

Shades of Immaturity-Late Preterm and Early Term Infants

By international convention a "term" infant is one born at 37-41 weeks of gestation. Therefore all infants born prior to 37 weeks of gestation are considered preterm. In recent years the recognition that rates of premature delivery (currently 12.5% of all deliveries) are increasing in the United States has led to further review of which infants are contributing to this increasing incidence of prematurity. Such review has demonstrated that 75% of all preterm deliveries occur in infants of 34-36 weeks gestation. It is this cohort

of infants that has contributed most to the overall increased incidence of preterm deliveries in the U.S. The 34-36 week cohort contributes significantly to intensive care admissions and many require prolonged stays in well newborn nurseries thereby contributing greatly to the overall expense of newborn care. With the additional understanding that this cohort is at risk for a number of complications related to their immaturity a National Institutes of Health workshop was convened in July 2005 entitled "Optimizing Care and Outcome

continued on page 10

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continued from page 9

of the Near Term Pregnancy and Near Term Newborn Infant". One of the conclusions from this workshop was the new designation for infants born 34-36 completed weeks of gestation. This group of infants is now referred to as being "**late preterm.**"

Concurrent with the delineation of the late preterm infant and health concerns associated with this cohort has come recognition that even term infants can suffer from similar problems of immaturity. This recognition is supported by a number of articles addressing respiratory problems of infants born by elective cesarean section at 37-41 weeks of gestation. Thirty seven and 38 week infants are at significantly higher risk of respiratory morbidity and death than their 39-41 week colleagues. To emphasize their relative immaturity I will refer to the 37-38 week infants as being "**early term.**" Overall the definition of term and preterm has lead to significant confusion. Physicians who care for newborns have long recognized that many infants at 37-38 weeks gestation are relatively immature and can suffer from a variety of morbidities if not simply the need for a longer length of stay than infants born at 39-41 weeks gestation.

The purpose of this article is to delineate some of the complications encountered in infants born at 34-38 weeks gestation. One should think of newborn physiologic maturity as a spectrum with 34 week infants the least mature and 38 week infants being the most mature of this cohort, recognizing that some 38 week gestation infants are at risk for some of the immaturity associated morbidities that are frequently observed in late preterm infants.

Late Preterm Infants

Within the late preterm cohort it is recognized that 34 week gestation infants are significantly less mature than their 36 week counterparts. Nearly 50% of infants born at 34 weeks gestation will require some degree of intensive care support after birth whether this is simply care for feeding or care for issues of respiratory distress. However, by 35 weeks gestation this number drops to 15% and is only 8% at 36 weeks gestation. This cohort however is at particularly increased risk for other neonatal complications including hypoglycemia, hyperbilirubinemia, feeding difficulties, and problems with temperature instability. The risk of each of each of these morbidities decreases as gestation increases, however since these infants can be relatively

large in size they are frequently managed in ways that are similar to the management of the more mature term infant. Frequently 35 and 36 week infants are considered abnormal when they are slow to feed, have bilirubin problems or hypoglycemia when in fact those issues could all have been predicted because of immaturity. A close look at the cohort of late preterm infants demonstrates that a significant number of these infants are delivered by cesarean section or after induction of labor. The indications for these early deliveries have not been well delineated; however it is generally assumed that they occurred because of improved ascertainment of problems with fetal well being or of maternal conditions.

Respiratory Issues Related to Relative Immaturity

Though only about 12% of infants born at 33-34 weeks gestation have a true surfactant deficiency the fact that many late preterm infants are born by cesarean section in the absence of labor puts them at significantly increased risk for respiratory morbidities. In addition to maturation of the surfactant system, the fluid handling of the lung as gestation progresses is an important factor in determining respiratory response after delivery. Since the fetal lung is a fluid secreting organ it is important that this fluid production decrease then discontinue prior to delivery. This generally occurs at term and this process of transition from the lung being a fluid secreting organ to a fluid absorbing organ begins to occur prior to the onset of labor. However, in the absence of labor the lung can continue to secrete fluid as it has not undergone the transition to the more mature state of fluid absorption. Though the incidence of surfactant deficiency is approximately 12% in a 33-34 week baby, and 2% in the 35-36 week baby these infants can suffer additional respiratory morbidities in the form of transient tachypnea of the newborn and other "unspecified respiratory failure". Since transition from fetal to newborn life also requires improved pulmonary blood flow these infants are at increased risk for developing persistent pulmonary hypertension of the newborn. This respiratory illness in the late preterm infants can be very severe, and may progress to severe hypoxic respiratory failure requiring extra corporeal membrane oxygenation (ECMO). A recent review of the data maintained by the Extracorporeal Life Support Organization (ELSO) demonstrated that 14.5% of infants placed on ECMO between 1989 and 2006 were late preterm infants. In this cohort the mortality rate was twice that of the cohort of term infants placed on ECMO during the same period. The late preterm infants were at increased risk for neurological problems, primarily intraventricular hemorrhage, compared to the term infants placed on ECMO.

