The Late Preterm Infant: Not Really Full term

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Objectives

• Recognize the changes in obstetric demographics in the US over the last 2 – 3 decades
• Understand why this has occurred
• Recognize the need to better define a specific group of infants
• Understand the unique problems of these infants

US birth statistics in the last 2 – 3 decades

More Babies are Being Born in the US

CDC/NCHS, National Vital Statistics System

Gestational Age-Specific Distribution
All Singleton Live Births

Preterm Birth is Increasing
United States 1994-2004

Source: March of Dimes PeriStats
Additional Terminology

- Near Term ?32-36; 33-37; 34-36
- Early term
- Moderate preterm (CDC 32-36 wk)
- Mild preterm
- Borderline preterm

Why Change the Terminology?

- “Near-Term” suggests that infants are almost term and almost mature
- Could lead to false sense of comfort:
  - less rigorous assessment
  - early discharge
  - inadequate follow-up plans
- “Late Preterm” suggests that infants are still premature and vulnerable (and they are !)

Current Accepted Definitions

- Term: 37⁰/₇ through 41⁶/₇ week gestation
- Preterm: less than 37 weeks

Late Preterm (Near Term) Infants

- 34 0/7 to 36 6/7 weeks
- 239 to 259 days

Late Preterm 34-36 wk

NICHD Workshop
July 2005

- Discontinue use of “near-term”
- Use “Late Preterm” for those born between 34⁰/₇ –36⁵/₇ weeks, or
  239—259 days counting from the first day of the last menstrual period

Engle WA. Semin Perinatol 2006; 30:2-7
Why 34, 35, and 36 completed weeks?

- Most obstetric interventions (e.g., antenatal steroids) are recommended for less than 34 weeks.
- Compared with term gestation, neonatal morbidity and infant mortality rates are higher for 34, 35, and 36 weeks.
- All definitions are arbitrary – maturation should be considered a continuum.

Raju et al. Pediatrics 2006;118:1207-14

The Magnitude of the Problem

- In 2004 ~ 250,000 births in US were late preterm.
- ~ ¼ preterm births in US are late preterm.


Distribution of All US Preterm Births, 2003

www.marchofdimes.com Late Preterm Birth: Every Week Matters 03/06

Why is this happening?

Possible Causes for Increased Preterm and Late Preterm Births

- Traditional Causes
  - Maternal and fetal disorders – better risk assessment and timing, reduce stillbirths
  - Multiple gestation
  - Errors in judgment
  - Convenience of the family and/or the obstetrician

- New causes
  - ↑ maternal age
  - ↑ use of reproductive technologies with ↑ age
  - ↑ multiple gestations (1992 2.4%, 2000 3.2% of live births) major contributor to preterm delivery

Triplet Birth Rate

![Triplet Birth Rate Graph]


Quadruplet and Higher Order Births

![Quadruplet and Higher Order Births Graph]


But, singleton rate of preterm birth is also increasing – why?

Preterm birth and Perinatal Mortality Among Singletons; US 1989-2000

- Reviewed 46,375,578 singleton births from Nat Center for Health Statistics of CDC
- Classified births < 37 weeks
  - Following preterm ROM
  - Medically indicated (labor induction, primary or repeat C-section)
  - Spontaneous preterm

Reasons for Singleton Preterm Births – USA 1989 - 2000

![Reasons for Singleton Preterm Births Graph]

Increase in preterm singleton births is due primarily to an increase in medically indicated preterm births

Effect of Medically Indicated Preterm Birth on Preterm Stillbirth and Perinatal Mortality*

<table>
<thead>
<tr>
<th></th>
<th>1989</th>
<th>2000</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stillbirth</td>
<td>33</td>
<td>24</td>
</tr>
<tr>
<td>Perinatal Mortality</td>
<td>50.6</td>
<td>36.2</td>
</tr>
</tbody>
</table>

* Per 1000 live births


Changing Birth Demographics

- < 37 wk ↑ 20% since 1990
- ↑ from multiples but also singletons
- All of ↑ in < 37 wk due to late preterm (34-36 wk)
- 29% ↓ in births ≥ 40 wk
- Shift to lower birthweight distribution in US in last 15 years

Leveno. Obstet Gynecol 2008;111:810

Are late preterm births a problem?

