Fetal Surgery for Myelomeningocele Repair

- What is the post-MOMS Trial State?
  - Why did we need the MOMS Trial?
  - How do the results shape discussion?
  - What are the implications for expansion of fetal surgery centers?
  - What implications for the future?
Fetal Myelomeningocele Repair: Short Term Outcomes

Natural History:

- variable cognitive impairment
- paralysis of legs & feet
- orthopedic deformities
- bowel & bladder incontinence
Fetal Myelomeningocele Repair: Short Term Outcomes

Spina bifida: experimental fetal lamb model

Nature Medicine 1, 342 - 347 (1995) In utero surgery rescues neurological function at birth in sheep with spina bifida
Martin Meuli¹, Claudia Meuli-Simmen¹-², Grover M. Hutchins³, Charles D. Yingling⁴, Kathleen McBiles Hoffman⁵, Michael R. Harrison¹ & N. Scott Adzick¹
Fetal Myelomeningocele Repair: Short Term Outcomes

Spina bifida: experimental fetal lamb model
Fetal Myelomeningocele Repair: Short Term Outcomes

Spina bifida: experimental fetal lamb model

Post fetal surgical repair


Fetal Surgery for Myelomeningocele and the Incidence of Shunt-Dependent Hydrocephalus
Joseph P. Bruner, MD; Noel Tulipan, MD; Ray L. Paschall, MD; Frank H. Boehm, MD; William F. Walsh, MD; Sandra R. Silva, MD; Marta Hernanz-Schulman, MD; Lisa H. Lowe, MD; George W. Reed, PhD JAMA. 1999;282(19):1819-1825
Fetal Myelomeningocele Repair: Short Term Outcomes

- **Selection criteria:**
  - gestational age < 26 wks
  - normal karyotype
  - absence of other major anomalies
  - ventriculomegaly < 17 mm
  - presence of type II Arnold-Chiari malformation
  - evidence of intact neurologic function in the lower extremities and absence of club foot deformity
Fetal Myelomeningocele Repair: Short Term Outcomes

Results (pre-operative):

- anatomic bony defect:
  - thoracic = 3 (T8 = 1, T11 = 1, T12 = 1)
  - lumbar = 34 (L1 = 3, L2 = 2, L3 = 7, L4 = 12, L5 = 10)
  - sacral = 6 (S1 = 6)
- Hindbrain herniation: moderate-severe = 5, severe = 38
- mean GA at surgery = 23 wks 0 day (20w0d - 25w4d)
- mean post-operative hospital stay = 4.5 days
- mean maximal ventriculomegaly = 11.1 mm (6.0 - 17.0)
Effect of Intrauterine Repair and Postnatal
Fetal Myelomeningocele Repair: Short Term Outcomes

**Results** (neonatal outcomes):
- mean ventriculomegaly at birth: 15.7 mm
- mean maximal change in ventriculomegaly: 5.3 mm
- reversal of hindbrain herniation: 40 (100 %)
- transient ventilatory support: 8 (mean age at birth = 31w5d)
- transient CPAP support: 5 (mean age at birth = 33w4d)
- discharged on caffeine and apnea monitor: 15 (37.5 %)
Fetal Myelomeningocele Repair: Short Term Outcomes

- **Results** (neonatal outcome):
  - ventriculoperitoneal shunt placement = 14/40  (35 %)
    - Actual shunt rate by level          predicted shunt rate
    - thoracic = 1/2  (50 %)             (100 %)
    - lumbar = 12/33  (36 %)             (88 %)
    - sacral (S1) = 1/5  (20 %)          (68 %)
  - observed vs. predicted leg function for thoracic-lumbar defects
    - better than predicted = 24/35  (69 %)
    - worse than predicted = 3/35  (9 %)
    - same as predicted = 8/35  (23 %)
  - club foot deformity = 8  (20%)
Fetal Surgery for Myelomeningocele Repair

- Limited supporting data
- Evangelical parents
- Belief in the ability of this operation to allow their child to walk and have a normal life
- Lack of appreciation of potential maternal or fetal risks
- Willing to assume any maternal risk
- Compromised informed consent
Management of Myelomeningocele: The MOMS Trial

- Trial stopped at 183 patients randomized for efficacy
- Primary endpoint: death or VP shunt at 1 year of age
- 2nd Primary endpoint: Bayley Mental Developmental Index and Motor level at 30 months

