Antenatal Corticosteroids: Expanding the Indications to Late Preterm Pregnancy and Beyond?

Cynthia Gyamfi, MD
22nd Annual NICHD Aspen Conference
August 26, 2010
Liggins and Howie, 1972

• Initial observation in sheep of accelerated lung maturity
• Randomized pts to betamethasone or placebo with low dose of hydrocortisone
• Dose arbitrarily chosen
### Incidence of RDS Related to Entry Delivery Interval

<table>
<thead>
<tr>
<th></th>
<th>Betamethasone</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>RDS (%)</td>
</tr>
<tr>
<td>Under 24 hrs</td>
<td>77</td>
<td>25%</td>
</tr>
<tr>
<td>24 hr - 7 days</td>
<td>182</td>
<td>8.8</td>
</tr>
<tr>
<td>&gt;7 days</td>
<td>172</td>
<td>5.0%</td>
</tr>
</tbody>
</table>

Liggins and Howie, 1972
## Beneficial Effects of Antenatal Corticosteroids

<table>
<thead>
<tr>
<th>Condition</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>RDS</td>
<td>0.5</td>
<td>0.4-0.6</td>
</tr>
<tr>
<td>Neonatal Mortality</td>
<td>0.6</td>
<td>0.5-0.8</td>
</tr>
<tr>
<td>IVH</td>
<td>0.4</td>
<td>0.2-0.9</td>
</tr>
</tbody>
</table>
NIH Consensus Conference 1994

- NICHD along with other NIH branches
- Reviewed literature on use of ACS
- Recommended that ACS use be standard of care
Requirements For Rapid Transition To Adult Breathing

• Lung Structure capable of diffusing oxygen from alveoli to capillaries
• Alveoli capable of remaining expanded with air
• Low resistance vasculature system
• Rapid removal of lung fluid
Steroids in Preparing the Fetal Lung for Adult Breathing

**Induction of Proteins and Enzymes**
- Increased Tissue and Alveolar Surfactant
- Accelerated antioxidant production
- Induction of $\beta$-receptor expression in Alveolar cells

**Induced Structural Changes**
- More mature parenchymal structure
- Increased compliance and maximal lung volume
- Decreased vascular permeability

Immature Lung

Mature Lung
Preparing for Birth
Alveolar Salt Transport

Term labor
Catecholamines
Oxygen
Steroids

Salt and Water

ENaC = Epithelial Sodium Channels
Quandaries in Antenatal Steroid Use: 2010

- Betamethasone vs. Dexamethasone?
- Is the Dose of corticosteroid optimal?
- Does the effect vary by obstetrical condition?
- Does the Beneficial Effect of treatment diminish with Time
  - Benefits and Risks of Repeat Dosing
- Should the Treatment Window be Expanded
  - Under 24 weeks
  - Over 34 weeks
Extreme Prematurity Revisited

April, 2008


Hayes, et.al. Obstet Gynecol 2008

- Retrospective cohort study
- Neonates born at 23 0/7 to 23 6/7 wks
- Dated by LMP c/w sonographic dating
- Survived to NICU admission
- Compared neonatal outcomes by steroid exposure
Results

- 149 mothers/181 neonates
- 63 mothers received steroids; 32 complete, 31 partial
- 181 neonates
  - 66 died in DR
  - 115 survived to NICU admission
  - 20 survived to discharge (11% survival)
### Results: Reduction in death

<table>
<thead>
<tr>
<th>Exposure to steroids</th>
<th>OR</th>
<th>95% CI</th>
<th>Reduction in odds</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any</td>
<td>0.32</td>
<td>0.12-0.84</td>
<td>68%</td>
</tr>
<tr>
<td>Partial</td>
<td>0.61</td>
<td>0.17-2.24</td>
<td>39%</td>
</tr>
<tr>
<td>Complete</td>
<td>0.18</td>
<td>0.06-0.54</td>
<td>82%</td>
</tr>
</tbody>
</table>
Recent data, Neonatal Network


- Prospective cohort
- Evaluate when to offer “intensive care”
- Neonatal Network Study (19 centers)
- Neonates born at 22 0/7 to 25 6/7 wks
- Dated by “best obstetric estimate”
- Included only those who required mechanical ventilation, considered “intensive care”
## Results: Death

