Medical Policy

Blue Cross Blue Shield Blue Care Network of Michigan

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*Current Policy Effective Date: 5/1/25
(See policy history boxes for previous effective dates)

Title: Prenatal (Fetal) Surgery for Diagnosed Malformations

Description/Background

Prenatal (fetal) surgery represents interventions that are performed to correct specific malformations or conditions, which without intervention may result in irreversible organ damage or are a threat to the life of the fetus. Historically, fetal surgery involved an invasive operation on the mother in order to open the uterus and access the fetus. A growing body of knowledge related to specific prenatal disease processes, and advances in prenatal testing, imaging, and specialized surgical tools enables treatment which improves the likelihood of survival. Surgical techniques now include minimally invasive fetoscopic surgery, which requires very small incisions and is guided by fetoscopy and sonography; and percutaneous fetal therapy, which involves placing a catheter under continuous ultrasound guidance. Most identified prenatal conditions do not require fetal intervention, and most anatomic malformations are best managed after birth. The exceptions are conditions for which early correction in utero is feasible and may be of significant benefit in the future development and survival of the fetus.

This policy pertains to fetal surgery performed for the following clinical conditions:

Fetal Urinary Tract Obstruction
Few cases of prenatally diagnosed urinary tract obstruction require prenatal intervention. However, distal obstruction can lead to megacystis (distention of the urinary bladder), and is often associated with serious disease. Fetuses with megacystis due to distal obstruction with concurrent oligohydramnios, who have adequate renal function reserve and no other lethal or chromosomal abnormalities, may be candidates for prenatal surgery. The most common surgical approach is decompression through the percutaneous placement of a shunt or stent. Vesicoamniotic shunting bypasses the obstructed urinary tract, permitting fetal urine to flow into the amniotic space. The goals of shunting are to protect the kidneys from increased pressure in the collecting system and to assure adequate amniotic fluid volume for lung development.

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Congenital Diaphragmatic Hernia
Congenital diaphragmatic hernia (CDH) results from abnormal development of the diaphragm, which permits abdominal viscera to enter the chest, frequently resulting in hypoplasia of the lungs. Congenital diaphragmatic hernia can vary widely in severity, depending on the size of the hernia and the timing of the herniation. For example, late herniation after 25 weeks' gestation or smaller defects that result in less herniation of abdominal contents may be adequately managed postnatally. In contrast, a significant amount of liver herniation into the chest prior to 29 weeks' gestation is associated with a poor prognosis, and these fetuses are considered candidates for fetal surgery. Temporary tracheal occlusion using a balloon is the intervention used for the most severe cases of isolated CDH. Occluding the trachea prevents the normal efflux of fetal lung fluid, which results in a build-up of secretions in the pulmonary tree and increases the size of the lungs, gradually pushing abdominal viscera out of the chest cavity and back into the abdominal cavity, promoting lung maturation. Due to improvements in neonatal management, only the most severe cases of CDH are considered candidates for prenatal surgery. Preliminary data from Europe suggests that overall survival of severe or extreme CDH is improved from the expected 20% to 47% with prenatal treatment.[1]

Congenital Pulmonary Airway Malformation
Congenital pulmonary airway malformations (CPAM) are a category that includes both congenital cystic adenomatoid malformations (CCAM) and bronchopulmonary sequestration (BPS); they are congenital anomalies of the lung that share the characteristic of a segment of lung being replaced by abnormally developing tissue. They may include a solitary lesion or many lesions. In CCAM, there is a connection to the pulmonary tree and they contain air; the tissue is served by blood vessels in the pulmonary circulation. In BPS, the mass of tissue is not connected to the airway and has blood flow from branches off the aorta as well as the pulmonary circulation. Lesions vary in size and appearance, but generally continue to grow during pregnancy. Only a small subset of patients with CPAM are candidates for in utero treatment. In severe cases, the lesions increase in size and may result in the development of hydrops fetalis (abnormal accumulation of fluid in two or more fetal compartments). This may also result in the development of maternal mirror syndrome (a severe form of pre-eclampsia) in the mother. Mortality increases with the development of hydrops fetalis. Surgical intervention differs depending on the type of CPAM but includes the placement of a thoraco-amniotic shunt to decompress the lesion in order to treat macrocystic lesions with a CPAM volume ratio (CVR) > 1.6. Rarely, a fetus is a candidate for ex utero intrapartum treatment (EXIT procedure) or prenatal resection, and this is based on a much larger CVR. Prenatal resection of CPAM is rarely performed since the discovery that steroids may prevent or reverse hydrops fetalis.

Sacrococcygeal Teratoma
Sacrococcygeal teratoma (SCT) is both a neoplasm with the power of autonomous growth and a malformation made up of multiple tissues foreign to the region of origin and lacking organ specificity. It is the most common tumor of the newborn and generally carries a good prognosis in infants born at term. Almost all prenatally diagnosed SCTs are resected in the neonatal period. However, in utero fetal mortality approaches 100% with large or vascular tumors, which may become larger than the fetus. In the most severe cases, when the fetus displays decreased cardiac function or impending hydrops, based on increased cardiac output, prenatal resection via an open fetal surgery may allow survival. An alternative approach, which is dependent on the specific type of teratoma, is in utero radiofrequency ablation of the feeder vessels.

Myelomeningocele
Myelomeningocele is a neural tube defect in which the spinal cord forms abnormally and is left open, exposing the meninges and neural tube to the intrauterine environment. Myelomeningocele is the most common cause of spina bifida, and based on the location, results in varying degrees of neurologic impairment to the legs and bowel and bladder function, brain malformation (ie, hindbrain herniation), cognitive impairment, and disorders of cerebrospinal fluid circulation (ie, hydrocephalus requiring placement of a ventriculoperitoneal shunt). Traditional treatment consists of surgical repair after term delivery, primarily to prevent infection and further neurologic dysfunction. The National Institute of Neurological Disorders and Stroke reports that children as young as 6 years who underwent prenatal surgical repair for myelomeningocele are more likely to walk independently, are less likely to require early hunting for ventriculomegaly and have fewer follow-up surgeries when compared to those who had corrective surgery at birth.[2]

Cardiac Malformations
In utero interventions are being investigated for several potentially lethal congenital heart disorders, including critical aortic stenosis with evolving hypoplastic left heart syndrome (HLHS), HLHS with intact atrial septum, and critical pulmonary stenosis or pulmonary atresia.[3] Critical pulmonary stenosis or atresia with intact ventricular septum is characterized by a very narrow pulmonary valve without a connection between the right and left ventricles. Critical aortic stenosis with impending HLHS is a very narrow aortic valve that develops early during gestation that may result in HLHS, a complex spectrum of cardiac anomalies characterized by hypoplasia of the left ventricle and aorta, with atretic, stenotic, or hypoplastic atrial and mitral valves. In utero aortic balloon valvuloplasty may relieve aortic stenosis with the goal of preserving left ventricular growth and halt the progression to HLHS. Hypoplastic left heart syndrome with intact atrial septum is a variant of HLHS that occurs in about 22% of all HLHS cases in which blood flow across the foramen ovale is restricted, leading to left atrial hypertension and damage to the pulmonary vasculature, parenchyma, and lymphatics. For HLHS with intact atrial septum, fetal balloon atrial septostomy is designed to reduce the left atrial restriction, resulting in lower mortality.

