Developmental Outcomes of Children Born Prematurely

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Context

- Incidence of preterm birth in the US is 1 in 10 (~400,000/year)
- Significant disparities exist in preterm birth (14% non-Hispanic black vs. 9% white)
- Preterm birth/low birth weight accounts for 17% of infant mortality (#2 cause) and an even higher proportion of morbidity
Context

• Incidence of preterm birth in the US is 1 in 10 (~400,000/year)

~6,000 babies born per year with trisomy 21
Context

• Incidence of preterm birth in the US is 1 in 10 (~400,000/year)

https://thephilanews.com/

~39,000 people die due to firearms per year
Context

• Incidence of preterm birth in the US is 1 in 10 (~400,000/year)

~39,000 people diagnosed with HIV per year
Context

- Incidence of preterm birth in the US is 1 in 10 (~400,000/year)

~1 in 6 Americans have blue eyes
Incidence

Blue Eyes
Prematurity
Gun Deaths
HIV
Down’s Syndrome
Outline

1. Terminology

2. Neurodevelopmental Outcomes

3. Other health outcomes of prematurity that contribute to neurodevelopmental risk

4. Where to refer
Terminology

Gestational Age:
• ≥37 weeks = Term
• 34-37 weeks = Late Preterm
• <28 weeks = Extremely Low Gestational Age

Weight:
• <2500g = Low Birth Weight
• <1500g = Very Low Birth Weight
• <1000g = Extremely Low Birth Weight

Gestational Age + Weight:
• AGA: Birth weight 10-90th Percentile for gestational age
• LGA: >90th Percentile for gestational age (Gestational diabetes, genetic disorders)
• SGA: <10th Percentile for gestational age (pre-eclampsia, maternal medications and drugs, genetic syndromes)
Corrected Gestational Age

• Chronologic age = how many days, weeks, months since birth
  – Example: Born 6 weeks ago → Chronologic age = 6 weeks

• Corrected age = Chronologic age - # of days premature
  – Example: Born 6 weeks ago, at 36 0/7 weeks (i.e. 4 weeks early) → Corrected age = 6 weeks – 4 weeks = 2 weeks

• Correct until 2-3 years old
Survival of Extremely Low Gestational Age Newborns
Short and Long-Term Outcomes for Extremely Preterm Infants
Patel et al, American Journal of Perinatology 2016
Developmental Outcomes of Extremely Low Gestational Age Newborns
Brain Development

• Premature brain smaller & smoother

• Brain volume 60% of term size at 32w

• 1/3 of brain size gained in last 2 months of pregnancy

Seminars in Perinatology, 2016
Factors associated with poor neurodevelopmental outcome

- Low gestational age and birth weight
- Multiple birth
- Male
- IVH
- PVL
- Infection/inflammation
  - Chorioamnionitis
  - BPD
  - Sepsis
  - NEC
- Poor prenatal care
- Maternal obesity
- Nonwhite race
- Smoking
- Drug abuse
- Teen mom
- Low Socioeconomic Status
- Low education level of mom (< 12 years)
- Single mom
Recent Research Examining Premie Outcomes

- Examined 4,272 infants born at 22-24 weeks gestational age.
- Examined neurodevelopmental outcomes at 18-22 months
- Survival without neurodevelopmental impairment 16-29%
- Survival with neurodevelopmental impairment 4-16%

CONCLUSION: Among extremely preterm infants, many but not all babies who survive are at risk for developmental differences, however risk is improving with time
## Neurodevelopmental Outcome in Extremely Preterm Infants at 2.5 Years After Active Perinatal Care in Sweden

**CONCLUSION:** Infants born at higher gestational ages typically do better. However, even babies born very preterm may have no or only very mild difficulties.
Academic attainment and special educational needs in extremely preterm children at 11 years of age: the EPICure study