<table>
<thead>
<tr>
<th>Variables</th>
<th>Odds Ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>GA</td>
<td>0.62</td>
<td>0.53-0.74</td>
</tr>
<tr>
<td>25 v. 24 wks</td>
<td>0.62</td>
<td>0.53-0.74</td>
</tr>
<tr>
<td>24 v. 23 wks</td>
<td>0.61</td>
<td>0.52-0.73</td>
</tr>
<tr>
<td>23 v. 22 wks</td>
<td>0.54</td>
<td>0.32-0.92</td>
</tr>
<tr>
<td>Birth weight</td>
<td>0.60</td>
<td>0.55-0.65</td>
</tr>
<tr>
<td>Female sex</td>
<td>0.64</td>
<td>0.55-0.75</td>
</tr>
<tr>
<td>ACS</td>
<td>0.55</td>
<td>0.45-0.66</td>
</tr>
<tr>
<td>Singleton</td>
<td>0.77</td>
<td>0.65-0.92</td>
</tr>
</tbody>
</table>
# Results: Death or profound impairment

<table>
<thead>
<tr>
<th>Variables</th>
<th>Odds Ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>GA</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>25 v. 24 wks</td>
<td>0.66</td>
<td>0.55-0.78</td>
</tr>
<tr>
<td>24 v. 23 wks</td>
<td>0.58</td>
<td>0.46-0.73</td>
</tr>
<tr>
<td>23 v. 22 wks</td>
<td>0.50</td>
<td>0.26-0.98</td>
</tr>
<tr>
<td><strong>Birth weight</strong></td>
<td>0.61</td>
<td>0.56-0.66</td>
</tr>
<tr>
<td><strong>Female sex</strong></td>
<td>0.55</td>
<td>0.48-0.65</td>
</tr>
<tr>
<td><strong>ACS</strong></td>
<td><strong>0.54</strong></td>
<td><strong>0.44-0.66</strong></td>
</tr>
<tr>
<td><strong>Singleton</strong></td>
<td>0.76</td>
<td>0.64-0.91</td>
</tr>
</tbody>
</table>
### Results: Death or impairment

<table>
<thead>
<tr>
<th>Variables</th>
<th>Odds Ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>GA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>25 v. 24 wks</td>
<td>0.70</td>
<td>0.59-0.84</td>
</tr>
<tr>
<td>24 v. 23 wks</td>
<td>0.56</td>
<td>0.42-0.74</td>
</tr>
<tr>
<td>23 v. 22 wks</td>
<td>0.56</td>
<td>0.22-1.44</td>
</tr>
<tr>
<td>Birth weight</td>
<td>0.61</td>
<td>0.56-0.66</td>
</tr>
<tr>
<td>Female sex</td>
<td>0.48</td>
<td>0.41-0.56</td>
</tr>
<tr>
<td>ACS</td>
<td><strong>0.53</strong></td>
<td><strong>0.42-0.66</strong></td>
</tr>
<tr>
<td>Singleton</td>
<td>0.70</td>
<td>0.58-0.85</td>
</tr>
</tbody>
</table>
The Late Preterm Infant: 34 0/7 to 36 6/7 wks

- Peak Shifted: 40 to 39 weeks
- Late Preterm: 34 0/7 to 36 6/7

Source: NCHS, final natality data
Prepared by March of Dimes Perinatal Data Center, April 2006.
US preterm births: Change 1992-02

MOD: Davidoff 2005
Increasing incidence of late preterm birth

* % US Singleton live births

Tomashek et al, J Peds, 2007; CDC
Increase in LP birth per state


NOTE: Singleton births only.
Late preterm birth by plurality, 2005

Percent of live births

Peristats, March of Dimes, 2008
Late preterm birth: singletons

Percent of live births


Percent: 7.0, 6.9, 7.2, 7.3, 7.4, 7.3, 7.6, 7.6, 7.8, 7.9, 8.1

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Late preterm birth: multiples

Percent of live births

- 1995: 33.2
- 1996: 33.7
- 1997: 34.6
- 1998: 35.1
- 1999: 36.0
- 2000: 35.9
- 2001: 36.3
- 2002: 36.6
- 2003: 37.4
- 2004: 37.7
- 2005: 37.8

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US Late Preterm Singleton Births

- <32 weeks: 14%
- 32 weeks: 7%
- 33 weeks: 5%
- 34 weeks: 13%
- 35 weeks: 13%
- 36 weeks: 22%

75% of all pts!