Note: Twin to Twin Transfusion Syndrome (TTTS) is addressed in medical policy, "In Utero Laser Therapy for the Treatment of Twin to Twin Transfusion Syndrome (TTTS)." The policy was retired in 2003.

Regulatory Status

N/A

Medical Policy Statement

Prenatal (fetal) surgery for specific congenital abnormalities or conditions is considered **established** when criteria are met.

Inclusionary and Exclusionary Guidelines

Inclusions:
The following prenatal surgical interventions are considered established, when there are no maternal contraindications to the surgery and criteria for the surgery are met:

Fetal Urinary Tract Obstruction
Vesicoamniotic shunting is considered established when ALL of the following are present:
- Megacystis due to urinary tract obstruction,
- Progressive oligohydramnios,
- Adequate renal function,
- No other lethal abnormalities or chromosomal defects.

Congenital Pulmonary Airway Malformation
Placement of a thoraco-amniotic shunt or in utero resection of malformed pulmonary tissue is considered established when ALL of the following are present:
- Congenital pulmonary airway malformation (CPAM) is identified,
- The malformations are progressing in size,
- CPAM volume ratio (CVR) >1.6,
- Gestational age of:
  - 32 weeks or less for shunting, OR
  - less than 27 weeks for in utero resection with plan for continuing pregnancy, OR
  - greater than 32 weeks for EXIT procedure.

Sacrococcygeal Teratoma
In utero resection of sacrococcygeal teratoma is considered established when ALL of the following are present:
- Cardiomegaly with compromised cardiac output,
- Gestational age of:
  - 28 weeks or less for resection, OR
  - 32 weeks or less for radiofrequency ablation.

Myelomeningocele
Repair of myelomeningocele is considered established when ALL of the following are present:
- Myelomeningocele is identified, with an upper boundary located between T1 and S1 with evidence of hindbrain herniation,
- Gestational age of 26 weeks or less,
- No other clinically significant fetal abnormalities.

Congenital Diaphragmatic Hernia
Tracheal occlusion in the treatment of congenital diaphragmatic hernia is considered established when ALL of the following are present:
- Gestational age is less than 30 weeks,
- Evidence of liver herniation,
- Lung-to-head ratio (LHR) observed-to-expected for gestational age is ≤ 15%.

Prenatal surgery should only be performed by facilities with the expertise, multidisciplinary teams, services and facilities to provide the intensive care required for these patients.

Exclusions:
- Prenatal (fetal) surgery that does not meet criteria listed above.
- All other applications of prenatal (fetal) surgery, including but not limited to, treatment of congenital heart defects.

Note: **Twin to Twin Transfusion Syndrome (TTTS)** is addressed in medical policy that was retired in 2003, "In Utero Laser Therapy for the Treatment of Twin to Twin Transfusion Syndrome (TTTS)."

CPT/HCPCS Level II Codes *(Note: The inclusion of a code in this list is not a guarantee of coverage. Please refer to the medical policy statement to determine the status of a given procedure.)*

Established codes:

59076	59897	S2400	S2401	S2402	S2403
S2404	S2405	S2409			

Other codes (investigational, not medically necessary, etc.):

N/A

Note: Individual policy criteria determine the coverage status of the CPT/HCPCS code(s) on this policy. Codes listed in this policy may have different coverage positions (such as established or experimental/investigational) in other medical policies.

Rationale

This policy was originally based on 1998 and 1999 BCBSA TEC Assessments[4,5] and updated periodically with literature searches of the MEDLINE database.

The evidence related to the use of fetal surgery is limited by the rarity of the conditions treated and the extremely specialized nature of the procedures, although randomized controlled trials (RCTs) have been conducted for several conditions. The literature related to fetal surgery has been summarized in several systematic reviews. In addition to the 1998 and 1999 TEC Assessments, the Agency for Healthcare Research and Quality (AHRQ) published a technology assessment on fetal surgery in April 2011.[6]

FETAL URINARY TRACT OBSTRUCTION

Systematic Reviews
The 2011 AHRQ assessment identified 26 publications representing 25 unduplicated reports on fetal interventions for obstructive uropathy. From the 3 prospective cohorts and 8 retrospective cohorts identified, 24 fetuses had placements of shunts, 11 had other treatments for posterior urethral valves, 14 had no fetal intervention, and 13 pregnancies were terminated due to poor prognosis. Overall, 53% to 66% of infants who had shunt placement survived short

term. However, more than half of otherwise normal infants who have only isolated bladder outlet tract obstruction and do not have multiple anomalies or syndromes, do not recover normal renal function in childhood, and the majority require dialysis and renal transplantation. In addition, a proportion of affected infants have clusters of syndromic features that are not readily diagnosed prenatally, increasing morbidity among survivors. For example, in a follow-up of 18 male children who had survived prenatal vesicoamniotic shunting (follow-up ranged from 1 to 14 years), parents and physicians reported the children to be neurodevelopmentally normal, with the majority having acceptable renal and bladder function and satisfactory self-reported quality of life.[7] There is a need to better identify appropriate surgical candidates and clarify health outcomes in children who do and do not receive fetal intervention to inform decision making. At the time of the AHRQ assessment, 1 publication described the design of a multicenter randomized trial of percutaneous shunting for lower urinary tract obstruction (PLUTO) that will assess whether intrauterine vesicoamniotic shunting improves pre- and perinatal health outcomes in comparison with conservative, noninterventional care.[8]

Randomized Controlled Trials
Since publication of the 2011 AHRQ assessment, Morris et al (2013) published the results of the PLUTO trial.[9] The study was an unblinded RCT that included 31 women with male singleton pregnancies, complicated by an isolated lower urinary tract obstruction, recruited from centers in the United Kingdom, Ireland, and the Netherlands. Inclusion criteria were an ultrasound diagnosis of lower urinary tract obstruction (diagnosed on the basis of the visualization of an enlarged bladder and dilated proximal urethra, bilateral or unilateral hydronephrosis, and cystic parenchymal renal disease) about whom the treating physician was uncertain as to the optimum management. Women pregnant with fetuses with other major structural or chromosomal abnormalities were excluded. Women were randomly allocated to either prenatal intervention, consisting of placement of a vesicoamniotic shunt, or control, consisting of usual care. The primary outcome measure was survival to 28 days after birth, with secondary outcomes of survival at 1 and 2 years, and renal function at 28 days, 1 year, and 2 years (measured by serum creatinine, renal ultrasound appearance, and evidence of renal impairment based on need for medical treatment, dialysis, or transplantation). The original planned sample size for the trial of 75 pregnancies in each study group was based on calculations from a meta-analysis reported by the study authors in 2010[10] and was designed to detect a relative risk of survival with vesicoamniotic shunting of 1.55 with 80% power and an alpha level of 0.05. The study was terminated early due to poor enrollment. Concurrent with the RCT, study authors enrolled eligible subjects who elected not to participate due to either patient or physician preference in an observational registry. There was a high degree of crossover between groups: 3 of 16 women randomized to receive vesicoamniotic shunting did not receive it, and 2 of 15 women randomized to the control group received a vesicoamniotic shunt.

