Disclosures

• None
Learning Objectives

• Describe the missions of the North American Fetal Therapy Network

• Recognize the power of collaborative research in studying rare congenital anomalies

• Evaluate outcomes after prenatal repair of myelomeningocele

• Compare treatment strategies for twin-to-twin transfusion syndrome
North American Fetal Therapy Network

SMFM Meeting 2004 Fetal Therapy Working Group

NIH 2004 Workshop on Fetal Therapy

‘Formation of a cooperative group of clinical investigators to help set up a national agenda for research and clinical progress in the field of fetal therapy’
NAFTNet Missions

- Foster collaborative research between active fetal centers in USA and Canada
- Develop a peer review mechanism for study proposals
- Centralize data collection and study development
- Establish an educational agenda for medical professionals and the public

Johnson MP. Semin Fetal Neonatal Med 2010
Annual Data Collection

- Detailed annual report
  - Diagnostic imaging procedures
  - Diagnostic procedures
  - Open fetal surgery cases
  - Fetal anomalies and interventions
- Composite data posted on website

Johnson MP. Semin Fetal Neonatal Med 2010
Peer Review of Study Proposals

- Concept proposal to Executive Committee
- Detailed proposal to Steering Committee
- NAFTNet centers obtain local IRB approval and participate
- PI uses letter of support to obtain funding

Johnson MP. Semin Fetal Neonatal Med 2010
Active Research Studies

1. Fetal MMC registry
2. Complicated monochorionic twin pregnancy registry
3. Indications for delivery for TTTS after SFLP
4. Natural history registry for prenatally diagnosed LUTO with normal amniotic fluid volume
5. Natural history of stage 1 TTTS
6. Pregnancy outcomes in monochorionic twin undergoing selective reduction
Fetal Repair of MMC Registry

- PI: Julie Moldenhauer, MD (CHOP)
- Prospective data registry (REDCap format)
- Objectives:
  - Maternal outcomes, including subsequent reproductive outcomes
  - Fetal/Neonatal outcomes, including physical and neurodevelopmental outcomes
- ~100-200 cases per year
Myelomeningocele

- Open neural tube defect
- 3.4 per 10,000 live births in the U.S.
- Lower extremity motor & sensory deficits
- Bowel and urinary incontinence
- Sexual dysfunction
- Cognitive impairment
- Chiari II malformation
- Hydrocephalus (70-90%)
A Randomized Trial of Prenatal versus Postnatal Repair of Myelomeningocele

Moms and infants go to assigned center

Prenatal group
- Admitted to MOMS center
- In utero repair
- Remain near center until delivery
- Deliver by CD @ 37wks if undelivered

Postnatal group
- Return home
- Return at 37wks to MOMS center for delivery by CD
- Postnatal closure within 48h

Adzick NS et al. NEJM 2011
A Randomized Trial of Prenatal versus Postnatal Repair of Myelomeningocele

Primary outcomes

- Death or need for VP shunt (12 months)
- Composite score of mental development and difference b/w motor & sensory level (30 months)

Secondary outcomes

- GA at delivery
- Hindbrain herniation
- Ambulation
- Placental abruption
- Pulmonary edema
- Hysterotomy site
- Fetal bradycardia

Adzick NS et al. NEJM 2011
MOMS Results

- Early termination of trial (183/200 patients)

Prenatal repair:

- Reduced need for VP shunt at 12 months (40% vs. 82%)
- Reduced hindbrain herniation at 12 months (4% vs. 36%)
- Significantly higher Bayley MDI scores at 30 months
- Doubles ability to walk without orthotics (42% vs. 21%)
- More likely to have a level of function that was two or more levels better than expected according to anatomic levels

Adzick NS et al. NEJM 2011
MOMS Results

Prenatal repair associated with maternal & fetal risks

- Preterm birth: 80% vs. 15%
- Fetal bradycardia during repair (10%)
- Oligohydramnios
- Chorioamniotic separation (26%)
- Thinning or uterine dehiscence at surgical site (35%)

Adzick NS et al. NEJM 2011
Post MOMS Experience at CHOP

- 100 fMMC repairs - Jan 2011 → Mar 2014
- Average GA: repair 23.4 weeks → delivery 34.3 weeks

