Innovative Care Models in the Advancement of Maternal Fetal Interventional Offerings

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Introduction

At present, approximately 4 million babies are born in the United States.[1] Unfortunately, 120,000 face a major birth defect and 23,000 babies die within the first year.[2] Birth defects are the leading cause of death of babies in their first year of life. For the past 40 years, maternal fetal specialists have explored ways to intervene prior to birth to resolve defects identified in unborn fetuses. Advanced fetal imaging, prenatal sampling techniques, and genetic testing have aided in this effort. These technological advances have provided new insights into the physiology of fetuses, allowing for easier identification of correctable anomalies, and opening opportunities for medical teams to explore ways to intervene earlier when detecting life-threatening malformations.[3] Fetal intervention, however, is still in its infancy with only about 600 cases taking place each year. Early pioneers in the field on the verge of retirement and a new generation of talent is needed to only take their place, but also expand access to these life changing interventions. The burgeoning field faces tremendous headwinds; however, as these procedures are expensive, NIH research funding is limited, and the next generation of therapies will raise additional ethical concerns as genetics and cellular treatments are investigated. That said, maternal fetal intervention plays a key role in the field of pediatric medicine and must be appropriately supported as it continues to evolve.

Early History of Fetal Surgery

The first fetal surgery operation to take place in the United States occurred in 1981 at University of California San Francisco (UCSF). The surgical team partially removed the fetus from a pregnant woman's uterus, corrected a urinary obstruction, and surgically sealed the fetus back into the woman's womb. While the operation ultimately proved unsuccessful, it launched a novel approach of using surgical intervention to save the life of an unborn fetus facing certain death. During this time, care teams were quick to put in place strict criteria to ensure surgical interventions were worth the risk in saving the life of the fetus while protecting the mother.

Fetal surgeries attempting to improve the quality of life of a baby once born – not just saving a fetus from imminent death – did not occur until the mid-1990s, when a surgical team at Vanderbilt performed an operation on a fetus diagnosed with a severe case of spina bifida (myelomeningocele). While not life threatening, the fetus was identifying as having some of its bone and skin not fully enclosing the nerves of the spinal cord, resulting in an exposed hole or lesion. Closing this hole along the spinal cord would prevent additional spinal cord damage from occurring during fetal development and result in a higher quality of life. The operation, taking place in 1997, served as a key milestone moment for broadening the number of lives that could benefit from early fetal intervention. Findings from a federally sponsored Management of Myelomeningocele (MOM) study published in 2011 later confirmed this significant improvement in quality of life. In 2015, fetal surgery received additional promotion and interest through a documentary series, Twice Born, aired by PBS and following the lives of families facing fetal defects and considering early fetal intervention.