Analyses were conducted on both an intention-to-treat and per-protocol basis. For the study's primary outcome of 28-day survival, there was no significant difference between the groups: of the 16 pregnancies randomly assigned to vesicoamniotic shunting, 8 neonates survived to 28 days, compared with 4 from the 15 pregnancies assigned to the control group (relative risk [RR], 1.88; 95% confidence interval [CI], 0.71 to 4.96; p=.27). Analysis based on treatment received showed a stronger association between shunting and survival (RR=3.2; 95% CI, 1.06 to 9.62; p=.03). The authors conducted a Bayesian analysis, combining data from their trial with elicited priors from experts, and found an 86% probability that vesicoamniotic shunting increased survival at 28 days. Overall, the authors concluded that "survival seemed higher in

the fetuses receiving vesicoamniotic shunting, but the size and direction of the effect remained uncertain." While strengths of this study included its randomized controlled design, and tracking of longer (2-year) outcomes, it was limited by its failure to reach enrollment targets and the significant crossover between treatment and control groups. As such, it is difficult to conclude that the lack of significant association between shunting and survival was not due to underpowering.

Morris et al (2013) reported on secondary outcomes from the PLUTO trial in a complete health technology assessment of the PLUTO trial and the associated registry for patients who elected not to participate in the randomized trial portion.[11] Secondary objectives of the trial included cost-effectiveness of vesicoamniotic shunting compared with conservative management; effect of vesicoamniotic shunting on short-term morbidity; survival and development of chronic renal failure at 1 year of age; identifying prognostic markers of outcome; determining clinicians' prior beliefs about the effectiveness of vesicoamniotic shunting; and assessing influences on women's decision making with respect to opting for termination of pregnancy, randomization and the acceptability of the intervention. For the secondary outcomes of the randomized portion of the trial, there were no statistically significant differences in mortality from 28 days to 1 year, although the point estimate for the RR was in the direction of benefit (RR=2.19; 95% CI, 0.69 to 6.94). Of those babies who survived to 1 year, 2 had no evidence of renal impairment (vesicoamniotic shunt arm), while 4 in the vesicoamniotic shunt arm and 2 in the conservative arm required medical management for renal impairment. One baby in the conservative arm had end stage renal failure at 1 year.

Forty-five women were entered into the concurrent registry; of those, 78% had conservative management. Women who were in the registry cohort differed from those randomized: registry patients who had conservative management were more likely to have a normal (>5th percentile) amniotic fluid volume at diagnosis than those who received vesicoamniotic shunting (p=.07) or randomized (p=.05). Women in the registry arm were more likely to be diagnosed at 24 or more weeks among these women than among those in the randomized group (p=.003).

Section Summary
For fetal vesicoamniotic shunting as a therapy for urinary tract obstruction, evidence from retrospective and prospective cohort studies summarized in the 2011 AHRQ technology assessment on fetal surgery suggests that vesicoamniotic shunting improves survival, at least in the short term. A subsequent small RCT found limited benefit from the procedure.

CONGENITAL DIAPHRAGMATIC HERNIA (CDH)

Tracheal Obstruction for Congenital Diaphragmatic Hernia
In 1999, the TEC Assessment[5] concluded that temporary tracheal obstruction met the TEC criteria as a treatment of congenital diaphragmatic hernia, based in part on a case series (Flake et al [2000]).[12] However, in Harrison et al (2003), the same authors who reported on the original case series, reported the results of a randomized trial of fetoscopic tracheal occlusion compared with standard postnatal care.[13] Enrollment was stopped at 24 women due to the unexpectedly high 90-day infant survival rate with standard care, and thus the safety monitoring board concluded that further recruitment would not result in a significant difference between the groups. In addition, the fetal surgery group had higher rates of prematurity and lower birth weights. The survival rate in the standard treatment group was 73%, considerably higher than the estimated survival rate of 37% based on historical controls. The survival of

infants with a lung-to-head ratio (LHR) greater than 1.0 was 100% in both groups. In contrast, Deprest et al (2006)[14], reported survival to be approximately 10% for children with isolated CDH who have left-sided lesions, liver herniation, and an LHR of less than 1.0 during mid-gestation. In this subgroup, temporary placement of a detachable balloon to occlude the trachea was reported to result in a survival rate of 55% (35 cases), compared with 8% survival in a group of contemporary controls treated by postnatal therapy. Based on the results of the Harrison et al randomized trial, the policy statement was revised to indicate that tracheal occlusion is considered established.

More recent evidence for tracheal occlusion for CDH includes a 2011 AHRQ technology assessment which identified 25 publications with 21 unduplicated populations from 10 U.S. sites, 9 European sites, 3 multinational sites, and 5 other countries, for a total of 335 cases. The single randomized controlled trial (RCT) was by Harrison et al (2003)[13] (previously described), with follow-up reported by Cortes et al (2005).[15] Growth failure occurred in 56% of controls and 86% of infants who had occlusion. No neurodevelopmental differences were observed between groups with follow-up at 1 or 2 years of age. This randomized study reinforces the importance of a concomitant control group, as the survival for CDH with postnatal repair also improved over time. Also noted were results of the Fetal Endoscopic Tracheal Occlusion (FETO) Task Group in Europe, which used a control group of 86 fetuses with left-sided CDH and liver herniation, managed expectantly and live born after 30 weeks of gestation. In this control group, the survival rate increased from 0% for LHR of 0.4 to 0.7 to approximately 15% survival for LHR of 0.8 to 0.9, 65% for LHR of 1.0 to 1.5, and 83% survival for LHR of 1.6 or more. This ongoing series currently has an 11% survival for LHR less than 1, which can be used as a reference value for Europe, but not for the United States.

Since publication of the AHRQ assessment, several studies have been published that address fetal endoscopic tracheal occlusion in CDH. Ruano et al (2011) published a small randomized controlled study to evaluate the feasibility of percutaneous fetal endoscopic tracheal occlusion with a 1-mm fetoscopy.[16] Thirty-five women were enrolled from 2006 to 2008, of whom 17 were intended for fetal intervention and 16 underwent successful fetal tracheal occlusion. Nine of 17 (52.9%) of fetal intervention infants and 1 of 18 (5.6%) of control group infants survived to 28 days, and the authors concluded the intervention was feasible.

In a subsequent study, Ruano et al (2012) reported a small randomized trial that compared percutaneous fetal endoscopic tracheal occlusion (FETO) with postnatal management in 41 patients whose fetuses had severe congenital diaphragmatic hernia, lung-to-head ratio (LHR) less than 1.0 and at least one third of the fetal liver herniated into the thoracic cavity).[17] All fetuses in the FETO group were delivered by *ex-utero* intrapartum therapy to remove the tracheal balloon; controls were delivered by Cesarean section at a maximum gestational age of 38 weeks. The primary outcome, survival to 6 months of age by intent-to-treat analysis, was 50% (10/20) in the fetal surgery group and 4.8% (1/21) in controls (relative risk [RR]=10.5). Mean delivery was about 2 weeks earlier in the fetal surgery group compared to controls (35.6 weeks vs 37.4). There was a trend for a higher frequency of premature delivery (<37 weeks, 50% FETO vs 28.6% controls) and extreme premature delivery (<32 weeks, 15% FETO and 0% controls) in the FETO group. For the 10 survivors in the FETO group, the mean age at hospital discharge was 34.7 days.

