Late Preterm Infants: More than “nearly term”

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Definitions:
Term — GA between 37 weeks and 41 6/7 weeks
Preterm - GA earlier than 37 weeks
  *Late preterm birth — GA between 34 and less than 37 weeks
  *Very preterm birth — GA less than 32 weeks
  *Extremely preterm birth — GA at or below 28 weeks
The risks of prematurity: Alphabet Soup

• Respiratory Distress Syndrome (RDS)
• Retinopathy of Prematurity (ROP)
• Patent Ductus Arteriosus (PDA)
• Bronchopulmonary Dysplasia (BPD)
• Necrotizing Enterocolitis (NEC)
• Intraventricular Hemorrhage (IVH)
• Periventricular Leukomalacia (PVL)

So can we stop worrying about these conditions once a baby reaches a GA of 34 weeks and 1 second?

**NO.** Still higher risk than term infants but other problems more likely.
In the US, premature births increased from 10.6% in 1990 to 12.8% in 2006. Increase primarily due to rise in late preterm births from 7.3% to 9.1% of all live births in 2006.

Why?
- Increased obstetrical surveillance: fetal assessments, prenatal U/S, electronic fetal heart monitoring
- Consensus recommendations regarding GA for delivery to optimize maternal, fetal, and neonatal outcomes
- Increased maternal obesity → medical and antenatal complications
- Maternal diabetes
- Maternal HTN
- Multifetal pregnancy → multiple births → delivery at earlier GA
- Increased maternal age, assisted reproductive technology

Potential maternal and newborn consequences of late preterm or early term birth compared with potential maternal and fetal consequences of continued pregnancy.

- Neonatal morbidity and mortality (immaturity-related)
- Maternal morbidity and mortality (prolonged or failed induction, cesarean delivery)
- Maternal morbidity and mortality (hemorrhage, hypertension crisis, uterine rupture)
- Fetal morbidity and mortality (stillbirth, uteroplacental insufficiency)
Are “Late preterm” and “Near term” synonymous?

• The term “near term” can be misleading, making it seem like they are “almost term”
  • Underestimation of risk
  • Less diligent evaluation, monitoring, and follow-up

(Optimizing care and outcome for late-preterm (near-term) infants: a summary of the workshop sponsored by the National Institute of Child Health and Human Development)
Late preterm infants can often be the **same size and weight** as term infants

So what are the risk s of being **late premature**?

- Respiratory morbidity
- Hypothermia
- Hypoglycemia
- Apnea
- Hyperbilirubinemia
- Feeding difficulties
- Readmission

- Long term outcomes
Respiratory Morbidity

Stages of Lung Development

week 4 – 5: embryonic
week 5 – 17: pseudoglandular
week 16 – 25: canalicular
week 24 – 40: terminal sac
late fetal – 8: years alveolar

Note: Timing varies in different sources

• From 34 – 36 6/7 weeks GA, terminal respiratory units change from alveolar saccules with cuboidal and flat epithelial cells (terminal sac period) to mature alveoli with thin epithelial cells (alveolar period)

• During alveolar period, pulmonary capillaries begin to bulge into each terminal sac and mature pools of surfactant develop

• Late preterms can develop RDS, TTN, PNA, respiratory failure, and need for ventilator
Hypothermia

BROWN FAT

• **Thermogenin** is a protein that uncouples oxidative phosphorylation from ATP production.

• Brown fat is specialized for **non-shivering thermogenesis** due to higher # of mitochondria than typical cells and higher-than-normal concentration of **thermogenin** in these mitochondria.

• Makes up 5% of newborn body mass.

• Located on back, upper half of spine, and shoulders.

• At term, brown-fat accumulation and maturation peaks.
  
  • Same w/ prolactin, leptin, NE, triiodothyronine, cortisol, etc.
  
  • These proteins are responsible for **brown fat metabolism**.

• **So late pre-term infants have less brown fat and less effective at generating heat from what they do have.**

Also...

* Late preterm infants have less white adipose (→ less insulation).
* Higher SA:weigh ratio → more heat loss.
Hypoglycemia

• Can occur in any GA due to insufficiently responding to loss of maternal glucose after birth

Late Preterm Infants
• Risk 3x greater in late-preterm than term
  • Immature hepatic gluconeogenesis
  • Immature adipose tissue lipolysis
  • Immature glucose regulation due to increased need for glucose infusion during initial birth hospitalization
Apnea

• Incidence in late-preterm infants is 4-7% (1-2% in term infants)
  • More episodes of Apnea and Bradycardia
  • Greater risk for SIDS

WHY?
• Increased susceptibility to hypoxic respiratory depression
• Immature pulmonary irritant receptors
• Increased respiratory inhibition sensitivity to laryngeal stimulation
• Decreased upper airway dilator muscle tone

• Decreased central chemosensitivity to CO
  • Immature CNS (fewer sulci/gyri, smaller brains)
Development of sulcation and gyration with increasing GA. Transverse T2 weighted FSE images at the level of the central sulcus at: (A) 25 weeks GA; (B) 28 weeks GA; (C) 30 weeks GA; (D) 33 weeks GA; (E) 39 weeks GA.

Hyperbilirubinemia

- Delayed maturation and lower concentration of **UDP glucuronyltransferase**
  - Decreased conjugation of bilirubin \(\rightarrow\) hyperbilirubinemia

- Relatively **immature BBB** and lower amounts of **bilirubin-binding albumin**
  - Greater risk for kernicterus at a given bili level

- Immature **orobuccal coordination** and **swallowing mechanisms**
  - Poor feeding \(\rightarrow\) increased risk for hyperbilirubinemia
Long term outcomes

Increased risk for:
• Neurodevelopmental impairment (CP, MR)
• Schizophrenia
• Failure to thrive

• Asthma
  • Association of Late-Preterm Birth with Asthma in Young Children: Practice-Based Study (Goyal, et al; Pediatrics June 2011)

  • Retrospective cohort analysis of infants born 34-42 weeks GA
    • 31 practices within CHOP Pediatric Research Consortium
    • Eligibility: seen by PCP within first 30 days of life, subsequently monitored for 18 months

  • Measured diagnoses of asthma and persistent asthma, prescriptions of inhaled corticosteroids, and # of acute office visits in the first 18 months of life
• Late-preterm status NOT significantly associated with increased dx of asthma

• Was associated with increased dx of persistent asthma, receipt of 1 or more inhaled corticosteroid prescriptions, and more acute outpatient visits with a wheeze

• “association of asthma severity with late prematurity”
FIGURE 2
Standardized proportions of asthma outcomes. Standardized proportions of asthma-related outcomes according to gestational-age category are shown. Estimates were standardized for all covariates. Brackets represent 95% CIs. * Risk differences are statistically significant compared with the reference group at 39 to 42 weeks of gestation (P < .05).
Summary

• Late preterm infants are born between 34 week and 36 6/7 GA

• Increasing rates over last few decades due to increased rates of OB surveillance, maternal obesity, and multiple births

• While their premature GA puts them at similar risks to those born before 34 weeks, there are more common issues that this group faces
  • Respiratory morbidity
  • Hypothermia
  • Hypoglycemia
  • Apnea
  • Hyperbilirubinemia
  • Feeding difficulties
  • Readmission
  • Long term outcomes (asthma, FTT, neurodevelopmental impairments)

• Despite this information and official discharge AAP recommendation, there are still high rates of early discharge of late-preterm infants


