Management of children with spina bifida and hydrocephalus

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Management of children with Spina bifida and Hydrocephalus
Spina Bifida and Neural Tube Defects

- **Epidemiology**
  - One of the most common birth defects: 1-2 cases/1,000 births
    - Certain populations have a greater risk:
      - Highest incidence in Ireland and Wales
      - More common in girls
      - U.S.: 0.7/1,000 live births
      - Higher on the East Coast than on the West Coast
      - Higher in whites (1/1,000 births)
      - Lower in African-Americans (0.1-0.4/1,000 births)
Spina Bifida and Neural Tube Defects

- Epidemiology
  - Risk factors:
    - Race and ethnicity
    - Family history of neural tube defects
    - Folate deficiency
    - Medication/teratogenic effect: valproic acid
    - Maternal age
    - Diabetes
    - Obesity
    - Increased body temperature

Hol FA et al, Clinical Genetics, 2008
Management of children with spina bifida in the age of fetal intervention

- **Embryology of spina bifida**
  - **Weeks 3-4 of gestation**
    - “Primary Neurulation”
    - **Canalization**
  - **Weeks 6 – 10 of gestation**
    - “Secondary Neurulation:
      - **Retrogressive differentiation**
Embryology of the Filum terminale

- Around 6 weeks of gestation:
  Caudal extension of the spinal cord and "more" neural tube formation — "Secondary neurulation"

- Around 9 to 10 weeks of gestation:
  Cell necrosis causes a decrease in the size of the caudal neural tube and will form the Filum Terminale — Retrogressive differentiation
Spina Bifida and Neural Tube Defects

- **Definitions and Classification**
  - Open spina bifida (Aperta)
    - Meningocele in 5%
    - Myelomeningocele (cord and cauda equina exposed) in 95%
  - Closed spina bifida (Occulta)
    - 50% have cutaneous stigmata
    - Cord is tethered through abnormal FILUM
Management of children with spina bifida and hydrocephalus

- Can it be diagnosed in utero?
  - Magnetic Resonance Imaging
Surgical Aspects MMC closure
Spina Bifida and Neural Tube Defects

Definitive repair of the open neural tube defect
- Closure within 24 hours
- No evidence that immediate/urgent closure improves function
- But: early closure reduces risk of infection
  - Wound colonization after 36 hours

Surgical technique: (neurosurgeon + plastic surgeon team)
- Placode dissected off arachnoid
- Allowed to drop into spinal canal
- Dura dissected off skin and lumbodorsal fascia
- Dura closed
- Muscular fascia closed
- Skin closed
Spina Bifida and Neural Tube Defects

- Definitive repair of the open neural tube defect
  - No Repair of posterior vertebral defect
  - Thecal sac
  - Cord extruded into the sac (placode)
    - Plate of embryonic epithelial cells: spinal cord
Formal repair of MMC
Another Example:
Spina Bifida and Neural Tube Defects

- Pathophysiology and associated disorders
- Hydrocephalus
  - 80-95% incidence in myelomeningocele
    - 100% of 35 thoracic lesions
    - 88% of 114 lumbar lesions
    - 68% of 40 sacral lesions
  - Significant in 20% at birth

Rintoul et al, Pediatrics 2002
Spina Bifida and Neural Tube Defects

- Management of hydrocephalus
  - Serial head ultrasounds in the newborn:
Treatment of Hydrocephalus

Acute: *External ventricular drain*
Treatment of Hydrocephalus

Chronic

VENTRICULAR SHUNTS

- Ventriculoperitoneal
- Ventriculopleural
- Ventriculoatrial

Weight >2.5 kg
No active infection
Medically stable
What is a shunt made of?

5cm
Spina Bifida and Neural Tube Defects

- Management of hydrocephalus
  - Types of shunts:
    - Adjustable valves
Endoscopic 3rd ventriculoscopy for obstructive Hydrocephalus
Spina Bifida and Neural Tube Defects

- Clinical – which organ systems does it affect?
  - Neuro-motor
  - Neurodevelopmental, hydrocephalus, CNS development
  - Urogenital
  - Gastrointestinal
    - Gastroesophageal reflux disease (GERD)
    - Constipation
    - More commonly: incontinence
  - Variability in severity for all systems (GI specifically)
Current management of spina bifida: **Spina bifida clinic**

