Extreme Prematurity: Perinatal Management, Outcomes and Approach on the brink of Viability

6th Annual Regional Neonatal Conference: Decision-Making for Optimal Care and Outcomes

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Objectives

• Discuss extremely premature infants and appropriate perinatal management
• Discuss appropriate perinatal counseling for extremely premature infants
• Define age of viability and discuss current guidelines
• Discuss comprehensive vs selective approach/management of extremely premature infants
• Discuss mortality and outcomes of extremely preterm infants
• Quick Glance: CMH Consensus Guideline for management of perivable infants

Antenatal/Perivable Counseling

• Discussions regarding care of perivable infants should be:
  - Well informed and thorough, ideally with physician present
  - Ethically sound and free of personal bias
  - Consistent within medical teams/institutional practices
  - Individualized, adaptive to change and considerate of long term mortality
  - Consistent with parents wishes; shared decision making
  - Inclusive of the option of comfort care, family bonding, palliative care and should include option of pregnancy termination from and OB standpoint

Antenatal/Perivable Counseling

<table>
<thead>
<tr>
<th>Antenatal/Perivable Counseling</th>
<th>Options</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antenatal counseling for perivable infants</td>
<td>Prevention</td>
</tr>
<tr>
<td>Perivable counseling for perivable infants</td>
<td>Intervention</td>
</tr>
<tr>
<td>Recommendations</td>
<td>Six months</td>
</tr>
</tbody>
</table>


What Actually Happens…

- Difficult questions and conversations for all involved
  - Including whether or not to initiate resuscitation
- Variation in practice
  - Driven by unclear outcomes
  - Individual bias with regard to these outcomes
  - Difficultly communicating to multidisciplinary team and parents during a stressful time
  - Emotionally charged environment


Periviable birth: executive summary of a Joint Workshop by the Eunice Kennedy Shriver National Institute of Child Health and Human Development, Society for Maternal-Fetal Medicine, American Academy of Pediatrics, and American College of Obstetricians and Gynecologists

Pub 2014. UPDATE 2016, 2017
- Periviable gestation (broadly defined as 20 0/7 through 25 6/7 weeks of gestation
- Described outcomes after periviable birth
- Provides current evidence and recommendations regarding interventions in this setting
- Provides outline for family counseling with the goal of incorporating parent preferences
  - A plan for follow-up counseling
  - Recommended developing educational curricula on the care and counseling of families facing the birth of a periviable infant.


Neonatal Survival and neurodevelopmental disabilities vary greatly and are significantly influenced by obstetric and neonatal management practices:

- Antenatal steroids
- Tocolytic agents
- Antibiotics
- Cesarean birth
- Local protocols for perinatal care
- Neonatal resuscitation
The Joint Workshop sought out to address these unresolved issues

- Where should women at risk for periviable birth be cared for?
- When should tocolytic agents and antenatal corticosteroids be given to delay delivery and to advance fetal lung maturatation?
- When should electronic fetal monitoring be instituted to assess the fetal status?
- When should cesarean delivery be offered for fetal indications? (including classical cesarean)
- How should the potential benefits to the infant and the risks to the mother from cesarean birth at a periviable gestation be balanced?
- When and how should the family be counseled regarding these complex issues and what should the contents of such counseling be?
- When and how should decisions regarding initial or continued intensive newborn care versus comfort care be made?
• 0.4-0.5% of all births occur before 27 wks of gestation and these account for over 40% of infant deaths and most neonatal deaths
• 20-21 wks do not survive irrespective of resuscitation efforts


Long-term Outcomes

• Wood et al reported a progressive decline (at 30 months of age) in the proportion of children with ‘severe’ disability (Bayley Scale score 54 or lower) with increasing GA
  - 27% at 23 wks to 17% at 25 wks
• Marlow et al reported overall disability (cognition, neuromotor, hearing and vision at 6yrs in same cohort
  - 25% at 23 wks and 18% at 25 wks
• In a systematic review, Moore et al evaluated long term neurodevelopmental outcomes at 4-8 yrs among survivors born btwn 22 and 25 weeks
  - Risk of mod to severe ND impairment decreased 6% for each week gained in gestation