Rocha et al (2014) published a retrospective case-control study to compare left heart structure size in patients with CDH who underwent fetal endoscopic tracheal occlusion with those

managed conservatively.[18] Based on observational data that infants born with CDH have small left heart structures, possibly due to direct compression by herniated abdominal organs and/or abnormal orientation of the inferior vena cava and foramen ovale, the authors postulated that increased lung size associated with fetal endoscopic tracheal occlusion may lead to increased left heart structure size in patients with CDH. The study included 9 cases with left-sided CHD and an LHR of 1 or less who underwent fetal endoscopic tracheal occlusion who were compared with 25 similar controls who did not undergo fetal intervention.

Mortality did not differ significantly between groups (67% in the fetal intervention group vs 52% in the control group, p=*NS*). At birth, the intervention group had larger left ventricular (LV) end-diastolic volume (indexed to body surface area) (16.8 vs 12.76 mL/m2, p<.05), LV length *z* score (-2.05 vs -4, p<.01), LV: right ventricular (RV) length ratio (1.43 vs 1.04, p<.05), left pulmonary artery diameter *z* score (+1.71 vs -1.04, p<.05), and better growth of the aortic valve (-2.18 vs -3.3, p<.01). The authors note that fetal endoscopic tracheal occlusion may have benefits in postnatal cardiac output and pulmonary hypertension but that the potential benefits of fetal treatment for CDH are still currently under investigation in several trials and must be weighed against the risks of prematurity and risk to the mother.

Shan et al (2014) reported on a systematic review and meta-analysis of RCTs evaluating fetal endoscopic tracheal occlusion for CDH.[19] The authors included 3 studies identified as RCTs, including Harrison et al (2003), Ruano et al (2011), and Ruano et al (2012). In pooled analysis, patients treated with fetal endoscopic tracheal occlusion had higher survival rates than patients treated with standard therapy: 27/48 versus 12/52 (OR for survival with fetal treatment, 5.95; 95% CI, 2.11 to 16.78; p<.000). Patients treated with fetal endoscopic tracheal occlusion had an earlier average gestational age at delivery than patients treated with standard therapy (mean difference, -3.43 weeks; 95% CI, -6.82 to -0.04; p<.05). However, the pooled estimates are difficult to interpret; 1 study categorized by the authors as an RCT was a controlled but nonrandomized study (Ruano et al [2011])[16].

Section Summary

Although noncomparative studies prior to 2003 suggested benefit from fetal endoscopic tracheal occlusion for the treatment of CDH, the most direct evidence related to the effectiveness of this procedure comes from 2 RCTs from 2003 and 2012 which report conflicting findings. The 2012 RCT demonstrated promising findings of improved survival at 6 months postdelivery in patients treated with fetal endoscopic tracheal occlusion. However, given the inconclusive results in the randomized trial by Harrison et al additional study is needed to determine the survival benefit with greater certainty. Longer follow-up is also needed to evaluate morbidity (eg, neurologic and pulmonary outcomes) in survivors. Due to the extreme rarity and urgent nature of the need for fetal endoscopic tracheal occlusion for the treatment of CDH, historically, this procedure has been considered an established service.

CONGENITAL PULMONARY AIRWAY MALFORMATION (CONGENITAL CYSTIC ADENOMATOID MALFORMATION OR BRONCHOPULMONARY SEQUESTRATION)

The 2011 AHRQ assessment identified 17 publications describing 6 distinct cohorts and 4 case series from 7 academic centers in the United States, South America, Europe, and Asia.[6] Of approximately 401 infants believed to have congenital cystic adenomatoid malformations(CCAMs), 54 had thoracoamniotic shunting and 3 had open procedures, with the goal of decompressing the lung lesion. An additional 13 fetuses with Bronchopulmonary Sequestration (BPS) were described. In the cohorts, 44% to 100% of infants who had

thoracoamniotic shunts survived to birth or through neonatal hospitalization; there was an overall survival rate of 54% in the literature. For fetuses with hydrops, survival was 20% to 30% following surgical treatment compared with 5.7% for untreated hydrops. Since some infants with large CCAMs respond to in utero medical treatment with steroids, failure to respond to steroids may be an entry criterion for future surgical interventions.

White et al (2014) reported outcomes after the use of a transabdominal, transuterine percutaneous thoracoabdominal shunt creation technique in 5 fetuses with nonimmune hydrops due to fetal thoracic abnormalities.[20] The study was a retrospective review of fetal thoracic abnormality cases treated with percutaneous shunt creation by a combination of interventional radiology and maternal-fetal medicine team at a single institution from 2007 to 2012. Eligible fetuses had to have a thoracic abnormality, no infection, an absence of lethal genetic abnormalities, and have a normal karyotype. All fetuses with type I congenital pulmonary airway malformation (CPAM) received betamethasone to attempt to decrease the CPAM size. Seven shunts were placed in 5 patients. There was 1 case of fetal distress requiring induction of labor at 31 weeks, 2 days gestation. After delivery, all of the shunts were in place in the thoracic cavity. Three of the infants underwent uncomplicated surgical resection of type I CPAMs and were discharged home. Two infants with chylothoraces had bilateral chest tubes placed after delivery and were discharged home after the chylothoraces resolved.

SACROCOCCYGEAL TERATOMA

At the time of the 1999 TEC Assessment, the published literature included only 4 cases of fetal surgery for sacrococcygeal teratoma (SCT). However, in utero surgery resulted in prenatal resolution of hydrops, healthy long-term survival, and normal development in some children. These results were impressive given the near-certain fetal mortality if fetal hydrops is left untreated. In a report of 4 cases of open surgical resection of SCT, Hedrick et al (2004) reported 1 neonatal death and 3 survivals with a follow-up range of 20 months to 6 years.[21] Complications other than the fetal death included 1 embolic event, 1 chronic lung disease, and 1 tumor recurrence. The 2011 AHRQ assessment identified a total of 7 retrospective cohorts and case series from 3 academic fetal surgery groups in the United States and the United Kingdom. The 17 fetuses reported to be treated with open surgery were compared with 94 cases with other interventions or no intervention; however, the expectant management cases were less severe. Other ablation methods included alcohol sclerosis (all 3 cases died), radiofrequency ablation (4 of 7 survived), and laser ablation (all 4 died). For open surgical procedures, the survival rates were 33% to 75%. All fetal and neonatal deaths occurred among patients with hydrops or with prodromal cardiovascular changes concerning for developing hydrops. Challenges in this area are the early and reliable detection of development of hydrops and the timing of the fetal intervention.[6]

Van Mieghem et al (2014) reported a case series of 5 fetuses with SCT treated with fetal interventions, along with a systematic review on fetal therapies for solid SCTs.[22] Cases included in the case series were women presenting between 17 5/7 and 26 4/7 weeks' gestation with fetuses found to have large SCT with evidence of fetal heart failure. Treatment was conducted with fetoscopic laser ablation (n=1), RFA (n=2), or interstitial laser ablation with or without vascular coiling (n=2). Two intrauterine fetal deaths occurred; the remaining 3 cases resulted in preterm labor within 10 days of surgery. Of those surviving to delivery, 1 death occurred and 2 infants survived without procedure-related complications but with complications of prematurity. In the authors' literature review, 21 case reports, case series, and cohort

studies were identified, which were generally assessed to be of poor to fair quality. Twenty-nine cases of minimally invasive procedures, with embolization of the SCT vasculature by a variety of therapies, for fetal SCT treatment were identified, which were associated with an overall survival rate of 44%. Twelve cases of open fetal surgery for SCT were identified, with survival of 55%. The authors note that, in the absence of treatment, fetal mortality with large fetal vascular SCTs approaches 100%, providing a rationale for fetal intervention.