Morbidity of Late Preterm Infants During Birth Hospitalization

Singleton Infants without Congenital Anomalies

Gestational age in weeks

Mortality Rates Excluding Congenital Malformations

<table>
<thead>
<tr>
<th></th>
<th>Ratio Late Preterm/Term</th>
</tr>
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<tbody>
<tr>
<td>Infant mortality (0-364d)</td>
<td>2.6</td>
</tr>
<tr>
<td>Early neonatal (0-6d)</td>
<td>5.0</td>
</tr>
<tr>
<td>Late neonatal (7-27d)</td>
<td>3.5</td>
</tr>
<tr>
<td>Post neonatal (28-364d)</td>
<td>2.2</td>
</tr>
</tbody>
</table>

Tomashek. J Pediatr 2007;151:450
Respiratory Morbidity in Northern CA Kaiser Permanente Cohort–Odds Ratios

<table>
<thead>
<tr>
<th>GA (wk)</th>
<th>O2 &gt; 1 hr</th>
<th>Asst Vent</th>
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<tbody>
<tr>
<td>38-40</td>
<td>reference</td>
<td>reference</td>
</tr>
<tr>
<td>37</td>
<td>2.04 (1.61-2.59)</td>
<td>2.35 (1.84-3.02)</td>
</tr>
<tr>
<td>36</td>
<td>4.95 (3.95-6.21)</td>
<td>5.24 (4.11-6.68)</td>
</tr>
<tr>
<td>35</td>
<td>8.76 (6.77-11.4)</td>
<td>9.04 (6.88-11.9)</td>
</tr>
<tr>
<td>34</td>
<td>18.67 (14.0-24.9)</td>
<td>19.8 (14.7-26.6)</td>
</tr>
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</table>

Gestational age, NICU admission

<table>
<thead>
<tr>
<th>Gestational age, NICU admission</th>
<th>Adjusted OR (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;34 weeks</td>
<td>0.96 (0.57,1.62)</td>
</tr>
<tr>
<td>34-36 wk, NICU &gt;24h</td>
<td>0.89 (0.54,1.46)</td>
</tr>
<tr>
<td>34-36 wk, NICU &lt;24h</td>
<td>1.31 (0.41,4.21)</td>
</tr>
<tr>
<td>34-36 wk, never in NICU</td>
<td>3.10 (2.38,4.02)</td>
</tr>
<tr>
<td>&gt;37 wk, NICU &gt;24h</td>
<td>0.79 (0.52,1.21)</td>
</tr>
<tr>
<td>&gt;37 wk, NICU &lt;24h</td>
<td>1.43 (0.73,2.81)</td>
</tr>
<tr>
<td>&gt;37 wk, never in NICU</td>
<td>reference</td>
</tr>
</tbody>
</table>

Late Preterm Rehospitalization Rates

n = ~33,000 infants

Effect of Gestational Age on Newborn Morbidity (LOS > 5 nights + life threatening DRG, TF to NICU, died)

Excess Hospital Costs by Week of Gestation, Compared with Hospital Costs at 38 Weeks California 1996

Risk of Being Readmitted For Phototherapy

30,000 Discharges from Well Baby Nursery 1988-94
4.2/1,000 Readmitted for Phototherapy

<table>
<thead>
<tr>
<th>RISK FACTOR</th>
<th>ODDS RATIO*</th>
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</thead>
<tbody>
<tr>
<td>33-36 wks</td>
<td>13.2</td>
</tr>
<tr>
<td>37 - 38 wks</td>
<td>7.6</td>
</tr>
<tr>
<td>Breast feeding</td>
<td>4.2</td>
</tr>
<tr>
<td>Jaundice in nursery</td>
<td>7.8</td>
</tr>
<tr>
<td>Length of stay &lt; 72 h</td>
<td>3.2</td>
</tr>
</tbody>
</table>

Kernicterus in Late Preterm Infants

- 119 cases of kernicterus in infants discharged from the well baby nursery 1992 - 2003
- 52/119 (44%) were 35 – 38 weeks gestation
What about developmental outcome?