"Outcomes following a comprehensive versus a selective approach for infants born at 22 weeks of gestation"

• Objective: To examine outcomes at two institutions with different approaches to care among infants born at 22 weeks of gestation.
• Study Design: Retrospective, cohort study (2006–2015)
  • Enrollment limited to mother-infant dyads at 22 weeks
  • Proactive Care: defined as provision of antenatal corticosteroids and neonatal resuscitation and intensive care.
  • Uppsala, Sweden; UUCH: provided proactive care to all mother–infant dyads (comprehensive center)
  • Nationwide Children’s Hospital, USA; NCH: initiated or withheld treatment based on physician and family preferences (selective center). Differences in outcomes between the two centers were evaluated.
"Outcomes at 18-22 months of Corrected Age for Infants born at 22 to 25 weeks of Gestation in a Center Practicing Active Management"

- **Objective:** to assess outcomes in actively managed extremely preterm infants after admission to a NICU
- **Study design:** Retrospective Cohort (n=255) btwn 22-25 wga 2006-2015; single study institution.
- **Results:**
  - 70 infants born at 22-23wks (22w n= 20; 23w n=50) and 178 infants born at 24-25wks (24w n=79; 25w n=99) were included.
  - Survival to hospital discharge of those surviving to NICU admission was 78% (55/70) at 22-23wks and 89% at 24-25wks (P=.02).
  - No or mild neurodevelopmental impairment in surviving infants was 64% at 22-23w and 76% at 24-45w.
- **Conclusion:** although survival was lower in infants born at 22-23 weeks than at 24-25 weeks of gestation, the majority of survivors in both groups had positive outcomes with no or mild neurodevelopmental impairments.

**In a perfect Perivable infants do not survive without life sustaining interventions immediately after delivery**

- All perivable births should occur in at least a tertiary care center
- With experts in MFM to manage maternal complications and highest level of NICU services for baby
- Protocols should be developed to clarify processes for consultation and transfer as well as perinatal management

Obstetric Care

Obstetric interventions

• Measures to delay delivery and improve outcomes when delivery is anticipated:
  • Emergent cerclage
  • Tocolytic therapy
  • Antibiotics
  • Antenatal Corticosteroids
  • Willingness to intervene while preventing stillbirth and fetal trauma

Cervical Cerclage

Why? Prolong pregnancy when fetal membranes are seen to bulge to or past the external cervical os in the absence of contractions

• Observational studies show that physical exam indicated cerclage, performed at an average of 22 weeks
  • can be associated with mean pregnancy prolongation of 7-9 weeks compared to 2-3 weeks for those managed without cerclage placement
  • Increased live birth and neonatal survival

Tocolytic Therapy

Why? To reduce uterine activity and delay delivery to increase time for steroid effects.

- Data regarding current therapeutic tocolytic agents fail to consistently demonstrate either pregnancy prolongation beyond 24-48 hours or newborn benefits.
- No studies address women with PTL or PROM at 20-25 wks.


Intrapartum Antibiotics/GBS Prophylaxis

Why? Reduces newborn infection and can prolong pregnancy in conservative management of PPROM.

- Studies of these interventions have limited numbers of women near limit of viability and specific data for those at 20-25 wks are lacking.


Antenatal Corticosteroids (ACS)

Why? Accelerates Fetal Lung Maturity.

- One of the most effective antenatal interventions to improve outcomes.
- Lung tissue in explant culture (12-24 week human fetuses) + corticosteroids = increase in epithelial thickness and the appearance of lamellar bodies.
- NICHD data revealed reduction in death and neurodevelopmental impairment at 18-22 months in infants exposed to ACS when born 23.0-23.6 wga (83.4% vs 90.5%), 24.0-24.6 wga (68.4% vs 80.3%), and 25.0-25.6 wga (52.7% vs 67.9%). In this study antenatal corticosteroid exposure decreased incidence of death, IVH, PVL and NEC in infants born between 23.0-25.6 wga.
- Mori et al. reported that infants exposed to ACS before birth at 24-25 weeks of gestation had less frequent RDS.
- Tyson et al. estimated that ACS increased the “functional” (in terms of maturity) gestational age of those born at 22-25 weeks by 1.1, 1.2 and 1.3 weeks for survival, death or profound impairment, and death or any impairment, respectively.
- Optimal timing Days 1-7 before birth.
Magnesium Sulfate

Why? To improve neurological outcomes

• Has been studied among women at risk for imminent early preterm birth in 5 RCTs including women recruited at 24-25 weeks of gestation.
• Reduced cerebral palsy and substantial gross motor dysfunction among survivors who increasing mortality
• Similar effects were seen with administration before 30 weeks of gestation for any cerebral palsy moderate-to-severe cerebral palsy and death
• However, data specific to those treated at 20–25 weeks are not available.

