Fetal Surgery for Myelomeningocele?
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The possibility of surgical repair of fetal anomalies in utero has long tantalized obstetricians and pediatric surgeons, especially since the development of high-resolution real-time ultrasonography. The presumption has been that earlier in utero repair would provide superior outcomes for the offspring than would postnatal surgery. However, postnatal treatment is much simpler and is not traumatic to the mother. Successful fetal surgery for any condition thus requires an accurate identification of which fetuses are at highest risk for a poor outcome if repair is delayed until after birth. Despite the promise of fetal surgical procedures, such repair of structural malformations has not been shown to be better than postnatal repair at improving the outcome in randomized, controlled trials (e.g., fetal tracheal occlusion for congenital diaphragmatic hernia).

Myelomeningocele is not lethal to a fetus, but postnatal repair is associated with a less-than-desirable long-term neurologic outcome. Early studies of open fetal surgery to repair myelomeningocele, which involved relatively small, non-randomized cohorts and the use of a relatively large hysterotomy to access the fetus, reported serious maternal and fetal complications. Thus, questions remained regarding the overall risk-benefit ratio of the procedure.

In this issue of the Journal, Adzick et al. report the results of the Management of Myelomeningocele Study (MOMS), which was designed to assess outcomes of prenatal surgery, as compared with postnatal repair. Women in this trial had a singleton fetus of 19.0 to 25.9 weeks of gestation with myelomeningocele located between T1 and S1 and evidence of hindbrain herniation; all fetuses had a normal karyotype. Of 1233 women who were initially screened, 183 (15%) were randomly assigned to undergo either prenatal surgery through the use of hysterotomy and open fetal repair or repair after delivery.

In the intention-to-treat analyses, prenatal surgery resulted in a significant reduction in the composite primary end point of infant death or the need for placement of a cerebrospinal-fluid shunt at 1 year, a finding entirely driven by the substantially lower frequency of shunt placement in the prenatal-surgery group (40% vs. 82%). Prenatal surgery, as compared with postnatal surgery, also resulted in significant improvement in a composite score based on the Bayley Mental Development Index and assessment of motor development at the age of 30 months (a coprimary outcome), although the earlier surgery had no significant effect on mental development alone. There was less hindbrain herniation in the prenatal-surgery group than in the postnatal-surgery group (with no hindbrain herniation in 36% and 4% of the infants, respectively, and severe herniation in 6% and 22%, respectively). The percentages of children who were able to walk independently at the age of 3 years were 42% in the prenatal-surgery group and 21% in the postnatal-surgery group. However, the prenatal-surgery group had higher rates of maternal and certain fetal complications: spontaneous membrane rupture (46% in the prenatal-surgery group vs. 8% in the postnatal-surgery group), oligohydramnios (21% vs. 4%), preterm birth (79% vs. 15%), and more complications associated with prematurity, such as the respiratory distress syndrome. More than a third of mothers in the prenatal-surgery group showed dehiscence or a very thin uterine wall at the hysterotomy site.

To what extent can these results be general-
ized? Caution is necessary here. For the decade of this trial, all cases nationwide were funneled to the three study centers, which by now should have developed near-optimal prowess. With the trial complete, other U.S. centers are likely to initiate their own programs, diluting experience and necessitating individual center-specific learning curves. Fetal results may not be as good as those in MOMS, and maternal complications could be increased. In addition, most women who expressed interest in the trial were either ineligible or declined to participate, with only 15% participation of those who were screened. This percentage may or may not increase as access extends beyond the three centers.

Earlier diagnosis of myelomeningocele and the performance of open fetal surgery earlier than that performed in MOMS might further improve outcomes, but the potential benefits of even earlier intervention must be weighed against the greater likelihood of maternal complications and possibly increased difficulty of fetal repair. More work is also needed to determine whether baseline characteristics could predict which fetuses would be more or less likely to benefit from prenatal surgery. But surely the greatest benefit would derive from a less traumatic approach.

Our job as physicians is to communicate options and available data to patients as lucidly as possible while assiduously adhering to the principles of nondirective genetic counseling. For many women, the 20% absolute improvement in ambulation at the age of 3 years and the decreased need for shunting may be perceived as sufficient to justify the increased risk of maternal complications, but it should be recognized that outcomes after prenatal surgery were less than perfect in MOMS. Couples who do not elect to terminate a pregnancy unavoidably feel pressured “to do everything possible” and hence may be inclined to interpret even marginal benefit favorably. It is also human nature to overestimate the likely benefit for one’s own fetus and to underestimate the associated risks. Counseling should involve not only precise quantitative statements comparing outcomes of prenatal versus postnatal surgery on the basis of this report but also the provision of information on centerspecific experience.

The degree to which intrauterine repair will transform outcomes for fetuses with myelomeningocele remains unclear. The study by Adzick et al. is a major step in the right direction, but the still suboptimal rates of poor neonatal outcome and high maternal risk necessitate the use of less invasive approaches if such procedures are to be widely implemented.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

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This article (10.1056/NEJMe1101228) was published on February 9, 2011, at NEJM.org.


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