Developmental Outcomes in Premature Infants: A Life Course Perspective

Emily Myers, MD
Assistant Professor, Developmental and Behavioral Pediatrics
emily.myers@seattlechildrens.org
Educational Goals

• Review life course perspective in low birth weight infants
• Discuss biology behind prematurity and low birth weight
• Discuss developmental outcomes of prematurity and low birth weight
• Integrate outcomes within a life course perspective
Life Course!

- Framework for describing health outcomes
- Intergenerational health connection
- Fetal exposures/adverse events: critical period!
- Childhood events affect long term health
- Perpetuation to future generations

http://genealogy.about.com/od/free_charts/ig/genealogy_charts/family_tree.htm
Commentary

Racial and Ethnic Disparities in Birth Outcomes: A Life-Course Perspective

Michael C. Lu, MD, MPH,¹,³ and Neal Halfon, MD, MPH²
Life Course and Birth Outcome

- Maternal health and development → birth outcome
- Exposures and experiences during critical periods
- Fetal programming → future reproductive health?
- Women who were born low birth weight → Low birth weight infants
- Maternal low birthweight increases risk
Life Course and Birth Outcome

- Stress and hardships “add up”
- Effects of physical and social environments during critical periods
- Chronic exposure to stress $\rightarrow$ reactivity
- Cardiovascular disease, Immune system dysfunction
- Homeless correlated with increased risk of having low birth weight babies
Prematurity

- Full term infant: 40 weeks
- Preterm infant: 38 weeks or earlier
- Late Preterm: 35 and 38 weeks
- Resuscitation initiated at 22-23 weeks
- Gestational age: first day of last menstrual period = day 1
- Timing of ovulation and fertilization → difficult to measure

Low Birth Weight (LBW)

- LBW:<2500g
- Distinct from prematurity
- Etiology of low birth weight differs from prematurity
- Different outcomes
- Very Low Birth Weight (<1500g, 3.3 lb): VLBW
- Extremely Low Birth Weight (<1000g, 2.2 lbs): ELBW
- Often discussed interchangeably despite differences
- Much of the life course research focuses on low birth weight

https://carmenwiki.osu.edu/display/hdfs361sp20119489/Group+9
Risks for Preterm Birth

MULTIFACTORIAL

• Maternal environment
• Maternal health and habits
• Maternal and fetal genomes
• Intrauterine environment
• Fetal health
• Other
• Some similarity to LBW risk factors

Risks of Low Birth Weight

- African American
- Low SES, low level of education
- Maternal age less than 16 or greater than 35
- Unmarried status
- Lack of prenatal care
- Short time interval between pregnancies
- Low pre-pregnancy weight
- Poor weight gain during pregnancy
- Cigarettes, alcohol, illicit drugs
Prematurity Trends

- Preterm birth rate has increased by 30% from 1980 to 2004
- CDC 1 in 9 Births in US
- Mean gestational age at birth decreased from 39.2 weeks to 38.8 between 1985-1988 and 1995-2000
- Highest rates of preterm births among African Americans
- Highest rate of increase in preterm birth rates is occurring in Caucasians, rate of preterm birth decreasing in African
- Increase in preterm birth the greatest between the gestational ages of 33 to 36 weeks
- Preterm birth related to: maternal age, assisted reproductive technology, multiple gestations, increased birth rates for term births with intrauterine growth restriction
Prematurity/LBW Survival

- Medical and technologic advances → improved survival
- LBW infants make up approximately 7% all births but represent 2/3 of neonatal death
- VLBW represent 1% all births but account for 50% of neonatal deaths
- Risk of death in VLBW infants is over 200 times higher than normal birth weight infants

http://www.bronx-ieb.org/Highlights.html
Medical Morbidities of Preterm Birth

- Injuries from etiology of preterm birth
- Delivery complications
- Immature organ systems
- Interventions needed to sustain extra-uterine life
Medical Morbidities: Acute

- Brain injury
- Blindness or visual impairment
- Hearing impairment
- Respiratory distress syndrome
- Necrotizing enterocolitis
- More vulnerable to infection
- Nutritional compromise with difficulties feeding

Medical Morbidities—The Brain

- Anoxic brain injury: maternal hemorrhage, placental abruption, cord prolapse during delivery
- Brain hemorrhage: Grades 1 through 4
- Hydrocephalus: Abnormal fluid buildup in the brain

http://www.politedissent.com/archives/2315
Grade 3 Intraventricular Hemorrhage: in ventricles and dilation

Courtesy of Kapiolani Medical Center For Women And Children
University of Hawaii John A. Burns School of Medicine
Hydrocephalus