- Relatively recent: now that these children survive long-term
- The most difficult – chronic vigilance
- CNS monitoring:
  - **VP shunt management and Management of tethered cord (10%)**
- Physical therapy evaluation/motor function of lower extremities
- Preventive medicine – insensate lower body
- Psychological support
- Gastroesophageal reflux disease (GERD)
- Incontinence (urine and stool)
  - Rectum and bladder share parasympathetic (S2-S4) and sympathetic (L1-L3) nerve roots
  - Dysfunctional Elimination Syndrome (DES)
Spina Bifida and Neural Tube Defects

- Current management of spina bifida: SURGICAL

- Management of tethered cord: Second Detethering surgery for decline in function and/or before correction of scoliosis

Tethering at the MMC closure site

after surgery
Spina Bifida and Neural Tube Defects

- Pathophysiology and associated disorders
- Chiari II malformation
  - 99% of myelomeningocele have radiographic Chiari II
  - Only symptomatic ones require treatment (30% at 5 years)
  - Responsible for 15-20% of deaths in children with MMC
    - Respiratory failure/arrest
  - Syringomyelia
Peripheral effects of open neural tube defect

- Exposed spinal cord during gestation
- (Progressive?) damage to the exposed neural tube
- Variable paresis, urine & stool incontinence
- CSF leak into amniotic cavity
  - Basis for prenatal testing: leakage of alpha-fetoprotein (AFP)
Can it be prevented?

- Progressive development theory
  - Is only one theory – and the most simplistic one
  - Prolonged in utero exposure of the neural tube leads to
    - Chronic leakage of CSF
    - Gradual siphoning and hindbrain herniation
    - Increased risk of hydrocephalus
    - Progressive damage to the neural placode
    - Progressive peripheral nerve damage
      - Lower extremity function
      - Sphincter function
Animal experiments – Fetal sheep

- Creation of a neural tube defect in a mid-gestation lamb:
  - Leads to phenotype resembling clinical spina bifida
  - Causes hind limb paralysis
  - Causes hydrocephalus
Management of children with spina bifida in the age of fetal intervention

• Animal experiments – Fetal sheep
  o Creation of a neural tube defect in a mid-gestation lamb:
    ▶ Leads to phenotype resembling clinical spina bifida
    ▶ Causes hind limb paralysis
    ▶ Causes hydrocephalus
  o Closure of the defect in utero:
    ▶ Corrects all these problems

  o Caveat: because this is a surgical created, then corrected defect, it may not be the same as the clinical syndrome

Management of children with spina bifida in the age of fetal intervention

- Fetal surgery for spina bifida: from sheep to man
  - Proof of concept in animal model
  - Progress in fetal surgery for other indications
    - Endoscopic fetal surgery for Twin-to-twin Transfusion Syndrome
  - 1998: Vanderbilt reports on endoscopic repair of MMC
    - 2/4 survivors – technique abandoned

Management of children with spina bifida in the age of fetal intervention

Fetal surgery for spina bifida: from sheep to man

- Early 2000: anecdotal, then non-randomized series
  - Vanderbilt, CHOP, UCSF
  - In utero repair is feasible
  - Possible improvement over postnatal repair? Less hydrocephalus?
  - Final conclusion: it does NOT improve motor function
Management Of Myelomeningocele Study: The MOMS trial

- Started in 2003
  - Randomized to 3 prenatal centers or postnatal R/
  - Goal: 100 patients/arm
  - Prenatal closure at 19-25 weeks
  - All deliveries in a MOMS center
    - Vanderbilt, Nashville
    - University of California San Francisco
    - Children’s Hospital of Philadelphia
- Hypothesis:
  - Fetal repair delays hydrocephalus, prevents Chiari II
  - Not: Better chance of walking!
Management Of Myelomeningocele Study: The MOMS trial

- **Started in 2003**
  - Was supposed to take only 3 years
  - By 2010: Still only 140 patients recruited (of 200 needed)
  - Late 2011: Study suddenly stopped at 85% recruitment
    - Why? Because of better-than-expected results!

New York Times 2011
### Results (%)

<table>
<thead>
<tr>
<th></th>
<th>Fetal</th>
<th>Control</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shunt criteria met</td>
<td>65</td>
<td>92</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Shunt placed</td>
<td>40</td>
<td>82</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Hindbrain herniation</td>
<td>64</td>
<td>96</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Moderate or severe</td>
<td>25</td>
<td>67</td>
<td></td>
</tr>
<tr>
<td>Baylor Psychomotor</td>
<td>64.0</td>
<td>58.3</td>
<td>0.03</td>
</tr>
<tr>
<td>Walking unassisted</td>
<td>42</td>
<td>21</td>
<td>0.03</td>
</tr>
</tbody>
</table>