MYELOMENINGOCELE

Systematic Reviews
As outlined in the 2011 AHRQ assessment, more than 200 fetuses with myelomeningocele have undergone open surgical repair in the United States.[6] All of the 25 reports on open surgery that were identified in the 2011 AHRQ assessment were based on 4 series of patients from 4 academic medical centers in the United States. Two of the studies had concurrent comparisons.[23,24] Bruner et al (1999)[24] analyzed the first 29 cases of open myelomeningocele repair at Vanderbilt University Medical Center, finding significant reductions in the need for postnatal shunt placement (51% vs 91%) and reduced hindbrain herniation (38% vs 95%). However, both prospective studies found that in utero repair was associated with greater rates of oligohydramnios (48% vs 4%), lower gestational ages (33 vs 37 weeks), and no difference in lower extremity function.

Randomized Controlled Trials
In 2011, results of the National Institutes of Health-sponsored RCT, the Management of Myelomeningocele Study (MOMS) comparing prenatal repair with standard postnatal repair were published.[25] The trial began in 2003 and was expected to enroll 200 women ages 18 years or older who were pregnant with fetuses with myelomeningocele. Women assigned to have prenatal surgery were scheduled for surgery within 1 to 3 days after they were randomized and stayed near the MOMS center until they delivered by C-section. Women in the postnatal group traveled back to their assigned MOMS center to deliver, also by C-section, around the 37th week of their pregnancies. Follow-up on the children was scheduled to be performed at 1 year and 2 ½ years of age to evaluate motor function, developmental progress, and bladder, kidney, and brain development. There was a voluntary moratorium in the United States on conducting in utero repair of myelomeningocele outside of this trial.[6]

The inclusion criteria for MOMS were singleton pregnancy, myelomeningocele with the upper boundary located between T1 and S1, evidence of hindbrain herniation, gestational age of 19.0 to 25.9 weeks at randomization, normal karyotype, U.S. residency, and maternal age at least 18 years. Major exclusion criteria were fetal anomaly unrelated to myelomeningocele, severe kyphosis, risk of preterm birth, placental abruption, body-mass index of 35 or greater, and contradiction to surgery including previous hysterotomy in the active uterine segment. Surgeons had performed at least 15 cases before this randomized study. Primary outcomes were a composite of fetal or neonatal death or the need for a cerebrospinal fluid shunt (shunt placement or meeting criteria for shunt) at 12 months and a composite score of the Mental Development Index of the Bayley Scales of Infant Development II and the child's motor function at 30 months adjusted by level of lesion. Secondary outcomes were surgical and pregnancy complications and neonatal morbidity and mortality. Women were randomized to treatment group in 1:1 ratio.

Recruitment for the trial, planned to include 200 subjects, was stopped at 183 subjects when a clear advantage of prenatal intervention was apparent. The report included 158 women randomized before July 1, 2009. Outcomes up to 30 months are based on 138 women randomized before December 1, 2007. Groups were similar other than that there were more female fetuses and the lesion level was more severe in the prenatal surgery group. Two perinatal deaths occurred in each treatment group. Both deaths in the prenatal surgery group occurred on the fifth postoperative day, a stillbirth at 26 weeks and a neonatal death due to prematurity at 23 weeks' gestation. Two neonates in the postnatal surgery group died with severe symptoms of the Chiari II malformation. Fetal or neonatal death or the need for shunt occurred in 68% of infants in the prenatal-surgery group and in 98% of the postnatal-surgery group (relative risk [RR]: 0.70; 97.7% confidence interval [CI]: 0.58 to 0.84; p<.001). Shunts were placed in 40% of the prenatal-surgery and in 82% of postnatal-surgery groups (p<.001). At 12 months, 4% of infants in the prenatal-surgery group had no evidence of hindbrain herniation versus 36% in the postnatal-surgery group. There was one death in each group between 12 and 30 months (coxsackie septicemia in a child who received prenatal surgery and complications of chemotherapy for choroid plexus carcinoma in a child who received postnatal surgery). The composite of score of Bayley Scales and motor function adjusted by lesion level at 30 months was significantly better in the prenatal surgery group: mean 148.6 +/- standard deviation (SD): 57.5 in the prenatal surgery group (n=64) versus mean 122.6 +/- SD: 57.2 in the postnatal surgery group (n=70) (p=0.007).

Maternal morbidity and complications related to prenatal surgery included oligohydramnios, chorioamniotic separation, placental abruption, and spontaneous membrane rupture. At delivery, an area of dehiscence or a very thin prenatal uterine surgery scar was seen at delivery in one third of mothers who had prenatal fetal surgery (with recommendation that all subsequent pregnancies should be delivered by cesarean before the onset of labor). The average gestational age of babies in the prenatal surgery group was 34.1 weeks, and 13% were delivered before 30 weeks of gestation. One-fifth of infants in the prenatal surgery group had evidence of respiratory distress syndrome, which was likely related to prematurity. The authors observed that "in the case of infants with low lumbar and sacral sessions, in whom less impairment in lower-limb function may be predicted, the normalization of hindbrain position and the minimization of the need for postnatal placement of cerebral spinal shunt may be the primary indication for surgery." They cautioned that the potential benefits of fetal surgery must be balanced against the risks of premature delivery and maternal morbidity and that continued assessment is required to learn if early benefits of prenatal surgery are sustained and the effects of fetal surgery on bowel and bladder continence, sexual function, and mental capacity. They warn that results of this trial should not be generalized to centers with less experience or to patients who do not meet eligibility criteria.

In follow-up to MOMS, Houtrow et al (2020) compared outcomes at school age (5.9 to 10.3 years) between prenatal versus postnatal surgery groups.[26] Of the 161 children who took part in the follow-up study, 79 had been assigned to prenatal surgery and 82 had been assigned to traditional surgery. Children in the prenatal surgery group walked independently more often than those in the traditional surgery group (93% vs 80%). Those in the prenatal surgery group also had fewer shunt placements for hydrocephalus (49% vs 85%), and fewer shunt replacements (47% vs 70%). The prenatal surgery group also scored higher on a measure of motor skills. The two groups did not differ significantly in a test measuring communication ability, daily living skills, and social interaction skills.

Uncontrolled Series

A report by Bruner et al (2004) described minimum 12-month follow-up of 116 fetuses after intrauterine repair of spina bifida (myelomeningocele or myeloschisis).[27] Sixty-one fetuses (54%) required ventriculoperitoneal shunt placement for hydrocephalus. Statistical analysis revealed that fetuses were less likely to require ventriculoperitoneal shunt placement when surgery was performed at 25 weeks' gestation or earlier, when ventricular size was less than 14 mm at the time of surgery, and when the defects were located at L4 or below. Johnson et al (2003) reported on the results of a series of 50 fetuses who underwent open fetal closure of a myelomeningocele between 20 and 24 weeks' gestation.[28] Fetal selection criteria included the presence of hindbrain herniation and sonographic evidence of intact neurologic function (ie, movement of the lower extremities), and absence of clubfoot deformities. Perinatal survival was 94%, with a mean age at delivery of 34 weeks. All fetuses demonstrated reversal of hindbrain herniation; 43% required ventriculoperitoneal shunting (compared to 68 to 100% in historical controls), depending on the location of the myelomeningocele. Tubbs et al (2003)[23], reporting leg function at longer follow-up, showed no difference between patients treated with fetal surgery at 20 to 28 weeks versus traditional surgery.