Early Term Infants

Early term infants are also at a significant risk of respiratory morbidity when delivered prior to 39 weeks gestation, particularly when the delivery occurs via elective cesarean section. One study demonstrated that infants born by elective cesarean section at 37-38 weeks are 120 times more likely to require ventilatory support for respiratory distress than infants born at 39-41 weeks gestation. Though multiple studies have demonstrated an increase in respiratory morbidities including severe hypoxemic failure, persistent pulmonary hypertension, and pneumothorax in infants delivered by elective cesarean section prior to 39 weeks gestation compared to infants delivered at 39 weeks and beyond the absolute rate of respiratory complications varies. However, approximately 15% of infants at 36 weeks gestation, 12% at 37 weeks gestation, 6% at 38 weeks gestation, and 3% at 39 weeks gestation will require NICU admission after elective repeat cesarean section. The American College of Obstetrics and Gynecology (ACOG) made recommendations in 1999 against elective deliveries prior to 39 weeks of gestation. This recommendation was reiterated in the 2002 5th Edition of The Perinatal Guidelines for Care, jointly published by the American Academy of Pediatrics (AAP) and ACOG. These recommendations and the recognition that there is significant morbidity associated with elective delivery of infants prior to 39 weeks gestation has prompted the Iowa Statewide Perinatal Care Program to encourage physicians and hospitals to adopt a “zero tolerance approach” to early inductions or cesarean sections prior to 39 weeks gestation without a solid medical indication.

Other Morbidities

As mentioned above, there are other complications associated with physiological immaturity in late preterm and early term infants. Approximately 10% of infants at 35-36 week gestation will have problems with temperature instability and require significant amount of swaddling or care in an incubator. This is particularly true when infants are small for gestational age. Other morbidities associated with prematurity include an 18% incidence of hypoglycemia in 35-36 week infants, and this is likely even higher in 34 week gestation infants. The risk for hypoglycemia is related to decreased stores of glycogen in preterm infants. Other complications of immaturity include risk for hyperbilirubinemia as over 16% of 35 and 36 week infants will have their discharge delayed secondary to jaundice. This population of infants also is well represented in the kernicterus registries. The risk for bilirubin related morbidity is likely secondary to relative immaturity of their systems for conjugating and eliminating bilirubin and to their increased risk for dehydration secondary

to poor feeding. The increased risk for hyperbilirubinemia in the 35 and 36 week cohort and the 37 and 38 week cohort of infants is recognized in recent guidelines published by the American Academy of Pediatrics regarding the management of hyperbilirubinemia. In this statement the 35-36 week infants are placed in a high risk category for hyperbilirubinemia whereas the 37-38 week gestation infants are placed in a moderate risk category compared to the low risk category which includes infants delivered at 39 weeks gestation and beyond.

Neurological Issues

Infants at 34-35 weeks gestation have brains that are only 60% the size of their term cohorts. Since a significant amount of brain growth occurs in the last 5-6 weeks of gestation, investigation into the effects of late preterm delivery on brain development is of interest. Autopsy data has demonstrated significant incidences of periventricular leucomalacia in late preterm infants. This may explain some of the difficulties observed in children that were born at 34-37 weeks gestation, which include increased risk of subtle neurological abnormalities, learning difficulties, poor scholastic achievement, and behavioral problems. Over 19% of infants born between 34-37 weeks gestation have clinically significant behavioral problems at the age of 8. Other important issues of neurological immaturity in the late preterm infants include poor feeding, uncoordinated suck and swallowing and general poor vigor with feeding. It is difficult for these infants to initiate and continue breast feeding. This lack of maturity with regards to feeding issues is often overlooked as a cause for prolonged hospitalization in the late preterm infants. I'm sure that many of us have observed 34-36 week gestation infants who are slow to begin feeding and in whom several days if not a week or two was needed before they were able to “take off” with their feeds. This is particularly true when attempting breast feeding. The average hospital length of stay for the 36 week infant is approximately twice that of the 38 week infant. Many times this increase is attributed to poor feeding. Given the risk of poor feeding for the late preterm infant, it is particularly important that they be followed closely after discharge for feeding and growth issues.

In these cases of immature physiology it is important to recognize that the encountered problem will improve with time and that there is little that one can do to hasten improvement other than to support the infant as time progresses. It is important to recognize that in every group of infants there is a spectrum of maturities. Just as some 36 week infants are relatively mature and some are physiologically very immature the same can be said for infants at 37 -40 weeks. When these patterns of immaturity are recognized it can be

very helpful in explaining the infant's response to his or her environment (this is reassuring to parents) and to help predict when the infant will be physiologically mature and ready for home discharge.

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WHEN: April 9-10, 2008 (Wednesday-Thursday)

WHERE: West Des Moines Marriott Hotel

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