Late Preterm Infants

Special Issues & Concerns for this Growing Patient Population

Robert V. Hingre, M.D.
SUNY Upstate Medical University

- This group of infants have been called:
  - “Near Term”
  - “Moderately Preterm”
  - “Minimally Preterm”
  - “Marginally Preterm”


Recent Definitions

- WHO, ACOG, and AAP consider Full-Term to be birth at/after 37/0/7 weeks (or 280 days) through 41/6/7 weeks or 294 days

- Late Preterm infants are those born between 34/0/7 to 36/6/7 weeks

- “Early Term” infants are those born between 37/0/7 to 37/6/7 weeks


U.S. Births in 2005

<table>
<thead>
<tr>
<th>Preterm Births in 2005</th>
<th>Premature Births &lt;37 wks GA in the United States, 2005</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preterm Births = 522,913</td>
<td>&lt;28 weeks = 31,588</td>
</tr>
<tr>
<td>12.6%</td>
<td>28-31 weeks = 51,820</td>
</tr>
<tr>
<td>Term</td>
<td>32-33 weeks = 65,853</td>
</tr>
<tr>
<td>Preterm</td>
<td>34-36 weeks = 377,000</td>
</tr>
<tr>
<td>Total Births = 4,138,349</td>
<td></td>
</tr>
</tbody>
</table>

Distribution of Preterm Births
2005 United States

- 71.4% Late Preterm
- 6.6% < 28 wks
- 9.9% 28-31 wks
- 12.9% 32-33 wks
- 11.4% 34-36 wks

Total Births = 4,138,349
Preterm Births = 522,913

Late Preterm & Preterm Births

<table>
<thead>
<tr>
<th>Year</th>
<th>&lt; 34 weeks</th>
<th>34-36 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>2005</td>
<td>12.7%</td>
<td>9.1%</td>
</tr>
<tr>
<td>2000</td>
<td>11.6%</td>
<td>3.4%</td>
</tr>
<tr>
<td>2005</td>
<td>10.6%</td>
<td>3.3%</td>
</tr>
<tr>
<td>1995</td>
<td>11.0%</td>
<td>3.3%</td>
</tr>
<tr>
<td>1990</td>
<td>9.3%</td>
<td>3.3%</td>
</tr>
<tr>
<td>1981</td>
<td>6.3%</td>
<td>3.1%</td>
</tr>
</tbody>
</table>


Late Preterm Births by Age

Factors Contributing to Late Preterm Births

- Teen Mothers
- Advanced Maternal Age (AMA)
- Over 69% of late preterm infants are born to mothers < 20 years and ≥ 40 years

- Pregnancy interval of < 12 months:
  - Increases risk > 4 times
- Previous preterm delivery:
  - Increases risk > 7 times
- Multiple Gestation (twins, triplets, etc.)

Multiple Gestation and Late Preterm Births

- Multiple births in the U.S. are approximately 5 times more likely to result in Late Preterm births compared to singleton pregnancies
  - One factor is the contribution of IVF and assisted reproductive technologies
- Between 1990 to 2005 in the U.S:
  - Twin births increased by 42%
  - Triplet/Higher births increased 122%

Maternal Conditions Contributing to Late Preterm Births

- Maternal Obesity
  - Body Mass Index (BMI) > 30
  - Woman who is 5 ft, 5 inches + >180 lbs.
- Maternal Diabetes
  - Increased risk of underdeveloped lungs
  - Need assessment for lung maturity if delivery is at < 39 weeks
- Maternal Asthma
- Maternal Smoking

Factors Contributing to Late Preterm Births

- Maternal Hypertension (HTN) in U.S.
  - If there is pregnancy-induced hypertension: 4% - 6% will have late Preterm births
- Maternal Pre-eclampsia (Toxemia)
  - 10% - 11% have Late Preterm births
- Gestational HTN AND Pre-eclampsia:
  - 9% - 14% have Late Preterm births

