Objectives

- Identify the latest neonatal research influencing care in the NICU:
  - In the delivery room
    - Cord Blood Gas Screening and HIE
    - Oxygen targeting and tidal volume
  - Respiratory interventions
    - Inhaled Budesonide
    - Inhaled Nitric Oxide
  - Blood Pressure and the Kidneys:
    - Isolated Hypotension to treat?
    - Acute Kidney Injury

Umbilical Cord Gases

- Delivery of an infant after induction of labor at 38 weeks gestation due to pregnancy induced hypertension. Labor and delivery are uneventful. Apgars 8/9.
- Do you send umbilical cord gases?
  1. Yes
  2. No
  3. Maybe

How do you detect infants with HIE?

- History
- Physical exam
TABLE 4-1 Clinical Staging of Hypoxic-Ischemic Encephalopathy

<table>
<thead>
<tr>
<th>Variable</th>
<th>Stage I</th>
<th>Stage II</th>
<th>Stage III</th>
</tr>
</thead>
<tbody>
<tr>
<td>Level of consciousness</td>
<td>Alert</td>
<td>Hypotonic</td>
<td>Comatose</td>
</tr>
<tr>
<td>Muscle tone</td>
<td>Normal or hypertonic</td>
<td>Rigid</td>
<td>Flaccid</td>
</tr>
<tr>
<td>Tonic reflexes</td>
<td>Increased</td>
<td>Increased</td>
<td>Absent</td>
</tr>
<tr>
<td>Flexor reflexes</td>
<td>Present</td>
<td>Present</td>
<td>Absent</td>
</tr>
<tr>
<td>Seizures</td>
<td>Absent</td>
<td>Absent</td>
<td>Absent</td>
</tr>
<tr>
<td>Complex Seizures</td>
<td>Absent</td>
<td>Absent</td>
<td>Absent</td>
</tr>
<tr>
<td>Brainstem</td>
<td>Absent</td>
<td>Absent</td>
<td>Absent</td>
</tr>
<tr>
<td>Autonomic function</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blood pressure</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heart rate</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Met all criteria: 412

To Detect Moderate/Severe Encephalopathy

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH ≤ 7.10</td>
<td>74.2 %</td>
<td>98.7 %</td>
</tr>
<tr>
<td>pH &lt; 7.00</td>
<td>37.6 %</td>
<td>99.8 %</td>
</tr>
<tr>
<td>Base Deficit ≥ 12</td>
<td>30.1 %</td>
<td>99.3 %</td>
</tr>
<tr>
<td>Base Deficit ≥ 16</td>
<td>10.8 %</td>
<td>98.9 %</td>
</tr>
</tbody>
</table>

Umbilical Cord Gases

- Delivery of an infant after induction of labor at 38 weeks gestation due to pregnancy induced hypertension. Labor and delivery are uneventful. Appars 8/9.
- Do you send umbilical cord gases?
  1. Yes
  2. No
  3. Maybe

Umbilical Cord Gases

- Delivery of an infant after induction of labor at 38 weeks gestation due to pregnancy induced hypertension. Labor and delivery are uneventful. Appars 8/9.
- Do you send umbilical cord gases?
  1. Yes
  2. No
  3. Maybe

Retrospective Cohort

- One institution — 2008-2015
  - Standard practice of universal cord gas testing on ALL LIVE BIRTHS
  - IF Arterial Cord Blood Gas pH ≤ 7.1
    - Neonatologist is notified
    - Mandatory Encephalopathy screening for first 6 hours of life
    - Therapeutic Hypothermia if encephalopathic exam
  - > 36 weeks gestation
  - Out of 27,028, only 560 (2%) of births with pH ≤ 7.1
  - 412 met all study criteria

You are called to a delivery

- Infant is 26 weeks gestation to be born via SVD due premature rupture of membranes and progressive labor.

- When setting up your ventilation equipment and the likely need for positive pressure ventilation, what settings do you plan to use?
  - A. PIP 16 PEEP 4
  - B. PIP 20 PEEP 5
  - C. PIP 24 PEEP 6
  - D. PIP 28 PEEP 8

Tidal Volume in the Delivery Room

- Observational Study at one center in Canada
- Infants < 29 weeks who received PPV for at least 2 minutes
- Measure Tidal Volume delivered to infants in DR with T-piece with fixed PIPs of 24 and PEEP of 6.
  - Started at FiO2 of 30%

What they found:

- 75% received a high TV >6mL/kg (124 patients)
- 25% received a TV <6mL/kg (41 patients)

TV in the DR and Brain Injury

<table>
<thead>
<tr>
<th>IVH</th>
<th>TV &lt;6mL/kg</th>
<th>Total 41</th>
<th>TV &gt;6mL/kg</th>
<th>Total 124</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Grades</td>
<td>5(13%)</td>
<td>63(51%)</td>
<td>0.008</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade I</td>
<td>2(5%)</td>
<td>30(24%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade II</td>
<td>1(2%)</td>
<td>8(7%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade III</td>
<td>0(0%)</td>
<td>3(2%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade IV</td>
<td>2(5%)</td>
<td>22(18%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe IVH</td>
<td>2(6%)</td>
<td>53(27%)</td>
<td>0.01</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade III or IV</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

You are called to a delivery

- Infant is 26 weeks gestation to be born via SVD due premature rupture of membranes and progressive labor.