Long-Term Medical and Social Consequences of Preterm Birth

Moster et al. NEJM 2008;359:262-273

- National registry of Norway
- 903,402 live born infants without congenital anomalies 23 – 37+ weeks
- Born 1967-83 and followed through 2003

<table>
<thead>
<tr>
<th>Disability</th>
<th>34-36 6/7 weeks vs ≥ 37 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RR</td>
</tr>
<tr>
<td>Cerebral palsy</td>
<td>2.7</td>
</tr>
<tr>
<td>Retardation</td>
<td>1.6</td>
</tr>
<tr>
<td>Schizophrenia</td>
<td>1.3</td>
</tr>
<tr>
<td>Autism spectrum</td>
<td>0.8</td>
</tr>
<tr>
<td>Abnormal psychological development, behavior, emotion</td>
<td>1.5</td>
</tr>
<tr>
<td>Other major disabilities</td>
<td>1.5</td>
</tr>
<tr>
<td>Any medical disability affecting work capacity</td>
<td>1.4</td>
</tr>
</tbody>
</table>

All adjusted for sex, year of birth, multiple births, single mother, maternal age, parents level of education, immigrant status

Early School-Age Outcomes of Healthy Infants – LOS ≤ 72 hr

Morse et al. Pediatrics 2009;123:e622-e629

Brain Weight During Gestation

Brain volume compared to term infants:
- 34 weeks – 65%
- 36 weeks – 80%

Kinney HC Semin Perinatol 2006; 30:81-88

Development of the Human Cerebral Cortex Showing Immaturity of Laminar Position and Dendritic Arborization of Neurons

Kinney HC Semin Perinatol 2006; 30:81
Breastfeeding Concerns

Decreased milk transfer:
• Poor latch
• Poor sucking effort and coordination
• Decreased milk production
• Alters bonding

Late Preterm Nutritional Concerns

Decreased milk transfer
• Prolonged artificial milk supplementation
• Weight loss
• Failure to thrive
• Delayed stooling
• Dehydration
• Hypernatremia

Developmental and Physiologic Immaturity of Late Preterm Infants

• Brain growth and development
• Lung water, surfactant – retained fluid, RDS
• Respiratory control – apnea
• Less white and brown fat – hypothermia
• Glucose regulation – hypoglycemia
• Gastrointestinal function – feeding issues
• Bilirubin metabolism - jaundice

Should We Consider Changes in Obstetric Management?

• Tocolysis and antenatal steroids routine at ≤ 33 weeks but no tocolysis or steroids at ≥ 34 weeks
  – (is gestational dating so accurate?)
• Up to 50% of infants at 34 weeks may require intensive care

Summary

Late preterm infants are immature and have
• ↑ mortality
• ↑ morbidity: hypothermia, hypoglycemia, respiratory distress, apnea, jaundice, feeding difficulties
• ↑ readmission for jaundice, feeding difficulties, dehydration, suspected sepsis
• ↑ poor neurodevelopmental outcomes including CP, retardation and other disabilities

? Design randomized controlled trial of labor induction at 34 – 36 weeks for specific maternal or fetal indications

Kramer J Pediatr 2009;154:159-60
**Obstetric Implications**

- “...preterm delivery should only occur when an accepted maternal or fetal indication for delivery exists”
- Examples include nonreassuring fetal status or a maternal condition that is likely to be improved by delivery
- Collaborative counseling by both obstetric and neonatal clinicians about the outcomes of late-preterm births is warranted unless precluded by emergent conditions”.

Committee on Obstetric Practice. ACOG Committee Opinion No.404, April 2008.