A Randomized Trial of Prenatal versus Postnatal Repair of Myelomeningocele
Percentage of Infants Requiring Ventriculo-Peritoneal Shunts at One Year of Age

- Postnatal Surgery
- Prenatal Surgery
Bayley Mental Developmental Index and Motor level at 30 months

- Composite of both significantly better in prenatal surgery group
- No difference in the Bayley Mental Developmental Index
- Difference between anatomic defect and motor level better in prenatal surgery group
  - > 2 vertebral bodies
    - 32% prenatal
    - 12% postnatal
  - Walking with /without orthotics
    - 71% prenatal
    - 57% postnatal
Fetal and Neonatal Complications of Prenatal MMC Repair

- Fetal mortality 3% vs 2%
  - IUFD and prematurity vs Brainstem dysfunction
- Prematurity
  - 34 weeks mean GA vs 37 weeks GA at delivery
  - <30 weeks 13% vs 0%
  - 30-34 weeks 33% vs 5%
  - 35-37 weeks 33 vs 10%
  - <37 weeks 79% vs 15%
- Birth weight
  - 2383g vs 3039 g
- Respiratory distress syndrome
  - 21% vs 6%

46%
Obstetrical Complications of Prenatal MMC Repair

- Chorioamnionotic separation 21% vs 6%
- Pulmonary edema 6% vs 0%
- Oligohydramnios 21% vs 4%
- Placental abruption 6% vs 0%
- PPROM 46% vs 8%
- Blood transfusions at delivery 9% vs 1%
- Hysterotomy site at delivery
  - Intact 64%
  - Very thin 25%
  - Partial dehiscence 9%
  - Complete dehiscence 1%
Prenatal MMC Repair Post-MOMS

MOMS Trail reported February 2011

- Increase in MMC referrals to MOMS Centers
- Only fraction of fetal MMCs evaluated chose fetal surgery
- CHOP 150 patients evaluated 50 underwent fetal MMC repair
- FCC 24 patients evaluated 5 underwent MMC repair
  - 2 others went to MOMS centers
Prenatal MMC Repair Post-MOMS

MOMS Trail reported February 2011

- 3 MOMS Centers
- 7 other new centers performing prenatal MMC repair
  - Most had established fetal programs
  - Some never had done open fetal surgery
- One center has abandoned MOMS trial criteria
  - No longer require hindbrain herniation
Prenatal MMC Repair Post-MOMS

MOMS Trail reported February 2011

- White paper on recommended requirement for Centers performing fetal surgery for MMC
  - ACOG, APSA, IFMSS, AAP,
- NAFTnet registry for all post-MOMS trial patients
- 20 centers in NAFTnet most participating
- MOMS II funded for long term follow up
Prenatal MMC Repair Post-MOMS

MOMS Trial reported February 2011

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New Programs for Prenatal MMC Repair

• Why?
  • Service to patients in region served by center
  • Travel to MOMS centers will continue to be an obstacle to access what may become standard of care treatment
  • MOMS centers can not accommodate all patients who may want to pursue this option
New Program for Prenatal MMC Repair

Who?

- Fetal Care Center
  - Prior experience with fetal surgery
  - Infrastructure in place to care for maternal-fetal surgical patients
  - Post-fetal surgical L&D-ICU setting
New Program for Prenatal MMC Repair

Who?

- Fetal surgical team:
  - Fetal Surgeon
  - Maternal-Fetal Medicine Specialist
  - Pediatric Neurosurgeon
  - Pediatric Cardiology
  - Obstetric Anesthesia
  - Spina Bifida Team
  - Obstetric Nursing team
New Program for Prenatal MMC Repair

- How?
  - Fetal surgery is just one option
  - Concern regarding hype and exaggerated perceptions regarding MOMS trial results
  - Critical review of the MOMS trial posted on web site and distributed to all patients
    - Reduction from 82% to 40% VP shunt rate
    - Remainder of findings may not be durable
    - Walking at 30 months is not walking at 16 years
    - Early days of MOMS results
A Model Program for Prenatal MMC Repair

• How?
  • Three phases of evaluation and counseling
  • Phase I
    • Ultrasound, fetal MRI and fetal echocardiogram
    • Genetic counselor
    • MMC clinic consult-Oppenheimer
    • Pediatric Neurosurgical consult
  • Team meeting
    - Pediatric Surgeon, MFM, Neurosurgeon, Neonatologist, Genetic Counselor, MSW, Coordinators
    - Review images
    - Review prenatal and postnatal natural history from
      - Obstetric
      - Fetal Surgery
      - Neonatal
      - Neurosurgical
      - MMC Clinic
A Model Program for Prenatal MMC Repair