Source: NCHS, final natality data
Prepared by March of Dimes Perinatal Data Center, April 2006.
Late preterm infants populate the NICU

Estimated Gestational Age (wks)

Clark R et.al, Pediatrix Database, 2005
Morbidity in LP infants

Safe Labor Consortium, JAMA, 2010

Objective: characterize short-term LP respiratory morbidity compared to term infants

Late preterm: 34 0/7 to 36 6/7 weeks

Retrospective cohort

8 years (2002-2008)
IVH, Grade 1 or 2

McIntire and Leveno, Obstet Gynecol, 2008;111:35-41
Culture-proven sepsis

McIntire and Leveno, Obstet Gynecol, 2008;111:35-41
Phototherapy

McIntire and Leveno, Obstet Gynecol, 2008;111:35-41
McIntire and Leveno, Obstet Gynecol, 2008;111:35-41
Ventilator use in LP infants compared to 39 wk infants

McIntire and Leveno, Obstet Gynecol, 2008;111:35-41

p<0.001
# Respiratory Morbidities Across Late Preterm & Term Gestations

## Table 4. Multivariate Logistic Regression Comparing Morbidities Across Gestational Ages

<table>
<thead>
<tr>
<th>Gestational Age, wk</th>
<th>RDS/HMD</th>
<th>Transient Tachypnea of the Newborn</th>
<th>Pneumonia</th>
<th>Respiratory Failure</th>
<th>Surfactant</th>
<th>Ventilator</th>
<th>Oscillator</th>
</tr>
</thead>
<tbody>
<tr>
<td>38</td>
<td>1.1 (0.9-1.4)</td>
<td>1.0 (0.8-1.2)</td>
<td>0.9 (0.6-1.2)</td>
<td>1.4 (1.0-1.9)</td>
<td>1.1 (0.8-1.4)</td>
<td>1.2 (1.0-1.5)</td>
<td>0.9 (0.6-1.3)</td>
</tr>
<tr>
<td>37</td>
<td>3.1 (2.5-3.7)</td>
<td>2.5 (2.1-3.0)</td>
<td>1.7 (1.3-2.4)</td>
<td>2.8 (2.0-3.9)</td>
<td>4.8 (3.8-6.1)</td>
<td>2.8 (2.3-3.4)</td>
<td>2.8 (2.0-3.9)</td>
</tr>
<tr>
<td>36</td>
<td>9.1 (7.5-11.1)</td>
<td>6.1 (5.1-7.4)</td>
<td>3.6 (2.6-4.9)</td>
<td>6.2 (4.4-8.6)</td>
<td>16.1 (12.7-20.4)</td>
<td>7.3 (6.0-8.8)</td>
<td>7.1 (5.1-9.9)</td>
</tr>
<tr>
<td>35</td>
<td>21.9 (17.8-26.9)</td>
<td>11.1 (9.1-13.6)</td>
<td>6.6 (4.7-9.3)</td>
<td>4.9 (3.2-7.6)</td>
<td>35.2 (27.1-45.6)</td>
<td>9.8 (7.9-12.1)</td>
<td>12.3 (8.5-17.7)</td>
</tr>
<tr>
<td>34</td>
<td>40.1 (32.0-50.3)</td>
<td>14.7 (11.7-18.4)</td>
<td>7.6 (5.2-11.2)</td>
<td>10.5 (6.9-16.1)</td>
<td>58.5 (44.1-77.6)</td>
<td>13.9 (11.0-17.6)</td>
<td>18.8 (12.6-28.1)</td>
</tr>
</tbody>
</table>

Abbreviation: RDS/HMD, respiratory distress syndrome/hyaline membrane disease.

