

# IN UTERO insights Special Edition

 The Children's Hospital of Philadelphia®

 CENTER FOR FETAL  
DIAGNOSIS & TREATMENT

Dear Colleague,

The field of fetal therapy is one of slow, steady progress, marked by decades of diligence and punctuated by rare moments of breakthrough.

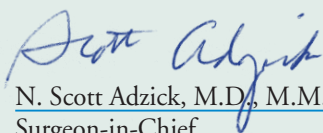
Once such moment occurred recently.

We are absolutely thrilled to announce that prenatal surgery for myelomeningocele (MMC) is now a standard of care at The Children's Hospital of Philadelphia. This represents the biggest single advance in the history of treatment for spina bifida, the most common birth defect of the central nervous system.

This breakthrough stems from the results of the nationwide Management of Myelomeningocele Study (MOMS), which has shown clear efficacy of the fetal procedure versus traditional postnatal repair. CHOP had the distinct honor to be one of three centers participating in the seven-year trial. Our team members pioneered the fetal repair procedure and have the greatest depth of collective experience — in both the surgery and all aspects of care surrounding it — in the world. This special issue of *In Utero Insights* presents the study findings, as well as information about prenatal repair at our center.

More than 20 years of working toward this advance have confirmed what we've always believed: the persistence of a dedicated and experienced team, combined with the courage of mothers determined to brave new frontiers for their unborn children, is a force that can change medical history.

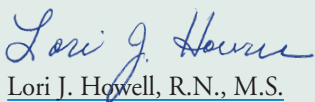
Sincerely,



N. Scott Adzick, M.D., M.M.M.

Surgeon-in-Chief

Director, Center for Fetal Diagnosis and Treatment



Lori J. Howell, R.N., M.S.

Executive Director, Center for Fetal Diagnosis and Treatment

## BIRTH OF A BREAKTHROUGH

*A landmark study, co-led by The Children's Hospital of Philadelphia, has found that prenatal repair of myelomeningocele (spina bifida) can substantially improve outcomes for this severely disabling condition.*

Director of the Center for Fetal Diagnosis and Treatment (CFDT), N. Scott Adzick, M.D., was lead author on the study, which appeared in the *New England Journal of Medicine* (N. Scott Adzick, M.D. et al., "[A Randomized Trial of Prenatal versus Postnatal Repair of Myelomeningocele](#)," *New England Journal of Medicine*, online Feb. 9, 2011; March 17, 2011 in print edition).

The long-awaited results validate the work pioneered by the CFDT team over more than 20 years: developing the prenatal repair technique, conducting extensive tests in animal models and then cautiously applying the therapy in select patients.

The Management of Myelomeningocele Study (MOMS) was conducted from 2003 to 2010 at CHOP and two other centers, Vanderbilt University and the University of California at San Francisco. It was sponsored by the Eunice Kennedy Shriver National Institute of Child Health and Human Development. The Biostatistics Center at George Washington University independently oversaw data collection and analysis.

So important was the learning gleaned from MOMS, that for the seven-year duration of the randomized, prospective trial, all U.S. fetal surgery programs agreed to suspend performing prenatal repair. The trial goal was to enroll 200 patients, but the NICHD ended the study after 183 patients based on clear evidence of efficacy for the prenatal procedure versus postnatal repair. In both study groups, surgeons used the same technique to close the MMC defect — the only difference was timing of the procedure. Fetal repair is performed between 19 and 26 weeks gestation.

Specifically, the study found that prenatal repair resulted in:

- **Reversal of the hindbrain herniation component of the Chiari II malformation.** During pregnancy, all fetuses in the trial had hindbrain herniation. At age 12 months, 36 percent of infants in the prenatal surgery group no longer had any evidence of hindbrain herniation, compared with only 4 percent in the postnatal surgery group.

- **Reduced need for ventricular shunting to relieve hydrocephalus.** At 12 months of age, 40 percent of children in the prenatal repair group had received a shunt, compared with 82 percent in the postnatal group.

*continued* ►

# BIRTH OF A BREAKTHROUGH *continued from front cover*

## • Reduced incidence or severity of potentially devastating neurologic effects.

At age 30 months, children in the prenatal surgery group scored significantly better in measurements of motor function. Forty-two percent in the prenatal group were able to walk independently, compared with 21 percent in the postnatal repair group.

**Miles to Go** • All children enrolled in the MOMS trial, whether they had pre- or postnatal repair, continue to be followed long after delivery. Clinic visits are scheduled at 12 months and 30 months of age, at which times a multidisciplinary team, blinded to which type of repair the child received, evaluates each patient on an extensive battery of physical and developmental measures. It is vital that patient families continue to participate in the extended follow-up schedule, as this data is key to gaining a comprehensive understanding of the long-term results of fetal therapy.

Under our Center's leadership, the NICHD will also fund the MOMS II study, which will follow patients from the initial MOMS trial well into school age. This study will yield invaluable new learning that will help us shape care for future generations.