Prevention of Late Preterm Births

- Limit in vitro fertilization (IVF) to twins or singletons
- No elective C-sections or inductions of labor < 39 weeks
## Late Preterm Infants

- For decades, late preterm infants have been sent to the “Term Nursery”, where they are treated the same as Full-term infants.
- Even if they are > 2,500 g, the late preterm infants are now recognized as being physiologically and metabolically immature.
- Very little research has been conducted on this group and new management guidelines “… are extrapolated from knowledge about extremely preterm and term infants…”

__Note:__

*NeoReviews. 2009;10:e280-e286.*

## Late Preterm Infants

### Clinical Problems: Short-term

- Hypothermia
- Respiratory Distress
- Apnea
- Sepsis
- Hypoglycemia
- Hyperbilirubinemia
- Feeding Problems
- EUGR

- Late preterm infants are 4 times more likely to have at least 1 short-term morbidity
- 3.5 times more likely to have 2 or more morbidities

__Note:__

*Pediatrics. 2007;120:1390-1401.*

*NeoReviews. 2009;10:e280-e286.*

## Morbidity After Birth

<table>
<thead>
<tr>
<th>Condition</th>
<th>35-36 weeks</th>
<th>37-40 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypothermia</td>
<td>20%</td>
<td>20%</td>
</tr>
<tr>
<td>Respiratory Distress</td>
<td>25%</td>
<td>25%</td>
</tr>
<tr>
<td>Apnea</td>
<td>30%</td>
<td>30%</td>
</tr>
<tr>
<td>Sepsis</td>
<td>10%</td>
<td>10%</td>
</tr>
<tr>
<td>Hypoglycemia</td>
<td>15%</td>
<td>15%</td>
</tr>
<tr>
<td>Hyperbilirubinemia</td>
<td>20%</td>
<td>20%</td>
</tr>
<tr>
<td>Feeding Problems</td>
<td>10%</td>
<td>10%</td>
</tr>
<tr>
<td>EUGR</td>
<td>5%</td>
<td>5%</td>
</tr>
</tbody>
</table>

__Note:__

*NeoReviews. 2009;10:e280-e286.*

## Admissions to NICU

<table>
<thead>
<tr>
<th>Gestational Age</th>
<th>34 weeks</th>
<th>35 weeks</th>
<th>36 weeks</th>
<th>37 weeks</th>
<th>38-40 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>88%</td>
<td>54%</td>
<td>25%</td>
<td>12%</td>
<td>2.6%</td>
</tr>
</tbody>
</table>

__Note:__

Late Preterm: Neonatal Assessment and Postnatal Care

- **34 weeks**: NICU assessment in the delivery room and admission to Level 2 or higher NICU for observation and management
- **2004 AAP Policy Statement**: Level 1 Nursery:
  - “Stabilize and provide care for infants born at 35 to 37 weeks’ gestation who remain physiologically stable”
  - “Stabilize newborn infants who are ill and those born at < 35 weeks’ gestation until transfer to a facility that can provide the appropriate level of neonatal care”


Late Preterm: Neonatal Assessment and Postnatal Care

- **35 weeks**: There are NO specific guidelines for levels of neonatal care required after birth
- **Options for Assessment and Management**:
  - Routine assessment by labor & delivery staff and transfer to Term Nursery if adequate weight
  - Delivery Room assessment by pediatrics or NICU team: transfer to the Term Nursery if clinically stable and adequate weight
  - Delivery Room assessment and “pitstop” for observation in NICU or transitional nursery for 4 - 24 hours, then transfer to Term nursery if stable


**Expert Opinion**

**Observation in NICU or Transitional Nursery for the first 24 hours if 34 weeks OR 35 - 36 weeks AND < 2,300 g***

***“Unless arrangements can be made to provide transitional care and close monitoring in the mother’s room.”


Late Preterm: Respiratory Distress

- 125 infants born at 35 - 36\(\frac{6}{7}\) weeks compared to 120 infants at 37 - 41 weeks