In three papers (Danzer et al [2008], Danzer et al [2009], Danzer et al [2010]), investigators at the University of Pennsylvania reported outcomes of myelomeningocele repair in 54 patients treated before the voluntary moratorium.[29,30,31] At median follow-up of 66 months (range 36 to 54 months), 37/54 (69%) walked independently, 13/54 (24%) were assisted walkers, and 4/54 (7%) were wheelchair dependent. The strongest factors predicting a lower likelihood to walk independently were higher level lesion (>L4) and the development of clubfoot deformity after fetal intervention. The majority of independent ambulators, and all children who require assistive devices to walk, experienced significant deficits in lower extremity coordination.[30] Thirty children returned at 5 years of age for neurocognitive examination. In this highly selected group, most children had average preschool neurodevelopmental scores, and children who did not require shunt placement were more likely to have better scores.[31] A survey of 48 families focused on hindbrain herniation-associated brainstem dysfunction (eg, apnea, neurogenic dysphagia, gastro-esophageal reflux disease, neuro-ophthalmologic disturbances).[29] Half of the children required shunting. At a median age of 72 months, 15 non-shunted and 10 shunted children were free of hindbrain herniation symptoms. There were no hindbrain herniation-related deaths, and no children developed severe persistent cyanotic apnea. Most children had no or only mild brainstem dysfunction. The authors concluded that reversal of hindbrain herniation after fetal surgery may help reduce the incidence and severity of brainstem dysfunction.

Mayer et al (2010), investigators at a German center, performed a retrospective analysis of expectantly managed patients who received surgical intervention within 2 days of birth at their institution and compared them with reports of outcomes after fetal surgery from other centers including those noted above and to data from historical controls.[32] Patients were born between 1979 and 2009 and were now 13.3 +/- 8.9 (mean +/- standard deviation [SD]) years old. Gestational age at birth in the expectantly managed group was 37.8 weeks, significantly higher than in the prenatal surgery patients. In the expectantly managed group, shunt placement was required in 69.8% at mean age of 16.0 +/- 10.7 days, which is less than for historical controls and comparable to data reported on patients who received fetal surgery. The authors suggest that inconsistency in clinical criteria for shunting used in studies might contribute to differences in this outcome. Among their expectantly managed patients, 56.4% were assisted walkers and 64.1% attended regular classes, both comparable to historical controls. Noting the discrepancy

in the rate of assisted walkers and wheelchair users between expectantly managed patients/historical controls and patients who received surgery, the authors observed that the mean age of the study population was 21.7 years for historical controls, 13.3 years for their population, and only 67.0 months after fetal surgery. They cited earlier papers reporting mobility decreases from early childhood to the early teens including one reporting that "the percentage of patients ambulating the majority of time decreased from 76% at 0 to 5 years to 46% at 20 to 25 years, with a flattening beyond 10 years".[33]

Following publication of the MOMS results, Moldenhauer et al (2014) published outcomes for a cohort of patients treated at single institution with fetal myelomeningocele repair from 2011 to 2014.[34] A total of 587 patients were referred for potential fetal myelomeningocele repair during the study period, of which 348 (59.3%) underwent on-site evaluations and 209 (35.6%) were excluded due to noncandidacy for the procedure (BMI >35, additional fetal anomalies, genetic diagnosis in the fetus, gestational age >26 weeks, preexisting maternal medical condition, multiple pregnancy, and no hindbrain herniation on magnetic resonance imaging). A total of 139 (23.7%) patients were considered potential candidates for fetal myelomeningocele repair, of which 101 underwent open fetal surgery, 13 had postnatal management, and 25 underwent pregnancy termination. The average gestational age at the time of fetal surgery was 23.4 weeks. Fetal resuscitation (intraoperative cardiac compressions and/or administration of atropine, epinephrine, or blood products via the umbilical vein) was successfully performed in 5 cases. Preterm premature rupture of membranes occurred in 31 of 96 (32.3%), and preterm labor occurred in 36 of 96 (37.5%). Sixteen patients had premature rupture of membranes with preterm labor. The perinatal loss rate was 6.1% (6/98), which included 2 intrauterine demises, 1 diagnosed at the conclusion of fetal myelomeningocele repair and 1 on postoperative day 1, and 4 neonatal deaths. Maternal complications included clinical chorioamnionitis (n=4), persistent oligohydramnios (n=6), pre-eclampsia/gestational hypertension (n=1), and placental abruption (n=2). For the 83 patients who were liveborn at the authors' institution, hindbrain herniation was reversed in 71.1%, and the functional level improved compared with prenatal sonographic bony lesion level in 44 of 80 (55%) neonates who were assessed. The authors concluded that their experience with fetal myelomeningocele repair was similar to that reported in the MOMS trial.

Bennett et al (2014) compared outcomes for a cohort of patients treated with fetal myelomeningocele repair in the post-MOMS era with those treated at the same institution during MOMS.[35] Outcomes were evaluated for 43 patients treated with fetal myelomeningocele repair from 2011 to 2013 and compared with those for 78 patients treated as part of MOMS. During the study time period, the repair technique was modified so that no uterine trocar was used, and uterine entry, manipulation, and closure were modified to reduce amniotic membrane separation. Although the mean gestational age at delivery was similar for the post-MOMS and the MOMS cohort (34.4 weeks vs 34.1 weeks, respectively), a greater proportion of post-MOMS cohort subjects were born after 37 weeks of gestation (39% vs 21%, p=.03). Post-MOMS cohort subjects had lower incidences of premature rupture of membranes (22% vs 46%, p=.011) and chorioamnion separation (0% vs 26%, p<.001). These results suggest that fetal myelomeningocele repair outcomes in practice can be comparable with or better than those obtained in the MOMS study.

Section Summary
The most direct evidence related to fetal myelomeningocele repair comes from an RCT, the MOMS study, which demonstrated significant benefits across multiple outcomes for fetal

repair. Single-arm studies have supported these findings. Fetal myelomeningocele repair in a selected population improves the net health outcome.

CARDIAC MALFORMATIONS

The 2011 AHRQ technology assessment included the following evidence on fetal surgery for cardiac malformations:

- Two case series (n=10) were identified on fetal surgery for pulmonary atresia and intact ventricular septum. The literature was described as scant, reflecting the early formative period of development of procedures for this rare condition.
- Eight prospective case series (n=90) were identified on balloon dilation for critical aortic stenosis. One center in the United Kingdom, 2 centers in Germany, 2 in Brazil, and 1 in the United States performed this procedure. Seventy patients are from Boston. The 2011 technology assessment concluded that it is difficult to determine whether the procedure changes long-term outcomes, since it appears to increase the risk of fetal loss but potentially prevents neonatal deaths. However, it did appear that technical success improves over time within a dedicated team and center. For example, the North American center improved their success rate from 25% to 90% over a period of several years. Overall, the literature was considered to be very early in development.
- Three case series from one U.S. institution with a cumulative total of 24 patients were identified on creation in utero of an atrial septal defect for an intact atrial septum. There were no reports of this procedure being performed outside of the U.S. The procedure appears to have technical success; however, mortality remains high, and no controlled trials were available to compare outcomes in patients treated prenatally with those treated postnatally.