*Adjusted for onset of labor, mode of delivery, number of fetuses, medical disorders, substance abuse, race, body mass index at delivery, birth weight, sex, anomalous infants, and hospital.*
Adjusted Odds of RDS by GA at Birth

The Consortium on Safe Labor, JAMA 2010;304:419-425.
CS and Labor Induction Rates United States, 1992 and 2002

Source: NCHS, final natality data
Prepared by March of Dimes Perinatal Data Center, April 2006.
Not All Respiratory Distress in Late Preterm Infants is Benign

Clark R et.al, Pediatrx Database, 2005
Healthcare Burden

Discharge Delays: 42% LP VS 5% at term

Mean difference in the cost of care for a late preterm infant: $3877

US projections based on 9.1% LP rate:

$1.4 billion dollars

Wang et al, Pediatr 114:372, 2004

McIntire and Leveno, Obstet Gynecol, 2008;111:35-41
Neonatal Mortality Rates

*p<0.001, †p=0.02

McIntire D, Leveno K. Obstet Gynecol, 2008;111:37-41
Mortality in Late Preterm Infants

Late Preterm births: 2,221,545 (7.3%)
Late Preterm deaths: 18,484 (9.8%)

Mortality in late preterm infants:
- Early Neonatal (0-6 d) Mortality: 6 x Term
- Late Neonatal (7-28 d) Mortality: 2 x Term
- Infant Mortality (birth – 1 year): 3 x Term

Higher risk persists even after excluding congenital anomalies

Tomashek et al, J Peds. 2007;151:460-6
What About Long Term Outcomes?

White and gray matter follow different tempos of maturation with only 65% of term brain volume at 34 wks.


Late Preterm infants (33-37 weeks) account for 74% of adult disability in Sweden at 23-29 yrs age (n=522,310)

*(Lindstrom K et al Pediatr 120:70,2007)*
Long term data on disabilities

Longitudinal cohort, linked national database
903,402 infants, born 1967 to 1983
Followed to 2003
Documented medical disabilities and outcomes related to social performance
## Medical Disabilities by GA

<table>
<thead>
<tr>
<th></th>
<th>31’0 – 33’6</th>
<th>34’0 – 36’6</th>
<th>≥37 wks</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CP</td>
<td>14.1</td>
<td>2.7</td>
<td>1.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mental retardation</td>
<td>2.1</td>
<td>1.6</td>
<td>1.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Psychosocial disorders</td>
<td>1.4</td>
<td>1.5</td>
<td>1.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Other disabilities</td>
<td>2.3</td>
<td>1.5</td>
<td>1.0</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Early School-Age Outcomes of LP Infants in FL (n=161,804)

<table>
<thead>
<tr>
<th>Early school-age outcome</th>
<th>Healthy Late Preterm (%)</th>
<th>Term (%)</th>
<th>Adjusted RR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Developmental delay/disability</td>
<td>4.24</td>
<td>2.96</td>
<td>1.36 (1.29-1.43)</td>
</tr>
<tr>
<td>Disability in pre-kindergarten</td>
<td>7.40</td>
<td>6.60</td>
<td>1.10 (1.05-1.14)</td>
</tr>
<tr>
<td>Not ready to start school</td>
<td>5.09</td>
<td>4.40</td>
<td>1.04 (1.00-1.09)</td>
</tr>
<tr>
<td>“Special needs” education</td>
<td>13.30</td>
<td>11.88</td>
<td>1.10 (1.07-1.13)</td>
</tr>
<tr>
<td>Retention in kindergarten</td>
<td>7.96</td>
<td>6.17</td>
<td>1.11 (1.07-1.15)</td>
</tr>
<tr>
<td>Suspension in kindergarten</td>
<td>1.80</td>
<td>1.22</td>
<td>1.19 (1.10-1.29)</td>
</tr>
</tbody>
</table>

Why are we delivering LP pregnancies?

Spontaneous PTB
Indicated PTB
*Elective* PTB?
Non-spontaneous, non-indicated (NS/NI) PTB
Columbia Data: Indication for Delivery in the LP Infant 2005-06

<table>
<thead>
<tr>
<th></th>
<th>Spontaneous (PTL, PPROM)</th>
<th>Indicated (NRFHT, severe preeclampsia/HELLP, abruption, previa)</th>
<th>Elective (NS/NI) (Repeat C/S, IUGR w/ normal testing, oligo, multiples)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Count</td>
<td>229/548</td>
<td>155/548</td>
<td>164/548</td>
</tr>
<tr>
<td>Percentage</td>
<td>41.8%</td>
<td>28.3%</td>
<td>29.9%</td>
</tr>
</tbody>
</table>
UT Houston Data: Indication for Delivery in the LP Infant 2007-08