Cesarean Delivery

Questions to consider?
• Is routine cesarean appropriate?
• If not, will emergency cesarean be considered to prevent trauma, stillbirth or fetal asphyxia?
• Published literature regarding cesarean for perivable birth is limited by lack of data in relation to periviability
• No RCTs of adequate size regarding planned C-section vs planned vaginal delivery for periviable infants
• Current data do not consistently support routine cesarean to improve perinatal mortality, neurological outcomes or other long term outcomes

Cesarean and Maternal Health/Outcomes

• Cesarean in the periviable period incurs greater maternal morbidity both immediately postoperatively and for future pregnancies which must be considered in the risk/benefit balance with counseling.
• Emergent cerclage or classical cesarean delivery
• Preterm birth associated with fetal malpresentation and higher need for a classical cesarean
• Recent data indicate that regardless of incision type, periviable cesarean delivery results in an increased risk of uterine rupture in a subsequent pregnancy
• Expectant management in setting of PPROM, severe preeclampsia
• Higher risk of maternal infection, HELLP

Neonatal Care

Levels of NICU Care

- Level I: Well Newborn Nurseries
- Level II: stable/moderately ill newborns ≥ 32 wks or >1500g with problems expected to resolve rapidly. No subspecialty level services available
- Level III: <32 weeks, <1500g, NNP and Neonatologist continuously available. Some sub-specialty services and advanced imaging modalities are available. Therapeutic Hypothermia is available
- Level IV: All services of level III with addition of full spectrum of pediatric and surgical subspecialties and availability of ECMO, cardiac surgery

THE GOLDEN HOURS

- First 48-72 hours
  - Apparent stability often followed by deterioration
  - Immature and noncompliant lungs lead to difficulties with ventilation often requiring HFOV and surfactant
  - Low MAP: no evidence based guidelines to define hypotension or it’s treatment
- Critical to survival
  - Thermoregulation
  - Respiratory and CV support
  - Fluid, electrolytes and nutritional management (diuresis, natriuresis, higher TBW, thinness of skin)
  - Acid-base balance
  - Cerebral protection measures to prevent ICH

ELBW Interventions

- Indomethacin
- Vitamin A
- Caffeine
- HFOV

Guidelines for the Management of Extremely Premature Deliveries: A Systematic Review

- 47 highly developed countries
- 34 guidelines from 23 countries and 4 international groups were identified
  - 3 did not state management recommendations
  - Remaining 31 guidelines, 21 (68%) supported comfort care at 22 weeks’ gestation, and 20 (65%) supported active care at 25 weeks’ gestation.
  - Between 23 and 24 weeks’ gestation, much greater variation was seen

- Conclusion: Although there is a wide variation in recommendations (especially between 23 and 24 weeks’ GA), there is general agreement for comfort care at 22 weeks’ GA and active care at 25 weeks’ GA.

CMH NICU PERIVIABILITY CONSENSUS GUIDELINE

12 weeks gestation
- comfort care only

13-20 weeks gestation
- Will offer sedation/counseling at parents request after counseling, but will not recommend sedation
  - Intravenous maternal counseling and sedation: administration of maternal corticosteroids and fetal monitoring as soon as possible regardless of mode of delivery

13-20 weeks gestation
- Will offer sedation/counseling after counseling unless parents decide comfort care or there is a physiological abnormality

13-20 weeks gestation
- Full delivery: more sedation will be provided if indicated; 12 weeks gestation
  - Recommended management of maternal corticosteroids and fetal monitoring as soon as possible regardless of mode of delivery
If you don't believe in Miracles, you've never met a NICU baby...

THANK YOU