The AHRQ report concluded that overall, procedures for severe fetal cardiac anomalies are in an early stage. Preliminary work is being reported in a few highly specialized centers that are establishing the groundwork for feasibility and future directions for outcomes research in this area. The authors concluded that the most pressing challenge in this area is the ability to identify the "right" patient whose care would be compromised by waiting to do a postnatal repair.

McElhinney et al (2009) analyzed their experience with 70 prenatal balloon aortic valvuloplasties attempted in midgestational fetuses between March 2000 and October 2008 for critical aortic stenosis with evolving hypoplastic left heart syndrome to identify factors associated with procedural and postnatal outcomes.[36] Median gestational age was 23.2 weeks (range, 20 to 31 weeks). Technical success was achieved in 52 fetuses. Compared to 21 untreated comparison fetuses, subsequent prenatal growth of the aortic and mitral valves, but not the left ventricle, was improved after intervention. Nine pregnancies did not reach viable term or preterm birth. Seventeen patients had a biventricular circulation postnatally, 15 of them from birth. Two of these patients had no neonatal intervention. Sixteen were alive at a median age of 2.1 years (range, 4 months to 7 years). The other patient died of unrelated causes. Guidelines for assessing the potential for a biventricular circulation changed over the period of the study and became more selective. Larger left heart structures and higher left ventricular pressure at the time of intervention were associated with biventricular outcome. The authors concluded that further investigation is required before it is possible to predict whether fetal intervention will result in improved left heart growth and postnatal survival with a biventricular circulation, and "the potential befits of fetal intervention must be weighed against the risk of

technical failure, fetal demise, aortic regurgitation, and potential long-term adverse events that have yet to be identified".

Marantz et al (2013) reported results from a case series of 5 prenatal balloon aortic valvuloplasties for fetuses with aortic stenosis and risk of progression to hypoplastic left heart syndrome.[37] The procedure was technically successful in all cases with no maternal complications or fetal demise. One pregnancy was terminated after the procedure; of the remaining cases, 1 progressed to hypoplastic left heart syndrome and 3 did not. Rates of longer term survival and complications are not provided. The authors concluded that fetal aortic valvuloplasty is safe and feasible.

Pedra et al (2014) reported a case series of 22 fetal cardiac interventions for several cardiac conditions in 21 fetuses in Brazil.[38] Fetal cardiac intervention was considered for the following echocardiographic findings in patients with isolated cardiac defects (ie, no other structural abnormality or marker for chromosomal abnormality): (1) critical aortic stenosis with evolving hypoplastic left heart syndrome (HLHS) (n=9); (2) critical aortic stenosis, massive mitral regurgitation, giant left atrium, and hydrops (n=4); (3) HLHS with intact interatrial septum or small patent foramen ovale (n=4); (4) pulmonary atresia with intact ventricular septum or critical pulmonary stenosis with impending hypoplastic right heart syndrome (HRHS) (n=4). Fetal interventions included atrial septostomy, aortic valvuloplasty, pulmonary valvuloplasty, or a combination of aortic septostomy and aortic valvuloplasty in 1 case. Technical success was achieved in 20 of 22 procedures (91%), with 1 failed aortic and 1 failed pulmonary valvuloplasty. There was 1 fetal death, and no maternal complications. Longer term outcomes were generally poor, even among those with successful interventions. Among the 20 with successful fetal interventions, 8 eventually achieved biventricular circulation, with 1 "probable" biventricular circulation, and 12 deaths occurred.

Chaturvedi et al (2013) reported outcomes from a series of 10 fetuses who underwent active perinatal management for HLHS with restrictive or intact atrial septum at a single institution from 2000 to 2012.[39] Four of the identified fetuses underwent percutaneous stenting of the atrial septum. No maternal complications occurred. At follow-up, 2 children were alive at 16 and 20 months. Two neonatal deaths occurred in fetuses with the highest left atrial hypertension before intervention and recurrence in utero of left atrial hypertension secondary to stent stenosis.

Kalish et al (2014) reported outcomes for 9 fetuses with HLHS with intact atrial septum who underwent prenatal atrial septal stent placement.[40] Atrial septal stent placement was attempted in 9 fetuses, with successful stent deployment in 5, of which 4 demonstrated flow across the stent at the time of intervention. In the remaining 4 cases, stent placement was technically unsuccessful, but in 75% of cases, atrial balloon septoplasty during the same procedure was successful. One fetal death occurred, along with 4 neonatal deaths, 2 of which had undergone stenting. No maternal complications were reported.

Section Summary
Evidence related to fetal interventions for congenital heart defects, particularly for evolving HLHS and critical pulmonary stenosis/pulmonary atresia, is limited to small case series. Although postnatal repair/correction of these severe cardiac defects is associated with very high morbidity and mortality, further studies are needed to demonstrate that health outcomes are improved with fetal interventions. Randomized trials are unlikely to be conducted, but

comparative studies with concurrent controls would provide further insight into the net benefit of and appropriate patient populations for fetal cardiac interventions.

Other

The use of prenatal surgery for other defects is expanding; recent case reports include prenatal correction of cleft lip and palate and decompression of the fetal trachea.[41,42]

Sacco et al (2019) performed a systematic literature review for maternal complications following open and fetoscopic fetal surgery.[43] One hundred sixty-six studies were included, reporting outcomes for open fetal (n=1193 patients) and fetoscopic surgery (n=9403 patients). No maternal deaths were reported. The risk of any maternal complication in the index pregnancy was 20.9% (95%CI, 15.22 to 27.13) for open fetal and 6.2% (95%CI, 4.93 to 7.49) for fetoscopic surgery. For severe maternal complications (grades III to V Clavien-Dindo classification of surgical complications), the risk was 4.5% (95% CI 3.24 to 5.98) for open fetal and 1.7% (95% CI, 1.19 to 2.20) for fetoscopic surgery. In subsequent pregnancies, open fetal surgery increased the risk of preterm birth but did not increase the risk of uterine dehiscence or rupture. Nearly one quarter of the reviewed studies (n=175) were excluded because maternal complication data were not reported. The reviewers noted that outcomes should be reported consistently for all fetal surgery studies in order to properly quantify maternal risks.