Respiratory Distress after Birth

- Late Preterm*  Term Infants
- 28.9% of infants  4.2% of infants

*Nearly 7 times greater need for intervention in the delivery room (p < 0.0001)


Respiratory Distress: Elective C/section vs. Vaginal Delivery

- Risk for respiratory morbidity with delivery by c/section late preterm with no labor = 35.5/1000 versus risk with term vaginal delivery 5.3/1000 (Br J Obstet Gynaecol. 1995;102:101-6.)
- Odds ratio = 6.8 for late preterm (p < 0.001)
- At 37 weeks gestation, infants born by c/section without labor had 5 times greater odds of severe respiratory morbidity compared to a vaginal delivery at 39 weeks (BMJ. 2008;336: 85-87.)


Respiratory Morbidity in Late Preterm Births (233,844 deliveries, 19 hospitals, 2002-2008)

- Risk for respiratory morbidity with delivery by c/section late preterm with no labor = 35.5/1000 versus risk with term vaginal delivery 5.3/1000 (Br J Obstet Gynaecol. 1995;102:101-6.)
- Odds ratio = 6.8 for late preterm (p < 0.001)
- At 37 weeks gestation, infants born by c/section without labor had 5 times greater odds of severe respiratory morbidity compared to a vaginal delivery at 39 weeks (BMJ. 2008;336: 85-87.)

A baby’s brain at 35 weeks weighs only two-thirds of what it will weigh at 39 to 40 weeks.

Late Preterm: Apnea/SIDS

- Periodic Breathing and Apnea:
  - Incidence in Term Infants: < 1% - 2%
  - Incidence in Late Preterm: 4% - 7%

- Should 35 week infants be kept on apnea monitors in the term nursery???

- Sudden Infant Death Syndrome (SIDS):
  - There is a 4 times greater risk of SIDS in Late Preterm Infants 34 - 36 weeks gestational age

Increased Risk for SIDS*

<table>
<thead>
<tr>
<th></th>
<th>Term</th>
<th>Late Preterm</th>
<th>Low BW (&lt; 2500 g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prone Sleep</td>
<td>2.6 times</td>
<td><strong>49 times</strong></td>
<td><strong>83 times</strong></td>
</tr>
<tr>
<td>Side Sleep</td>
<td>2 times</td>
<td><strong>40 times</strong></td>
<td><strong>37 times</strong></td>
</tr>
</tbody>
</table>


Late Preterm: Temperature Regulation

- Temperature regulation in late preterm infants is compromised by immature hypothalamic function.
- They have larger body surface area-to-weight ratios and limited stores of white (adipose) fat for insulation.
- Brown (adipose) fat is metabolized to generate heat: stores are limited and there are low levels of hormones (i.e. cortisol, norepinephrine, leptin, prolactin, triiodothyronine) which are needed for brown fat metabolism
Temperature Monitoring

- Approximately 10% of late preterm infants between 35 - 36 6/7 weeks gestation develop hypothermia requiring active intervention
  - Hypothermia can aggravate respiratory distress and cause hypoglycemia and metabolic acidosis
- Cold Stress: rectal temperature 36.0° - 36.4° C
  - Cold Stress may lead to increased metabolic rate and oxygen consumption and inability to gain weight


Temperature Recommendations

- Recommended room temperatures for preterm infants who are wearing appropriate sleepwear:
  - Ideal Range: 68° - 72° F
- Some recommend increasing room temperature to 75° F for infant bathing in a tub
  - **Area of Debate:** No tub baths until weight > 2,500 grams (5.5 lbs); sponge bath only
  - Keep exam rooms at the high end of the recommended temperature range (72° F)