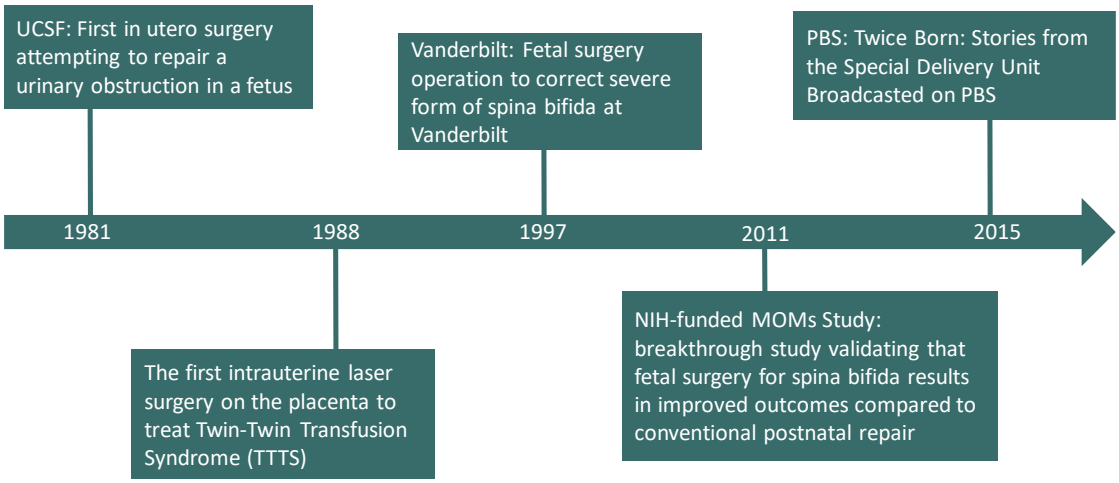

Table 1: Table of Major Firsts in Fetal Intervention

Conditions Treated

Over the last 25 years, over 20 conditions have been identified for fetal intervention. Selection criteria remains strict at many of the leading centers, where approximately 10 percent of those evaluated for a fetal intervention undergo an intervention. Below is a listing of many of the conditions currently treated recognizing that Congenital diaphragmatic hernia (CDH), Spina bifida (myelomeningocele), Congenital cystic adenomatoid malformation of the lung (CCAM), and Twin-twin transfusion syndrome (TTTS) make up the majority of patients treated.

Amniotic band syndrome	When an unborn baby (fetus) becomes entangled in fibrous string-like amniotic bands in the womb, restricting blood flow and affecting the baby's development
Bronchopulmonary sequestration of the lung	a piece of tissue that ultimately develops into lung tissue is not attached to the pulmonary arterial blood supply
Congenital cystic adenomatoid malformation of the lung (CCAM)	A benign lung lesion appearing as a cyst or lump in the chest that can vary in size
Congenital diaphragmatic hernia (CDH)	When the diaphragm muscle fails to close during prenatal development, and the contents from the abdomen (stomach, intestines and/or liver) migrate into the chest through this hole
Congenital high airway obstruction syndrome (CHAOS)	A blockage of the fetus's trachea or larynx
Lower urinary tract obstruction (LUTO)	a partial or complete obstruction of the urethra, the tube that connects the bladder to the amniotic fluid space around the fetus. This obstruction restricts or prevents the passage of urine.
Mediastinal teratoma	a solid growth (tumor) usually occurring within or near the thymus gland
Neck mass	A lump in the neck that can be benign (noncancerous), an infection, or a cancerous growth

Pulmonary agenesis	An incomplete development of the lungs, resulting in an abnormally low number or size of bronchopulmonary segments or alveoli
Sacrococcygeal teratoma	A tumor located at the base of the tailbone that can grow very large, but usually are not malignant
Spina bifida (myelomeningocele)	A defect of the backbone (spine) and spinal cord. Before birth, the baby's spine, the spinal cord and the spinal canal do not form or close normally
Twin reversed arterial perfusion sequence (TRAP sequence)	Occurs with twin pregnancies sharing a common placenta and when one twin is developmentally normal, and the other twin has a serious condition, either missing a heart (acardiac) or a head (acephalic) or both, that prevents it from surviving on its own.
Twin-twin transfusion syndrome (TTTS)	A rare, serious condition that can occur in pregnancies when identical twins share a placenta. Abnormal blood vessel connections form in the placenta and allow blood to flow unevenly between the babies.

Care Teams

Fetal surgery programs, predominantly located at flagship free standing children's hospital locations, consist of teams of perinatologists, neonatologists, pediatric anesthesiologists, and pediatric surgeons focused on providing superior care to the fetus while keeping the mom as stable and safe as possible. Select adult specialty resources, including adult anesthesiologists and obstetricians are on hand to support and care for the generally healthy mother.

Types of Surgical Intervention

Fetal surgery teams perform in utero surgery procedures ranging from open fetal surgery to minimally invasive procedures. Open fetal surgeries are typically performed to address myelomeningocele, SCT resection, and to remove CCAM. Minimally invasive fetoscopic surgery is generally used to address CDH, FRA and tumors. Ex utero intrapartum treatment is used for fetal cardiac intervention, stem cell transplantation, and Intrauterine blood transfusions.

Types of Interventions	**Description**
Open Fetal Surgery	A procedure where the mother is given anesthesia, then the surgeon makes an incision in the lower abdomen to access the uterus (as would be done during a Cesarean section). The uterus is opened with a special stapling device that prevents bleeding, the fetus is either partially or completely taken out of the womb, surgery is done, then the baby is returned to the uterus, and the incision is closed.
Fetoscopic Surgery	Minimally invasive procedures where surgeons use fiber optic telescopes and other specialized equipment to enter the uterus through small surgical openings, eliminating major incisions or the removal of the fetus from the womb.