S Johnson,¹,² E Hennessy,³ R Smith,² R Trikic,² D Wolke,⁴ N Marlow¹,²

- 307 children born at ≤25 weeks gestation
- Assessed school testing and special education needs at 11yo
- Compared premie scores against those of full term classmates
<table>
<thead>
<tr>
<th>Area of Assessment</th>
<th>Term Classmates</th>
<th>Preterm Children</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cognition:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No Impairment</td>
<td>84.3%</td>
<td>31.5%</td>
</tr>
<tr>
<td>Mild Impairment</td>
<td>14.4%</td>
<td>28.8%</td>
</tr>
<tr>
<td>Moderate/Severe Impairment</td>
<td>1.3%</td>
<td>39.7%</td>
</tr>
<tr>
<td><strong>Reading Skills:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No Impairment</td>
<td>88.9%</td>
<td>48.1%</td>
</tr>
<tr>
<td>Mild Impairment</td>
<td>9.2%</td>
<td>21.7%</td>
</tr>
<tr>
<td>Moderate/Severe Impairment</td>
<td>2.0%</td>
<td>30.1%</td>
</tr>
<tr>
<td><strong>Math Skills:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No Impairment</td>
<td>86.3%</td>
<td>30.2%</td>
</tr>
<tr>
<td>Mild Impairment</td>
<td>12.4%</td>
<td>26.0%</td>
</tr>
<tr>
<td>Moderate/Severe Impairment</td>
<td>1.3%</td>
<td>43.7%</td>
</tr>
<tr>
<td><strong>Special Education:</strong></td>
<td>11%</td>
<td>62%</td>
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</table>
• ADHD and Autism also at increased risk in preterm population

• Some suggestion that infants with cerebellar injury at particularly increased risk for Autism

Figure 1. Prevalence (with 95% confidence interval) of ASD by gestational age category. Dashed horizontal line represents ASD prevalence in the U.S. population.
Neurodevelopmental Outcomes of Late and Moderate Preterm Infants

- Infants born 32 0/7-36 6/7 weeks
- 80% of all premature infants
- Difficult to study due to low formal testing and follow-up rates
JAMA Pediatrics, 2017

Cohort study of 201 late preterm infants compared with term controls

Children recruited between 2009 & 2012 in Melbourne, Australia

Rate of serious neurodevelopmental delays very low (2 with CP, no children with blindness of deafness)
## Table 3. Developmental Delay and At-Risk Social-Emotional Development Compared Between the Birth Groups

<table>
<thead>
<tr>
<th>Variable</th>
<th>No./Total No. (%)</th>
<th>Odds Ratio (95% CI)</th>
<th>Adjusted P Value&lt;sup&gt;a&lt;/sup&gt;</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>MLPT Group (n = 198)</td>
<td>Term Group (n = 183)</td>
<td>Unadjusted</td>
</tr>
<tr>
<td>Neurodevelopment</td>
<td></td>
<td></td>
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<td>Cognitive delay</td>
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<td></td>
<td></td>
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<tr>
<td>Less than –1 SD</td>
<td>63/197 (32.0)</td>
<td>34/181 (18.8)</td>
<td>2.0 (1.2-3.3)</td>
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<td>Less than –2 SDs</td>
<td>11/197 (5.6)</td>
<td>4/181 (2.2)</td>
<td>2.5 (0.8-8.3)</td>
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<tr>
<td>Language delay</td>
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<td>85/190 (44.7)</td>
<td>34/178 (19.1)</td>
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<td>10/176 (5.7)</td>
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<td>Social-emotional competence</td>
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Health Outcomes of Prematurity

• Bronchopulmonary Dysplasia (BPD)
• Necrotizing Enterocolitis (NEC)
• Cerebral Palsy (CP)
• Intraventricular hemorrhage/Periventricular leukomalacia (IVH/PVL)
Bronchopulmonary Dysplasia (BPD)

- Chronic lung disease of prematurity
- Maldevelopment of lung tissue following preterm birth
- Most common serious morbidity affecting extremely preterm infants
- Increased work of breathing associated with increased nutritional needs
- Associated with increased risk of adverse neurodevelopmental outcomes
- Symptoms can persist into adolescence/adulthood (wheezing, decreased exercise tolerance)
Necrotizing Enterocolitis