J Perinatol. 2007;27:S45–S47

Temperature Monitoring: After Discharge

- Monitor preterm/low birth weight infants: axillary (skin) temperatures twice daily
  - **Range of normal for skin temps:**
    - 36.5° C - 37.5 C (+/- 0.5 degrees C)
    - 97.6° F - 99.6 F (+/- 1 degree F)
    - If skin temp falls outside of normal range, rectal (core) temperature should be taken

J Perinatol. 2007;27:S45–S47

Late Preterm: Hypoglycemia

- Incidence of Hypoglycemia is inversely correlated with gestational age, and late preterm infants are most at risk in the first 12 - 24 hours after birth
- Late Preterm infants have immature hepatic gluconeogenesis and adipose tissue lipolysis and limited glucose reserves


Late Preterm: Feeding Problems

- Potential feeding problems in late preterm:
  - Less alert-awake periods and decreased postural support
  - Poor oromotor tone (weak or burst-sucking)
  - Incoordinated suck-swallow-breathing patterns
  - Decreased gut motility, less stooling
  - At risk for excessive weight loss, feeding intolerance, hypoglycemia


Late Preterm: Sepsis

- Late preterm infants have 4 times greater odds of having a septic work-up versus term infants (36.7% versus 12.6%, p < .01)
- Empiric antibiotics were continued longer, despite having negative cultures
- New Group B Strep algorithm: (Nov 2010) calls for CBC with diff & blood culture if there was intrapartum antibiotics < 4 hours before birth


Fetal-Infant Growth Curves

Revised Babson-Benda a.k.a. Fenton Curves
- Meta-analysis of data from ALL studies between 1980 - 2002
- Use if < 40-42 wks post-conceptional age (PCA)

www.biomedcentral.com/1471-2431/3/13

Late Preterm: Sepsis

- New GBS Management Algorithm:
  - CBC with diff
  - Blood culture

MMWR. 2010;59(RR-10):1-32.
Late Preterm: Hyperbilirubinemia

- Late Preterm infants have delayed maturation & lower concentrations of UDP-glucuronyltransferase in the liver
- Poor feeding & slower gut motility may lead to delayed excretion of conjugated bilirubin and more enterohepatic recirculation
- Peak bilirubin levels occur later than in term infants (Day 5 to 7 of life)


Late Preterm: Hyperbilirubinemia

- Late preterm infants 2.4 times greater risk of significant hyperbilirubinemia compared to term infants
- Approximately 25% will require phototherapy
- Increased risk of kernicterus and bilirubin-induced neurotoxicity


Late Preterm: Readmissions

- Large study in U.K.: infants born at 35 - 37 wks were 1.7 times more likely to need readmission in the neonatal period (first 28 days of life)
- Late preterm infants NOT admitted to the NICU had the highest rates of readmission
- Having a home visit or well child check-up within 72 hours after discharge was associated with a decreased rate of hospitalization


Late Preterm: Readmissions

- Readmission rates were higher for late preterm infants (4.3%) versus term infants (2.7%) when infants were discharged after short stay (< 2-night hospital stay)
- Breastfed late preterm infants were 2.2 times more likely to need readmission than breastfed term infants
- There was NO significant difference in the readmissions between formula fed term and late preterm infants

Late Preterm Infants
Long-term Outcomes

- Infant Mortality
- Developmental Delays
- School Failure
- Behavioral Disorders
- School Disabilities


Comparison of Mortality Rates

<table>
<thead>
<tr>
<th></th>
<th>Neonatal Mortality (0 - 28 days)</th>
<th>Infant Mortality (birth - 1 year)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Late Preterm</td>
<td>Term</td>
</tr>
<tr>
<td>1995:</td>
<td>4.8 : 1,000</td>
<td>1.2 : 1,000</td>
</tr>
<tr>
<td>2002:</td>
<td>4.1 : 1,000</td>
<td>0.9 : 1,000</td>
</tr>
</tbody>
</table>

Mortality rates have declined since 1995, but remain 3 - 4 times higher in late preterm infants.