<table>
<thead>
<tr>
<th></th>
<th>Indicated</th>
<th>Elective (NS/NI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spontaneous (PTL, PPROM)</td>
<td>(NRFHT, severe preeclampsia/HELLP, abruption, previa, Repeat C/S, IUGR w/ normal testing)</td>
<td></td>
</tr>
<tr>
<td>277/514</td>
<td>155/514</td>
<td>42/514</td>
</tr>
<tr>
<td>53.9%</td>
<td>37.9%</td>
<td>8.2%</td>
</tr>
</tbody>
</table>

Holland M et al, AJOG. 2009;201:404.e1-4
Spontaneous LP birth

PTL

- No RCTs for LP PTL
- Concern for infection as etiology of PTL
- Standard of care
  - Related to efficacy of steroids
  - NIH: low risk of RDS, IVH, NEC >34 wks
  - ACOG: no steroids >34 wks
Spontaneous LP birth

PPROM

- Concern for infection as etiology of PPROM
- Neonatal sepsis
- Chorioamnionitis
Expectant Management of LP PPROM?

PPROM

- Spinnato et al., Obstet Gynecol 1987 (<36 wks)
  - Increased chorioamnionitis, ?neonatal sepsis
- Mercer et al., AJOG 1993 (32-36\(^6\) wks)
  - Increased chorioamnionitis, no increase in neonatal sepsis
- Naef et al., AJOG 1998 (34-37 wks)
  - Increased chorioamnionitis, no increase in neonatal sepsis
PPROMT Trial

• Morris et al., BMC Pregnancy and Childbirth
  – Published a protocol for a planned clinical trial
    • PPROM @ 34-37 wks, expectant management
  – Randomized, controlled trial $34^0-36^6$ wks
    • Sample size 1,812
    • Randomized to planned birth or expectant management
    • Primary outcome: neonatal sepsis
Upper limit of gestational age for *empiric delivery* of PPROM among MFM providers

Ramsey PS, AJOG, 2004
Indicated LP birth

- 25% of all preterm birth
  - Acute abruption: 7%
  - Severe preeclampsia: 40%
  - Nonreassuring fetal status: 25%
  - Other (elective? [NS/NI]): 29%
Non-spontaneous, non-indicated (Elective) LP delivery

- Mild preeclampsia
- Twin gestation
- Repeat cesarean delivery
  - Prior classical cesarean
  - Prior myomectomy
- IUGR with reassuring testing
- Oligohydramnios
Hypertensive Disorders of Pregnancy

- Chronic hypertension (CHTN)
- Preeclampsia/Eclampsia
  - Mild
  - Severe (Increased certainty of diagnosis)
- Preeclampsia superimposed on CHTN
- Gestational Hypertension

National High BP Education Program Working Group on High BP in Pregnancy; AJOG 2000

- 12.4% LP v. 4.0% 39 wks, P<0.001

McIntire D, Leveno K. Obstet Gynecol, 2008;111:37-41
Indications for delivery (Expert Opinion)

- Severe hypertension/preeclampsia
- PTL or PPROM
- IUGR or oligohydramnios
- Vaginal bleeding
- Abnormal fetal testing
  - Variable or late decels
  - AEDF or REDF
  - BPP \leq 6

Sibai, Semin Perinatol, 2006;30:16-19
## Potential risks of expectant management of LP mild PEC

<table>
<thead>
<tr>
<th>Complication</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eclampsia</td>
<td>0.5</td>
</tr>
<tr>
<td>HELLP</td>
<td>2-3</td>
</tr>
<tr>
<td>Abruption</td>
<td>1-2</td>
</tr>
<tr>
<td>Pulmonary edema</td>
<td>&lt;1</td>
</tr>
<tr>
<td>IUGR</td>
<td>10-12</td>
</tr>
<tr>
<td>Fetal death</td>
<td>0.5</td>
</tr>
</tbody>
</table>

