero reduction of intestines and closure of diaphragm : allows catch-up lung development.
 - Results in animal models promising; human application disappointing
 - Techniques (see chapter on pulmonary hypoplasia and diaphragmatic hernia):
 - Open fetal surgery/diaphragm repair: emulates postnatal treatment; too aggressive, poor results
 - Open fetal surgery/tracheal occlusion (metal clip): tracheal occlusion causes accelerated lung growth and development. Open fetal surgery too aggressive
 - Endoscopic tracheal clip placement: less invasive technique, but results unpredictable (too much, too little lung growth)
 - Fetal tracheoscopy/tracheal balloon: Elegant, minimally invasive technique, but results mixed at best. Results currently worse than with postnatal treatment (including ECMO) (see chapter 15)
- ***Large sacrococcygeal teratoma***
 - Teratoma: heterogeneous tumor composed of three primitive cell layers (endoderm, mesoderm, ectoderm)
 - If voluminous (esp. sacrococcygeal), may cause high output heart failure (hydrops)
 - Mother may develop placentomegaly and pre-eclampsia («mirror syndrome»)
 - In utero resection (open fetal surgery) potentially life-saving, but rarely successful
 - Significant morbidity: perineal necrosis described
 - If maternal complication (mirror syndrome) : fetal surgical resection vs. termination
- ***Myelomeningocele (spina bifida, or open neural tube defect)***
 - Not a life-threatening condition
 - Rationale: covering exposed neural tube may prevent damage by amniotic fluid
 - Elegant animal studies, but pathophysiology not fully understood
 - Results in human series:
 - No improvement in neuromotor function
 - No improvement of bladder/bowel control
 - Only possible benefit: reduction (not elimination) of shunt-dependent hydrocephalus
 - Highly controversial, despite large number of cases already performed (> 200 in U.S.)
 - Currently available only through randomized NIH study

- ***Congenital lung cyst***
 - Large congenital lung cysts/masses:
 - Congenital cystic adenomatoid malformation (CCAM)
 - Extralobar sequestration
 - Intralobar 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
 - Reported success in selected cases. Requires open fetal surgery and fetal thoracotomy
 - Experimental techniques: radiofrequency ablation

TECHNICAL ASPECTS OF INVASIVE FETAL INTERVENTION

- Most aggressive form of fetal intervention
- Decades of animal research (fetal lamb, rhesus monkey)
- Human applications since 1990's
 - General anesthesia; pregnancy-specific precautions (blood volume, uterine pressure on vena cava; halogenated inhalation anesthetics cause uterine relaxation)
 - Uterine trauma: major hemorrhage from hysterotomy, controlled with specialized clamps/staplers
 - Fragile fetus: dehydration, hypothermia when exteriorized
 - Postoperative uterine contractions/labor still major problem
- Clinical applications: bilateral urinary tract obstruction (no longer performed), diaphragmatic hernia (no longer performed), myelomeningocele/spina bifida, sacrococcygeal teratomas, large CCAM
- Significant rate of maternal complications: bleeding, infection, mandatory C-section
- Overall results poor – applicable only for very select indications

FETAL SURGERY SPIN-OFF: THE EXIT PROCEDURE

- EXIT: “EX-partum, Intra-uTerine” procedure (formerly – and unfortunately – named “Operation On Placental Support, or OOPS)
- If airway obstruction is anticipated at birth:
 - Planned C-section with placental/umbilical cord preservation
 - Obtain airway control
 - Intubation
 - Tracheostomy
 - Only then: clamp umbilical cord
- Indications: giant cervical teratoma, giant cystic hygroma, hemangioma
- Multidisciplinary team essential