SUPPLEMENTAL INFORMATION

Practice Guidelines and Position Statements

FETAL SURGERY

American College of Obstetricians and Gynecologists and American Academy of Pediatrics

ACOG's Committee on Ethics and AAP's Committee on Bioethics issued a committee opinion on Maternal-Fetal Intervention and Fetal Care Centers in 2011; reaffirmed in 2020.[44] The opinion recommended that:
- Fetal intervention cannot be performed without the explicit informed consent of the pregnant woman.
- Distinctions should be made to prospective parents between which protocols are standard or evidence-based therapies and which are innovative or experimental interventions.
- The informed consent process should involve thorough discussion of the risks and benefits for both the fetus and the pregnant woman.
- Safeguards should be in place to protect women considering fetal research.
- Access to support services such as social services, palliative care and perinatal hospice services, genetic counseling, and ethics consultation should be provided, when appropriate.
- The organization and governance of centers providing fetal interventions should involve a diverse group of professionals, including members without direct ties to the center involved.
- Cooperation between fetal care centers should be encouraged to establish collaborative research networks and to support multicenter trials to accumulate more robust short- and long-term maternal and fetal outcome data on all categories of fetal intervention. In addition, the establishment of centers of excellence for those procedures that are particularly challenging and rare may help to optimize fetal and maternal outcomes.

MYELOMENINGOCELE REPAIR

National Institute of Child Health and Human Development
The Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) convened the fetal myelomeningocele Maternal-Fetal Management Task Force in 2011, with representatives from the American Academy of Pediatrics, American College of Obstetricians and Gynecologists (ACOG), American Institute of Ultrasound in Medicine, American Pediatric Surgical Association, American Society of Anesthesiologists, American Society of Pediatric Neurosurgeons, International Fetal Medicine and Surgery Society (IFMSS), American Association of Neurological Surgeons/Congress of Neurological Surgeons, North American Fetal Therapy Network, Society for Maternal-Fetal Medicine, Society of Pediatric Anesthesia, and Spina Bifida Association. The Task Force provided recommendations about optimal practice criteria for maternal fetal surgery for myelomeningocele repair.[45]

Recommendations are related to 6 key considerations for teams providing in utero myelomeningocele repair:
1. Defining a fetal therapy center
2. Perioperative management for fetal myelomeningocele repair
3. Long-term care
4. Counseling
5. Reporting and monitoring
6. Access and regionalization

In general, the authors emphasize the need for access to multidisciplinary teams for prenatal, perinatal, and follow-up care and recommend that in utero myelomeningocele repair be performed under strict adherence to the MOMS protocol in terms of preoperative evaluation, intraoperative procedure, and immediate postoperative care.

American College of Obstetricians and Gynecologists
1. Committee opinion Maternal-Fetal Surgery for Myelomeningocele (2017)[46] Reaffirmed in 2022.[47] ACOG made the following recommendations:
- "Open maternal-fetal surgery for myelomeningocele repair has been demonstrated to improve a number of important pediatric outcomes at the expense of procedure-associated maternal and fetal risks.
- Women with pregnancies complicated by fetal myelomeningocele who meet established criteria for in utero repair should be counseled in nondirective fashion regarding all management options, including the possibility of open maternal-fetal surgery.
- Interested candidates for fetal myelomeningocele repair should be referred for further assessment and consultation to a fetal therapy center that offers this intervention and possesses the expertise, multi-disciplinary team, services, and facilities to provide detailed information regarding maternal-fetal surgery and the intensive care required for patients who choose to undergo open maternal-fetal surgery."

U.S. Preventive Services Task Force Recommendations
The U.S. Preventive Services Task Force has not addressed fetal surgery for prenatally diagnosed malformations.

Ongoing Clinical Trials
There are ongoing clinical trials for all conditions noted in this policy.

Government Regulations
National/Local:
There is no Medicare policy on this topic.

(The above Medicare information is current as of the review date for this policy. However, the coverage issues and policies maintained by the Centers for Medicare & Medicare Services [CMS, formerly HCFA] are updated and/or revised periodically. Therefore, the most current CMS information may not be contained in this document. For the most current information, the reader should contact an official Medicare source.)

Related Policies

- In Utero Laser Therapy for the Treatment of Twin to Twin Transfusion Syndrome (TTTS) (Retired)

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The articles reviewed in this research include those obtained in an Internet based literature search for relevant medical references through 1/2/25, the date the research was completed.

Joint BCBSM/BCN Medical Policy History

Policy Effective Date	BCBSM Signature Date	BCN Signature Date	Comments
11/05/01	11/05/01	11/05/01	Joint policy established
5/1/07	2/17/07	2/17/07	Routine Maintenance
5/1/08	2/19/08	4/26/08	Routine Maintenance
7/1/09	4/21/09	5/11/09	Routine Maintenance
7/1/10	4/20/10	4/20/10	Routine Maintenance
9/1/13	6/18/13	6/26/13	Policy updated, status changed from experimental/investigational to established for myelomeningocele. Name of policy changed to Fetal Surgery for Prenatally Diagnosed Malformations, replaces In Utero Repair of Fetal Myelomeningocele, In Utero Repair of Sacrococcygeal Teratoma – Retired, In Utero Repair of Congenital Cystic Adenomatoid Malformation and Extralobar Pulmonary Sequestration – Retired, In Utero Repair of Urinary Tract Obstruction in the Fetus – Retired and In Utero Treatment of Tracheal Occlusion for the Treatment of Congenital Diaphragmatic Hernia – Retired.
7/1/15	4/21/15	5/18/15	Routine maintenance • Tracheal occlusion as a treatment of congenital diaphragmatic hernia added to Inclusions and deleted from Exclusions
7/1/16	4/19/16	4/19/16	Routine maintenance
5/1/17	2/21/17	2/21/17	Routine maintenance Added cross-reference to "In Utero Laser Therapy for the Treatment of Twin to Twin Transfusion Syndrome (TTTS)"
5/1/18	2/20/18	2/20/18	Routine maintenance
5/1/19	2/19/19		Routine maintenance
5/1/20	2/18/20		Routine maintenance

5/1/21	2/16/21			Routine maintenance
5/1/22	3/11/22			Routine maintenance. Background section updated, Inclusions/Exclusions updated. Title change from "Fetal Surgery for Prenatally Diagnosed Malformations" to "Prenatal (Fetal) Surgery for Diagnosed Malformations" Ref 1,26,43 added.
5/1/23	2/21/23			Routine maintenance (jf) Vendor Managed: NA
5/1/24	2/20/24			Routine maintenance (jf) Vendor Managed: NA
5/1/25	2/18/25			Routine maintenance (jf) Vendor Managed: NA Edit to the MPS, removal of "safety and effectiveness"

Next Review Date:　　　　1st Qtr, 2026

BLUE CARE NETWORK BENEFIT COVERAGE
POLICY: PRENATAL (FETAL) SURGERY FOR DIAGNOSED MALFORMATIONS

I. Coverage Determination:

Commercial HMO (includes Self-Funded groups unless otherwise specified)	Covered; criteria applies
BCNA (Medicare Advantage)	See Government Regulations section.
BCN65 (Medicare Complementary)	Coinsurance covered if primary Medicare covers the service.

II. Administrative Guidelines:

- The member's contract must be active at the time the service is rendered.
- Coverage is based on each member's certificate and is not guaranteed. Please consult the individual member's certificate for details. Additional information regarding coverage or benefits may also be obtained through customer or provider inquiry services at BCN.
- The service must be authorized by the member's PCP except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Services must be performed by a BCN-contracted provider, if available, except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Payment is based on BCN payment rules, individual certificate and certificate riders.
- Appropriate copayments will apply. Refer to certificate and applicable riders for detailed information.
- CPT - HCPCS codes are used for descriptive purposes only and are not a guarantee of coverage.