At Children's Hospital, our commitment to our MMC patients, regardless of type of repair, is lifelong. Patients seen at CHOP have access to our [Spina Bifida Clinic](#), a comprehensive program that follows children into adolescence and adulthood — our oldest patients are now in their 40s. Led by renowned pediatrician [Patrick Pasquariello, M.D.](#), the Spina Bifida Clinic was the nation's first program to bring a multidisciplinary approach to long-term follow-up for these patients. The team includes experts from pediatrics, nursing, neurosurgery, orthopaedics, urology, physical therapy, social work and genetics. As needed, consultations are arranged with other subspecialties at Children's Hospital.

**The Promise of Research** • The results of the MOMS trial represent decades of meticulous research and clinical practice by our team and others in our field. They also reveal the vast frontier yet to be explored. Ongoing scientific investigation is essential and, like the advent of fetal repair itself, this work has the potential to completely alter once again the way we approach this devastating birth defect. Some highlights:

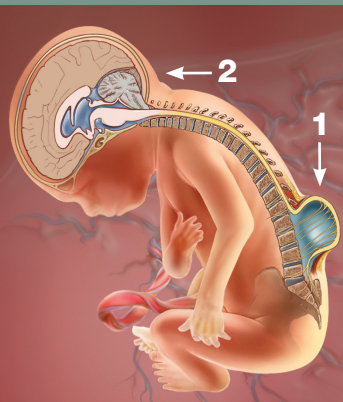
1. In the lab, CHOP researchers are pursuing better techniques for repair, including tissue engineering. Our team is developing materials that could be applied to seal the spinal defect early in gestation, through a minimally invasive procedure — providing effective protection to the spinal cord without the need for open fetal surgery.
2. By studying markers in the amniotic fluid, we can determine the amount of ongoing damage to the spinal cord within the uterine environment. Having a clearer understanding of a fetus' cord condition could help us make better-informed decisions about whether the benefits of prenatal surgery outweigh the risks in any given case. Our team hopes to initiate a multi-center collection of amniotic fluid samples to study this potentially important advance.

## EXPERIENCE *is* EVERYTHING

The complex requirements of caring for MMC pregnancies — from diagnosis through fetal surgery, from planned cesarean delivery through the N/IICU stay — require the expertise of a sophisticated multidisciplinary team. The Center for Fetal Diagnosis and Treatment includes specialists from fetal surgery, neurosurgery, obstetrics, maternal-fetal medicine, fetal cardiology, anesthesiology, neonatology and nursing. CHOP's facilities, including dedicated fetal ORs and the [world's first delivery unit created for birth defects](#), are also critical to providing the highest level of care.

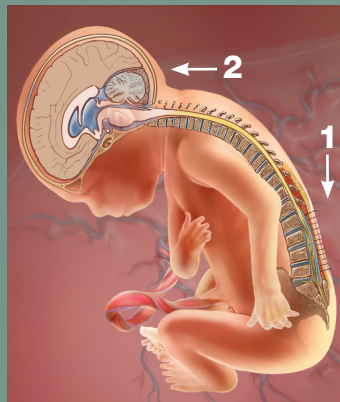


*The core team at the Center for Fetal Diagnosis and Treatment has been performing fetal MMC repair every year since 1998. No other program can offer this level of continuous experience.*



### ◀ FETUS WITH MYELOMENINGOCELE

1. Part of the spinal cord and spinal nerves, usually encased in a sac, protrude through an opening in the back and are exposed to the amniotic fluid.
2. The brain stem (hindbrain) descends, or herniates, into the spinal canal in the neck and blocks the circulation of cerebrospinal fluid. This can cause a damaging buildup of fluid in the brain called hydrocephalus.



### ◀ FETUS AFTER SURGICAL REPAIR

1. Fetal surgery repairs the defect, returning the spinal tissue to its proper place and covering the opening in the fetus' back.
2. The hindbrain herniation gradually reverses after repair, and the brain stem returns to its normal position.