<table>
<thead>
<tr>
<th>Delivery Outcomes</th>
<th>CHOP</th>
<th>MOMS</th>
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<tbody>
<tr>
<td>Membrane separation</td>
<td>22.9%</td>
<td>25.6%</td>
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<tr>
<td>PPROM</td>
<td>32.3%</td>
<td>46.2%</td>
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<tr>
<td>Preterm labor</td>
<td>37.5%</td>
<td>38.5%</td>
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<td>Hysterotomy at C/S</td>
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<tr>
<td>Intact</td>
<td>50.6%</td>
<td>64%</td>
</tr>
<tr>
<td>Thin</td>
<td>41.4%</td>
<td>25%</td>
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<table>
<thead>
<tr>
<th>Neonatal outcomes</th>
<th>CHOP</th>
<th>MOMS</th>
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<tbody>
<tr>
<td>Perinatal deaths</td>
<td>6.1%</td>
<td>3%</td>
</tr>
<tr>
<td>IUFD</td>
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<td>1</td>
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<tr>
<td>Neonatal deaths</td>
<td>4</td>
<td>1</td>
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<tr>
<td>Resp distress syndrome</td>
<td>51.8%</td>
<td>21%</td>
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<tr>
<td>Apnea</td>
<td>57.8%</td>
<td>36%</td>
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<tr>
<td>Shunt at discharge</td>
<td>2.4%</td>
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</tr>
<tr>
<td>No hindbrain herniation</td>
<td>71%</td>
<td>NR</td>
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Position statement on fetal myelomeningocele repair

MMC Maternal Fetal Management Task Force

- Established fetal therapy centers using a multidisciplinary approach
- Experienced fetal surgery team
- Adequate annual volume of open fetal and EXIT to maintain competency
- New centers must receive guidance and training
Position statement on fetal myelomeningocele repair

MMC Maternal Fetal Management Task Force

- Adherence to MOMS protocol
- Access to multi-disciplinary spina bifida clinics
- Non directive counseling with full disclosure
- Short term and long term outcomes data in a national registry
- Collaborative research between centers
Complicated Monochorionic Twin Pregnancy Registry

- PI: William Goodnight, MD (UNC Chapel Hill)
- Greg Ryan, MD (Toronto)- Chair, Database Committee
- MC twin pregnancies carry a disproportionate risk for adverse pregnancy complications
- Objectives: collect and analyze data
  - natural history
  - indications for fetal interventions
  - fetal/neonatal outcomes
Complicated Monochorionic Twin Pregnancy Registry

- Retrospective/Prospective data registry (REDCap format)
- Each NAFTNet center enters their data
- Each center ~ 50 patients annually
- Data:
  - TTTS
  - TAPS – twin anemia/polycythemia sequence
  - TRAP – twin reversed arterial perfusion
  - Conjoined twins
  - Monoamniotic twins
  - sIUGR – selective intrauterine growth restriction
Twin-to-Twin Transfusion Syndrome

- 5-15% of MC twin pregnancies
- 80-100% perinatal mortality, if left untreated especially if it presents prior to 20 weeks GA

Donor- oliguria, oligohydramnios, growth restriction and abnormal UA Doppler

Recipient- polyuria, polyhydramnios, abnormal venous Doppler, progressive TTTS cardiomyopathy
<table>
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<th>Stage</th>
<th>Donor</th>
<th>Recipient</th>
<th>Recipient Cardiomyopathy</th>
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<tr>
<td>I</td>
<td>Oligohydramnios</td>
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<tr>
<td>II</td>
<td>Bladder not visible</td>
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<tr>
<td>III</td>
<td>Abnormal Doppler</td>
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<tr>
<td>IIIIA</td>
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<td>Mild</td>
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<td>IIIIB</td>
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<tr>
<td>V</td>
<td>Death</td>
<td>Death</td>
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</tbody>
</table>
Treatment Options for TTTS

• Serial Amnioreduction
  - Improves uteroplacental blood flow
  - Variable results (37% to 83%)

• Microseptostomy of intertwin membrane
  - Restores amniotic fluid dynamics
  - Risk of monoamniotic sac & cord entanglement
Selective Fetoscopic Laser Photocoagulation

- Reserved for advanced TTTS
- Selective photocoagulation of direct a-a, v-v & unpaired a-v anastomosis
- Eurofetus trial
  - Higher survival in laser group
- NIH trial
  - no difference in 30 day survival
  - Advanced cases- poor prognosis
Summary

- NAFTNet represents a valuable paradigm in international collaborative research.
- Recognition of the power of cooperative research in studying rare congenital anomalies.
- Fetal MMC repair has become accepted as a standard of care option in selected patients.
- TTTS cardiomyopathy is central to the pathophysiology of TTTS and SFLP is an accepted treatment option.
Fetal Interventions:
Coming to a Center Near You

When: 3:00-5:00 pm, Saturday March 14, 2015

Faculty:

Anne C Boat- Cincinnati
Debnath Chatterjee- Colorado
Marla Ferschl- UCSF
Olutoyin A. Olutoye - Texas Children’s
Kha M Tran- CHOP