Mortality Rates & Risk Ratios for Death

<table>
<thead>
<tr>
<th>Gestation</th>
<th>Mortality rate (1 - 7 days)</th>
<th>Risk Ratio</th>
<th>Mortality rate (1 - 365 days)</th>
<th>Risk Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>34 wks</td>
<td>7.2*</td>
<td>25.5</td>
<td>12.5*</td>
<td>10.5</td>
</tr>
<tr>
<td>35 wks</td>
<td>4.5*</td>
<td>16.1</td>
<td>8.7*</td>
<td>7.2</td>
</tr>
<tr>
<td>36 wks</td>
<td>2.8*</td>
<td>9.8</td>
<td>6.3*</td>
<td>5.3</td>
</tr>
<tr>
<td>37 wks</td>
<td>0.8*</td>
<td>2.7</td>
<td>3.4*</td>
<td>2.8</td>
</tr>
<tr>
<td>38 wks</td>
<td>0.5</td>
<td>1.7</td>
<td>2.4*</td>
<td>2.0</td>
</tr>
<tr>
<td>39 wks</td>
<td>0.2</td>
<td>0.8</td>
<td>1.2</td>
<td>1.2</td>
</tr>
<tr>
<td>40 wks</td>
<td>0.3</td>
<td>- - -</td>
<td>1.4</td>
<td>- - -</td>
</tr>
</tbody>
</table>

* Significantly higher than 40 weeks


Death and/or Severe Neurologic Disability
150,426 singletons, France 2000-2008

Late Preterm: Long-term Outcome

- Cohort of late preterm infants who are now 20 - 36 yrs of age were compared to term infants:
- 900,000 births with 33,000 late preterm infants born between 1967 and 1983 in Sweden:
  - 2.7 times higher rate of Cerebral Palsy
  - 1.6 times higher rate of intellectual disability
  - 1.5 times higher rate of abnormal psychological, behavioral, emotional development
  - 1.3 times higher rate of schizophrenia
  - 1.4 times higher rate of disability affecting the capacity to work

Cost of Caring for Late Preterm Infants

- The average cost of caring for a late preterm infant in the year 2000 was 2.9 times greater than the cost of caring for a term infant:
  - $ 2,630 more per late preterm
- 1996 cost per 25-week preterm: $ 202,000 versus $ 4,200 per 35-week late preterm infant
  - Cost for ALL 25-week infants: $ 38.9 million
  - Cost for ALL 35-week infants: $ 41.1 million

Minimum Criteria for Discharge

- “A car safety seat study completed by a trained professional to observe for apnea, bradycardia, or oxygen desaturation has been passed.”
- Guidelines imply that infants should be kept on electronic monitoring: cardiac-apnea monitor + oximetry (or 3-channel event recording)
- Car seat evaluations should be done … “for a minimum of 90 - 120 minutes or the duration of travel, whichever is longer…”

Minimum Criteria for Discharge

- There are official recommendations from the AAP regarding management options if the car seat evaluation has NOT been passed.
- Possible options:
  - Delay discharge
  - Discharge on supplemental oxygen
  - Retest in an infant Car Bed
  - Retest with “blanket rolls”
Safe Transportation of Preterm and Low Birth Weight Infants

- Car Safety Seats are generally designed for infants weighing more than 4 to 5 lbs.
- Rear-facing seats should be reclined to around 45 degrees to minimize the potential for chin-on-chest position to compromise breathing.
- Blanket rolls can be placed under crotch strap and along both sides of infant to maintain proper positioning.


### Safe Transportation of Preterm and Low Birth Weight Infants

- "Many head-support systems, however, are sold as aftermarket products and may decrease the safety provided by the seat and harness system, because they introduce slack into harness straps. Only products that come with the seat or are sold by the manufacturer for use with their specific seat should be used."