Phase II
- Must meet all MOMS Trial criteria
- Independent Neonatal consultation
- Independent MFM consultation
- Availability of referral to MOMS center for consultation
- Psychosocial evaluation
- Oversight Committee approval

Phase III
- Consent Team meeting
- Prenatal MMC repair
A Model Program for Prenatal MMC Repair

- Oversight Committee
  - Maternal Fetal Medicine specialist
  - Chief of Pediatric Neurosurgery
  - Rehabilitation Medicine
  - Neonatologist
  - Bioethicist
A Model Program for Prenatal MMC Repair

- Role of Oversight Committee
  - Approve every patient to be offered prenatal MMC repair
  - Review outcome of every case
  - Review every adverse event
  - Approve Prenatal MMC Management Protocol
  - Approve any changes to protocol
  - Determine the length of oversight
Fetal Surgery for MMC Repair

Inclusion Criteria

- Myelomeningocele at T1 through S1 with hindbrain herniation, level of MMC confirmed by ultrasound and hindbrain herniation confirmed by MRI.
- Maternal age greater than or equal to 18 years.
- Gestational age 19 0/7 weeks to 26 6/7 at the time of prenatal surgery.
- Normal karyotype or FISH.
- Normal fetal echocardiogram.
- Singleton pregnancy.
- Willing to remain in greater Cincinnati area for remainder of pregnancy and deliver at The Fetal Care Center for postnatal management at Cincinnati Children’s.
Fetal Surgery for MMC Repair

Exclusion Criteria

- Significant fetal anomaly not related to MMC.
- Kyphosis in fetus of greater than 30 degrees.
- History of incompetent cervix, cervix less than 20mm or presence of a cerclage.
- Morbid obesity as defined as a BMI of greater than 35.
- Maternal – fetal Rh isoimmunization, Kell sensitization or a history of neonatal alloimmune thrombocytopenia.
- Maternal HIV, Hepatitis B, Hepatitis C due to increased risk of transmission to the fetus during maternal – fetal surgery.
- Uterine anomaly such as large or multiple uterine fibroids or mullerian duct abnormality.
- Maternal medical condition which is a contraindication to abdominal surgery or general anesthesia.
- No support person to stay with mother at Ronald McDonald House.
- Patient does not meet psychosocial criteria as determined by the social worker evaluation.
- Previous hysterotomy in the active segment of the uterus either from previous classical cesarean section, uterine anomaly such as an arcuate or bicornuate uterus, major myomectomy resection or previous open fetal surgery.
Fetal Surgery for MMC Repair

Criteria for VP Shunt Placement

- At least two of the following:
  - An increase in the greatest occipital-frontal circumference adjusted for gestational age defined as crossing percentiles. Patients who cross centiles and subsequently plateau do not meet this criteria
  - A bulging fontanelle (defined as above the bone assessed when the baby is in an upright position and not crying) or split sutures or sunsetting sign (eyes appear to look downward with the sclera prominent over the iris)
  - Head circumference >95th percentile for gestational age

or

- Presence of marked syringomyelia (syrinx with expansion of spinal cord) with ventriculomegaly (undefined).

or

- Ventriculomegaly (undefined) and symptoms of Chiari malformation (stridor, swallowing difficulties, apnea, bradycardia)

or

- Persistent cerebrospinal fluid leakage from the myelomeningocele wound or building at the repair site.
MOMS Trial:
Type I data that prenatal repair is better

Decrease in VP shunt rate at 1 year
Better neurologic level on exam
Better ambulation
Prenatal repair not for
MOMS Trial: Proof of Concept!

10 year moratorium on innovation
Early Gestation Fetoscopic Repair of MMC

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Early Gestation Fetoscopic Repair of MMC

Jose Peiro MD
Hospital Val Hebron Barcelona
Conclusions

- There is a need for more than the 3 MOMS trial centers

- Greater burden on new centers than MOMS centers

- Criteria for requirements for centers to start offering this treatment

- Safeguards for patients and the center and enhances informed consent

- Independent oversight is necessary

- Early gestation fetoscopic technique to prevent damage

- Europe will likely take the lead due to less regulatory burden