Fetoscopic-guided radiofrequency ablation	The use of radiofrequency energy to destroy or remove unwanted tissue and cells such as tumors. A fetoscope is used to guide the radiofrequency ablation probe.
Ex Utero Intrapartum Treatment (EXIT)	Procedure to correct a fetal airway obstruction, where utero-placental blood flow is kept intact, and the fetus remains on a maternal "heart-lung machine" while the airway is secured

Current Locations

Fetal Surgery has grown from a handful of designated locations (e.g., UCSF, CHOP) in the early 1990s to over 30 locations (as defined by institutions participating in the North American Fetal Therapy Network (NAFTNet). While considerably larger in nature this still represents less than 15% of children's hospitals.

Organizing Models

Service offerings and affiliation models between children's hospitals and adult health systems have varied across the country and continue to evolve. CHOP and Boston Children's, both standalone entities in major metropolitan areas, already provide in-house specialized fetal surgery offerings to lower risk mothers with high risk fetuses through their own special delivery units, and work with surrounding adult health systems as appropriate.

The Fetal programs at both institutions are internationally recognized, however, the surgical candidates receiving care are limited. Stanford and UCSF's children's hospitals, which are part of larger adult health systems, provide a more full-service delivery offering accommodating low to high risk patients. Sanford's Johnson Center includes a delivery platform accommodating nearly 5,000 annual deliveries with access of adult and children's specialty services from Sanford Medical Center and Lucille Packard accordingly. Benioff Children's Hospital is fully integrated into the Betty Irene Moore Women's Hospital at Mission Bay accommodating approximately 3,000 deliveries annually. Both hospitals offer a fetal surgery program that are comprehensive in nature aided by the integration of the children's hospitals within the larger adult health system platform. Please see Table 1 below:

NICU/Delivery Unit Examples	1. LP Children's / Johnson Center	2. UCSF / Betty Irene Moore Women's Hospital	3. CHOP / Garbose Family Special Delivery Unit	4. Boston Children's
Structure	Part of Adult Health System	Part of Adult Health System	Standalone	Standalone
University Affiliation	Stanford	UC	Penn	Harvard
Hospitals, Beds, CMI	1 hospital, 300-beds, 1.98 CMI	2 hospitals, 190-beds, 1.29 CMI	1 hospital, 520-beds, 1.86 CMI	1 hospital, 415-beds, 1.91 CMI
NICU Beds, Discharges	60-beds; 816 DXs	51-beds, 674 DXs	95-beds; 685 DXs	24-beds; 650 DXs
NICU ALOS, CMI	20 ALOS, 4.17 CMI	20 ALOS, NA	35 ALOS, 4.72 CMI	21 ALOS, 4.63 CMI
OB/MFM Stats	52 OB beds, 4,700 DXs	9 LDR, 36 PP, 2,800 DXs	6 LDRP, 2 PP; 350 DXs	NA (though adjacent to B&W)
OB/MFM Service Description	Full service delivery unit accommodating low to high-risk women, Stanford MFM providers integrated into LPCH	Full service delivery unit at Women's Hospital directly integrated into Benioff Children's at Mission Bay; UCSF MFM and Neonatologists	Focused only on low risk moms with high risk infants / fetal anomalies. Penn MFM and CHOP neonatologists have dual privileges	NA: NICU patients originate from CHN: Beverly, South Shore, Winchester Hospitals and transfers from BIDMC, B&W, and BMC
Fetal Program	Comprehensive care to expectant moms, complex fetal patients, high-risk newborns; integrated research and teaching platform	Open fetal surgery, gene therapy, research, etc.	Internationally recognized in fetal surgery and care offerings; comprehensive care to expectant moms, research and teaching platform	The Advanced Fetal Care Center (AFCC) focuses on treat the fetus with congenital anomalies and has 20 specialty areas
Neonatal Focus	**Comprehensive**	**Comprehensive**	**Specialized**	**Specialized**
Adult System Loyalty	Stanford though tries to remain neutral	UCSF	Neutral with network of adult health systems	Neutral with network of adult health systems

Table 1: Comparison of Mother, Baby, Fetal, NICU Service Offerings at Select Children's Hospitals

Future Opportunities

There are approximately 600 fetal surgical candidates identified each year. This represents less than 3% of total babies born with birth defects. The most immediate opportunities to provide advanced intervention to unborn babies is through gene and cellular therapy. Advanced Fetal Surgery programs demonstrating an ability to perform fetal interventions also have an opportunity to continue to look for ways to provide extend access to qualified candidates. Additional training, research, and innovation is needed to continue to advance this emerging field of care.

Sources:

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