- Inflammatory/infectious process affecting immature gut of preterm infants
- Affects ~2% of NICU population, up to 10% of extremely preterm infants\(^1\)
- High mortality in the neonatal period (30-40% with confirmed NEC in ELBW infants)
- Potential complications include intestinal stricture, short bowel syndrome (due to resection of diseased bowel)

\(^1\)Stoll et al. Pediatrics, 2010
Cerebral Palsy

- Permanent neurologic disorder that affects movement and muscle coordination
- Affects 8-9% of infants born 22-32w and 14% of infants born 22-25w\(^1\)
- Spastic diplegia most common

\(^1\)Stoll et al. Pediatrics, 2010
Risk of Cerebral Palsy Increases with Decreasing Gestational Age
Intraventricular Hemorrhage/Periventricular Leukomalacia

• IVH: Bleeding in brain
• Graded 1-4 (4=worst)
• Higher grade IVH associated with worse neurodevelopmental outcomes.
• PVL: “Holes” in white matter indicating brain injury
• PVL strongly associated with CP
## Characteristics of the 12-Year-Old Cohort

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<th>Term</th>
</tr>
</thead>
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<tr>
<td></td>
<td>Brain Injury</td>
<td>No Brain Injury</td>
</tr>
<tr>
<td>Subjects at study onset</td>
<td>58</td>
<td>408</td>
</tr>
<tr>
<td>Subjects followed up at 12 years</td>
<td>34</td>
<td>337</td>
</tr>
<tr>
<td>Cerebral Palsy</td>
<td>17/34 (50%)</td>
<td>17/337 (5%)</td>
</tr>
<tr>
<td>Hearing Aids</td>
<td>4/33 (12%)</td>
<td>8/323 (2.5%)</td>
</tr>
<tr>
<td>Blind Services</td>
<td>5/32 (16%)</td>
<td>4/325 (1%)</td>
</tr>
<tr>
<td>Any Neurosensory Impairment</td>
<td>21/34 (62%)</td>
<td>34/333 (10%)</td>
</tr>
</tbody>
</table>
Not all risk is biologic

Figure 61-1. Relationship of biological and demographic variables with mental development. Prematurity exerts a potent but short-lived influence on mental development; heritage and home environment have a more lasting effect beyond age 2 years. (Reprinted with permission from Wilson RS. Risk and resilience in early mental development. *Dev Psychol* 21:787, 1985. Copyright 1985 by the American Psychological Association.)
Most brain development occurs at home.

**THE NEURAL NETWORK**

The brain begins developing in the womb and achieves dramatic levels of growth during the first few years of life. During this time, positive experiences contribute to building a strong brain architecture.

**INTO ADULTHOOD**

The infant brain has many more synapses than the adult brain. These connections rapidly increase after birth, then begin a natural decline as the brain specializes. Active connections reinforced by experience stabilize, while weak ones disappear.

**THE FIRST YEAR**

Over time, a child acquires increasingly complex skills:
- Vision
- Hearing
- Touch
- Symbols, ideas
- Social relationships
- Talking
- Critical thinking
- Reflective thinking
- Considered response

GRAPHIC: LAWSON PARKER, NGM STAFF. SOURCE: CHARLES NELSON, HARVARD MEDICAL SCHOOL; PAT LEVITT, CHILDREN'S HOSPITAL LOS ANGELES SYNAPSE DRAWINGS BASED ON GOLGI STAIN PREPARATIONS FROM CONEL (1939-1967)
Where to refer for developmental concerns

• Birth to Three
• Infant Development Follow-up Clinic
  – <32w gestation
  – Intrauterine drug exposure
  – Physician concerns
• LAMBS Clinic (Late and Moderate Preterm Babies)
  – 32-37w gestation
Summary

• Preterm infants are at increased risk for motor, language, cognitive, sensory and behavioral delays/disturbances
• Late preterm infants are at increased risk primarily for language delays, learning disorders and behavioral disorders
• Medical complications of prematurity increase the risk of neurodevelopmental delays
• Please refer families to interdisciplinary support and assessment services, including the Infant Development Follow-up Clinic
Thank You
Resources


• Needelman H, Jackson B. Follow-Up for NICU Graduates. ISBN 978-3-319-73275-6