### Complications (%)

<table>
<thead>
<tr>
<th>Maternal complications</th>
<th>Fetal</th>
<th>Control</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulmonary edema</td>
<td>6</td>
<td>0</td>
<td>0.03</td>
</tr>
<tr>
<td>Placental abruption</td>
<td>6</td>
<td>0</td>
<td>0.03</td>
</tr>
<tr>
<td>Chorioamnionitis</td>
<td>3</td>
<td>0</td>
<td>0.24</td>
</tr>
<tr>
<td>Preecclampsia</td>
<td>4</td>
<td>0</td>
<td>0.12</td>
</tr>
<tr>
<td>Blood transfusion</td>
<td>9</td>
<td>1</td>
<td>0.03</td>
</tr>
</tbody>
</table>

### Complications

<table>
<thead>
<tr>
<th>Neonatal complications</th>
<th>Fetal</th>
<th>Control</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth weight (kg)</td>
<td>2.38</td>
<td>3.04</td>
<td>&lt;0.001</td>
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<tr>
<td>Respiratory distress (%)</td>
<td>21</td>
<td>6</td>
<td>0.001</td>
</tr>
<tr>
<td>Mean GA at birth (wk)</td>
<td>34.1</td>
<td>37.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Born &lt;30 wk (%)</td>
<td>13</td>
<td>0</td>
<td></td>
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<tr>
<td>Born 30-34 wk (%)</td>
<td>33</td>
<td>5</td>
<td></td>
</tr>
</tbody>
</table>

Management Of Myelomeningocele Study: The MOMS trial

### Complications (%)

<table>
<thead>
<tr>
<th>Pregnancy complications</th>
<th>Fetal</th>
<th>Control</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oligohydramnios</td>
<td>21</td>
<td>4</td>
<td>0.001</td>
</tr>
<tr>
<td>PROM</td>
<td>46</td>
<td>8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Uterine wound:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intact and healed</td>
<td>64</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Very thin</td>
<td>25</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Some dehiscence</td>
<td>10</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Management of children with spina bifida in the age of fetal intervention

- In utero repair of spina bifida: how is it done?
- Multidisciplinary team approach
  - Maternal Anesthesia
  - Maternal-Fetal Medicine
  - Pediatric Surgery
  - Pediatric Neurosurgery
  - Pediatric Plastic Surgery
  - Neonatalogy
In utero repair of spina bifida: how is it done?

Wide maternal laparotomy
- Full exposure of the uterus
Management of children with spina bifida in the age of fetal intervention

• In utero repair of spina bifida: how is it done?
• Partial exteriorization of the uterus
  ○ Ultrasound-guided mapping of the placenta, fetus
  ○ Stapled hysterotomy (preservation of membranes)
Management of children with spina bifida in the age of fetal intervention

- In utero repair of spina bifida: how is it done?
- Exposure of the neural tube defect
Management of children with spina bifida in the age of fetal intervention

- In utero repair of spina bifida: how is it done?
- Exposure of the neural tube defect
- Rapid closure
Post- vs. Prenatal repair

POSTNATAL challenges and conditions:

A) Separation of placode from Epithelium:
   - "trimming of the placode"
   - Use of surgical microscope

B) Preservation of the placode and vascular supply
   - "meticulous" hemostasis and microdissection
   - Use of surgical microscope

C) Anatomical reconstruction: Prevention of re-tethering, ischemia, CSF leak and infection!
   - Sufficient dissection of dural layer to prevent ischemia
   - Myofascial skin/subcutaneous fat dissection, preparation and closure important!

PRENATAL challenges and conditions:

A) YES,
   BUT much faster
   healthy spinal cord without epithelium, inflammation and infarction of placode, no trimming of the placode

B) YES,
   But NO significant dural vascular supply of placode ("bloodless")
   No use of surgical microscope!

C) NO!
   Only attempt to approximate DURA and SKIN (occasionally; Dural substitute and Skin substitute)

Counsel parents: Fetal repair is NOT formal and anatomical repair: Second Repair at birth or soon after necessary (e.g. skin breakdown etc.) and close watch for tethering

3 -4 hours!

0.5 hours!
MOMS II
- Further analysis of the results in the initial cohort
  - It improves motor function
- Does it improve GERD?
  - No real evidence (25% if shunted, v. 8% if not shunted)
- Does it improve continence?
  - No word yet – but the answer appears to be “no”
- Does it improve cognitive outcome?
  - No word yet – but the answer appears to be “no”
- Does it prevent/ Improve Tethering?
  - No word yet – but appears to be the opposite

Danzer E et al, Neuropediatrics 2008