- When setting up your ventilation equipment and the likely need for positive pressure ventilation, what settings do you plan to use?
  - A. PIP 16 PEEP 4
  - B. PIP 20 PEEP 5
  - C. PIP 24 PEEP 6
  - D. PIP 28 PEEP 8
Inhaled Budesonide for Preterm Infants

- RCT of 863 infants 23 weeks 0 days to 27 weeks 6 days
  - European study
- Randomized to early inhaled budesonide or placebo

Results

- Long term Neurodevelopmental impairment at 18-22 months – no difference
- BPD:
  - Budesonide had lower BPD rate of 28.2% vs. 37.4% for placebo group (p=0.01)
- Mortality
  - Budesonide had higher mortality rate of 19.9% vs. 14.5% for placebo group (p=0.04)

iNO as a vasodilator

- Retrospective cohort study of 22-29 week gestational age from 2004-2014
- Infants who received iNO in the first 7 days and case matched cohorts
- Results: Only 2.6% (993) of infants received iNO within the first 7 days
  - Infants who received iNO compared to the 39,916 who did not:
    - Less antenatal steroids
    - More PROM
    - More PPHN
    - More HFOV
    - More vasopressor therapy
Conclusion:

- The use of inhaled nitric oxide in preterm infants (22-29 weeks):
  - Does NOT improve mortality for infants with PPHN
  - is associated with increased mortality in infants with RDS without a diagnosis of PPHN.

Blood Pressure and the Kidneys

Neonatal Hypotension: To treat or not to treat?
- Extremely low birth weight infants frequently ~ 50% of the time have hypotension
- Can we have permissive hypotension?

The 26 week infant earlier:
Was intubated in the delivery room and given surfactant. Admitted to the NICU with umbilical lines placed. About 12 hours of life, the infant’s mean blood pressure is now 22 via umbilical arterial line correlating with cuff BP. The infant does not have any other signs of hemodynamic compromise.

What do you do?
A. Continue to monitor
B. Give 10mL/kg Normal saline bolus slowly
C. Start dopamine at 5 mcg/kg/min
D. B then C

EPIPAGE 2 Cohort
- French prospective study followed preterm infants 24-28 weeks gestation and at least one episode of hypotension in the first 72 hrs.
- Recruitment in 2011 in 60 NICUs
- Analyzed infants who received hypotension treatments like fluid resuscitation, inotropes or corticosteroids
- Matched cohorts
Total = 1633

Results

The 26 weeker

- 14 days of life - reintubated for mixed respiratory and metabolic acidosis
- Sepsis work up - cloxacillin, gent, and normal saline bolus
  - + culture for CONS got vancomycin X 7 days
- Creatinine went from 0.3 to max 0.8, then declined back to 0.3

Is this Acute Kidney Injury? Yes or No
Definition of AKI

Table 1. Definition of Acute Kidney Injury by Serum Creatinine and Urine-Output

<table>
<thead>
<tr>
<th>Stage</th>
<th>Serum creatinine</th>
<th>UOP over 24 hours</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No change in serum creatinine or rise &lt; 0.3 mg/dL</td>
<td>≥ 1 mL/kg/hour</td>
</tr>
<tr>
<td>1</td>
<td>SCR rise ≥ 0.3 mg/dL within 48 hours or SCR rise ≥ 2 x the reference SCR* within 48 hours</td>
<td>≥ 5 and &lt; 1 mL/kg/hour</td>
</tr>
<tr>
<td>2</td>
<td>SCR rise ≥ 2 x the reference SCR* or SCR rise ≥ 2 x the reference SCR* with a fall in SCR ≥ 0.5 mg/dL within 48 hours</td>
<td>0.5 to &lt; 0.3 mL/kg/hour</td>
</tr>
<tr>
<td>3</td>
<td>SCR rise ≥ 3 x the reference SCR* or SCR rise ≥ 2 x the reference SCR* with a fall in SCR ≥ 0.5 mg/dL within 48 hours</td>
<td>&lt; 0.3 mL/kg/hour</td>
</tr>
</tbody>
</table>

*Reference SCR is the lowest post 5 SCR measurement

Results:
AKI occurred in 605/2022 (30%)

The 26 weeker
- 14 days of life - reintubated for mixed respiratory and metabolic acidosis
- Sepsis work up - cloxacillin, gent, and normal saline bolus
  - + culture for CONS got vancomycin X 7 days
- Creatinine went from 0.3 to max 0.8, then declined back to 0.3

Is this Acute Kidney Injury?
Yes or No

Conclusions
- In the delivery room
  - Obtaining umbilical cord gases at all deliveries can identify more infants who would benefit from therapeutic hypothermia
  - Monitor the pressures delivered in the delivery room
- Respiratory interventions
  - Early use of inhaled budesonide is associated with lower rates of BPD, but high mortality
  - Off label use of inhaled iNO in the preterm infants does not improve survival
- Blood Pressure and the Kidneys:
  - Treatment of isolated hypotension in premature infants does not improve survival with severe morbidity.
  - Acute Kidney Injury in Neonates is Common associated with higher mortality

References:

Figure 4. Survival Outcomes
Survival curves for the entire cohort by any AKI (A) and by stages of AKI (B). *Survival was worse in infants with AKI than in those without AKI. Survival was worse in infants with stage 3 AKI than in those with Stage 2, 1 or no AKI.
Thank you!