*Sibai, Semin Perinatol,2006;30:16-19*
<table>
<thead>
<tr>
<th>Variable</th>
<th>35 weeks</th>
<th>36 weeks</th>
<th>37 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>NICU Admission</td>
<td>57.1%</td>
<td>33.3%</td>
<td>12.8%</td>
</tr>
<tr>
<td>NICU Stay (d)</td>
<td>5.3 ± 4.0</td>
<td>10.3 ± 8.6</td>
<td>5.7 ± 5.0</td>
</tr>
<tr>
<td>Total Stay (d)</td>
<td>4.9 ± 4.9</td>
<td>5.5 ± 4.8</td>
<td>3.9 ± 3.6</td>
</tr>
<tr>
<td>RDS</td>
<td>3.6%</td>
<td>9.5%</td>
<td>7.0%</td>
</tr>
<tr>
<td>Respiratory Support (O2/CPAP/vent)</td>
<td>28.6%</td>
<td>19.1%</td>
<td>15.1%</td>
</tr>
</tbody>
</table>

Twin Gestations

- Monochorionic (MC) v. dichorionic (DC)
- Barigye et al., PLoS Med 2005
  - 151 apparently normal MC twins
  - 4.6% fetal death >24 wks
  - 1/23 risk of IUFD >32 wks
- Hack et al, BJOG 2008
  - IUFD >20 wks: 7.6% MC v. 1.5% DC
  - IUFD >32 wks 8-fold increase MC twins
## Multiples and RDS

<table>
<thead>
<tr>
<th>Study</th>
<th>RR for RDS</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liggins 1972</td>
<td>0.63</td>
<td>0.29, 1.35</td>
</tr>
<tr>
<td>Collaborative</td>
<td>0.98</td>
<td>0.54, 1.77</td>
</tr>
<tr>
<td>1981</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gamsu 1989</td>
<td>0.44</td>
<td>0.02, 8.35</td>
</tr>
<tr>
<td>Silver 1996</td>
<td>0.97</td>
<td>0.65, 1.46</td>
</tr>
<tr>
<td>Total:</td>
<td>0.85</td>
<td>0.60, 1.20</td>
</tr>
</tbody>
</table>

167 cases, 153 controls  

Cochrane Database, 2006
NS/NI (Elective) Delivery

- **IUGR**
  - Delivery with non reassuring testing
  - Absence of fetal growth

- **Oligohydramnios**
  - Deliver at term; follow with testing
  - Term RCT suggests delivery can be delayed

- **Prior classical cesarean**
  - Deliver prior to onset of labor

- **Prior myomectomy**
  - GA at delivery?
“But I verified fetal lung maturity...”

Late preterm morbidity is more than RDS
Neonatal transition in the late preterm infant

Surfactant deficiency is *NOT* the only cause of respiratory distress in newborns

AF testing does not accurately predict respiratory distress from other causes

Delayed fetal lung fluid clearance is a significant part of RDS pathophysiology
Fetal Lung Fluid Dynamics

Bland RD, AJOG, 1979, 80.
Preparing for Birth
Alveolar Salt Transport

Term labor
Catecholamines
Oxygen
Steroids

Salt and Water

ENaC = Epithelial Sodium Channels
Effect of Steroid Depletion on Na Channels in AT2 Cells

Without Steroids

With Steroids

HSC

NSC

Impact of steroid exposure in late preterm infants

Rate of NICU admission among infants who received steroids at < 34 weeks and delivered 34 – 37 weeks:

- Steroid Exposed: 24%
- Steroid Unexposed: 81%

p < 0.0001

Steroids at >34 weeks and Fetal Lung Maturity Profiles

Shanks A et al, AJOG, 2010

- Randomized 32 women with neg FLM to steroids or no rx
- Repeated FLM studies in one week
- Significant increase in maturity indices

Shanks A et al. AJOG 2010;203 epub ahead of print
Can antenatal steroids reduce neonatal morbidity in TERM infants: ASTECS Trial

Stutchfield P. BMJ 331:7518, 2005
Why postnatal approaches may be less effective:

Limiting factor: number of sodium channels, other maturational changes

Transcription requires time (versus translation)

Secondary lung injury: atelectasis, oxygen-related injury, and PAH
SUMMARY:

Evaluate strategies to improve specific outcomes in LP infants perhaps by studying antenatal steroids

Re-evaluate indications for delivery for each diagnosis
Conclusion

*Are antenatal steroids the answer for the LP infant?*

No data (yet) to show benefit

Liggins and Howie did not show decrease in RDS;
Wrong outcome measure?

Will steroids decrease other morbidities?

Need data on long-term outcomes
Thank you!