# MAJOR MILESTONES BY CFDT TEAM MEMBERS

- 1993:** Creation of lamb model for fetal myelomeningocele (MMC)<sup>1</sup>
- 1995:** First large animal experiment demonstrating fetal repair of MMC<sup>2-4</sup>
- 1998:** First successful EARLY GESTATION fetal surgery for spina bifida in a human<sup>5</sup>
- 1999:** First clinical report showing fetal MMC closure resulted in improvement in hindbrain herniation as demonstrated by serial MRI scans<sup>6</sup>
- 2002:** Critical report of ventriculoperitoneal shunt percentages for children with MMC treated after birth – established baseline control data for MOMS<sup>7</sup>
- 2002:** First report on short-term outcomes for initial cohort of fetuses that underwent *in utero* MMC repair prior to MOMS trial<sup>8</sup>
- Feb. 2003: MOMS trial opens**
- 2003:** Fetal head biometry after fetal MMC repair<sup>9</sup>
- 2003:** Reversal of hindbrain herniation demonstrated in sheep MMC repair model<sup>10</sup>
- 2004:** Establishment of intraoperative fetal echocardiographic monitoring as standard of care for open fetal surgery<sup>11</sup>
- 2004:** First report on maternal reproductive outcomes following maternal-fetal surgery at CHOP;<sup>12</sup> second follow-up report in 2010<sup>21</sup>
- 2005:** Non-surgically induced fetal rat model for MMC<sup>13-16</sup>
- 2006:** First report of short-term (2 yr) neurodevelopmental outcomes in patients who underwent fetal repair of MMC at CHOP<sup>17</sup>
- 2008:** Examination of hindbrain herniation reversal and brain stem function in initial cohort of fetal MMC repair patients<sup>18</sup>
- 2009:** First report of longer-term (5 yr) neurodevelopmental outcomes in patients who underwent fetal MMC repair<sup>19</sup>
- 2009:** First report on lower extremity neuromotor function and ambulatory potential in infancy and early childhood for patients who underwent fetal MMC repair<sup>20</sup>
- 2010:** Report on the relationship of seizure activity and chronic epilepsy in early infancy and short-term neurodevelopmental outcomes following fetal MMC repair<sup>22</sup>
- Dec. 2010: MOMS trial stopped because efficacy of fetal MMC repair proven**
- Feb. 2011: MOMS trial published in the New England Journal of Medicine**<sup>23</sup>

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# EDUCATIONAL RESOURCES



## Online CME Now Available

### Fetal Myelomeningocele Repair: Tribulations and Trials

**Presenter:** N. Scott Adzick, M.D., M.M.M., Surgeon-in-Chief; Director, Center for Fetal Diagnosis and Treatment, The Children's Hospital of Philadelphia

**Purpose:** Provide participants practical, evidence-based techniques for the management of myelomeningocele (MMC) and enhance clinicians' skill in diagnosing, counseling and managing pregnancies complicated by MMC.

**Credit Available:** This activity has been approved for *AMA PRA Category 1 Credit*.™ The Children's Hospital of Philadelphia is an approved provider of continuing nursing education by the PA State Nurses Association, an accredited approver by the American Nurses Credentialing Center's Commission on Accreditation. This program is approved for 1.0 contact hour.

**Highlights:** Review the natural history of myelomeningocele diagnosed before birth • Identify the indications for fetal myelomeningocele repair • Discuss the results from the Management of Myelomeningocele Study (MOMS).

**This online CME activity is offered free of charge.** To take this course, go to: [fetalsurgery.chop.edu/fetal-ed](http://fetalsurgery.chop.edu/fetal-ed)

**Resources for Clinicians** • On our website, you can find more information about the MOMS trial and about fetal repair of MMC at CHOP. Visit our resource page at [fetalsurgery.chop.edu/spinabifida](http://fetalsurgery.chop.edu/spinabifida) for: fast facts about the study and procedure, MMC indication sheet, fetal MMC case study, referral guidelines and more.

**Educational Video Coming Soon** • In our new DVD, *Birth of a Breakthrough*, CFDT team members clearly explain the prenatal MMC repair procedure and the comprehensive, multidisciplinary care provided for both mother and baby at The Children's Hospital of Philadelphia. Created for clinicians and patients, it's essential information about this important treatment advance. To request your free copy, please call 1-800-IN-UTERO (468-8376).



## UPCOMING EVENTS

### National Conferences

**American Institute of Ultrasound in Medicine\***  
Annual Convention  
April 14-17, 2011, New York, NY

**American College of Obstetricians and Gynecologists\*** • Annual Clinical Meeting  
April 30-May 4, 2011, Washington, D.C.

**38th Spina Bifida Association Conference**  
June 26-29, 2011, Anaheim, CA  
N. Scott Adzick, M.D., M.M.M., presenting

*\*Stop by our exhibit for updated information.*

## BY THE NUMBERS

### CHOP Experience **1995 to Present**

#### Central Nervous System Anomalies

Referrals: **2142**  
Evaluations: **1650**

#### Suspected Myelomeningocele (MMC)

*from all 50 states and 12 countries*

Referrals: **1235**  
Evaluations: **561**  
Fetal Surgeries for MMC: **100**



The Center for Fetal Diagnosis and Treatment collaborates with top-ranked disciplines within The Children's Hospital of Philadelphia, one of only eight pediatric hospitals in the nation to be named to the prestigious *U.S. News & World Report Best Children's Hospitals Honor Roll for 2010-11*.

- Neonatology; pulmonology; diabetes and endocrine disorders — ranked best in the nation
- Heart and heart surgery; cancer; gastroenterology; urology — ranked second in the nation
- Orthopaedics; neurology and neurosurgery — ranked third in the nation
- Kidney — ranked sixth in the nation



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