Courtesy of Seattle Children’s Hospital
Medical Morbidities—The Eyes

- Retinopathy of Prematurity

  - 50% infants with birth weight below 1000g
  - Retinal detachment, cataracts, closed angle glaucoma
  - Strabismus (eyes not properly aligned), amblyopia (lazy eye), and visual acuity difficulties
Medical Morbidities—The Ears

• Severe hearing impairment: 1-9% of children born < 26 weeks gestation, or birth weight <1000g
• Moderate to severe hearing impairment → difficulties with language development
• Auditory processing and auditory discrimination → academic success
• Universal newborn hearing screening!

http://cochlearimplantonline.com/site/what-to-do-while-waiting-for-your-babys-cochlear-implant/
Developmental Consequences of Prematurity

• Severity of Prematurity: How early the infant was born
• Medical morbidities infant experienced

• How Life Course applies ➔ can you see the cycle continuing?
Developmental Complications of Prematurity

- Motor: Gross and Fine Motor
- Cognitive: Intellectual Disability and Learning Disabilities
- Adaptive: getting dressed, eating, organizing
- Language: Receptive and Expressive Language
- Social: Social Communication
Motor Morbidity of Prematurity: Cerebral Palsy

• “nonprogressive disorder of movement and posture that results from a fixed lesion of the immature brain” Marino et al 2004

Spastic Diplegia

Spastic Quadriplegia
Cerebral Palsy: Prevalence Estimates

- Oskoui et al, 2013 Meta Analysis
- 2500 g + → 1.33 per 1000 live births
- 1500g-2500g → 10.17 per 1000 live births
- 1000g-1500g → 59.18 per 1000 live births
- <1000g → 56.64 per 1000 live births
Cerebral Palsy: Research

• Mercier et al, 2010: prospective cohort study of very low birth weight infants (<1,500 grams), N=3,567, 18-24 months of age
• 8.5% had Cerebral Palsy
• 34.7% quadriplegia
• 42.7% diplegia
Motor Morbidities of Prematurity: Transient Dystonia, Mild Motor Impairment

- Affects how infants early on can explore and manipulate their environment (e.g. develop)
- 12% infants with transient dystonia at 7-9 months of age develop cerebral palsy
- 35%-50% children born below 1000g have evidence of mild motor impairment
- Children with neuromotor abnormalities → other developmental problems

Intellectual Consequences of Prematurity: Intellectual Disability (ID)

- Intellectual disability = IQ < 70
- Mild intellectual disability = IQ 50 - 70
- Moderate intellectual disability = IQ 35 - 49
- Severe intellectual disability = IQ 20 - 34
- Profound intellectual disability = IQ < 20
- +Additional Adaptive Impairment

- These categories set a person into different developmental trajectories
- Mild and moderate are often included in regular education classroom
- Severe/profound need more care
Intellectual Consequences of Prematurity: Intellectual Disability (ID)

- 4 increased risk of ID if born less than 2500 grams (Bilder et al, 2013)
- 1.4 increased risk of ID if born between 32-36 weeks gestation
- 6.9 increased risk of ID if born before 32 weeks gestation
- 2.3 increased risk of ID if birth weight between 1,500g-2,499g
- 11.6 increased risk of ID if birth weight less than 1,500g
Academic Consequences of Preterm Birth

- Language understanding
- Visual perceptual abilities
- Graphomotor skills
- Ability to learn
- Auditory memory
- Visual memory
- Complex language
- Abstract reasoning

How do these affect success of an individual, or promote risk?

http://www.pointoviewes.vbschools.com/
Academic Consequences of Preterm Birth

- Specific learning disabilities
- Grade retention
- Need for special education
- 27% of infants born below 2,500g need support services in classroom (3.5% normal birth weight)
- Hack et al, ELBW had lower achievement scores in spelling, applied mathematics
- Substandard learning progress in written language and mathematics in kindergarten (Hack et al, 2011)

SES predicted these learning problems in many cases
Executive Dysfunction

- The skills and behaviors necessary to organize goals
- Affects how we learn, work and socialize
- Increased risk of having executive dysfunction if born premature or have low birth weight

Kids/adults become more marginalized and cycle repeats
Behavioral Consequences of Preterm Birth

• Attention Deficit Hyperactivity Disorder: 2- to 6- increase in infants born between 1000g and 1,500g
• Children with ADHD are 3.1 times more likely to have been born with a birthweight less than 2,500g
• Hack et al: increased risk of ADHD, generalized anxiety, autistic symptoms, Asperger’s Syndrome symptoms in extremely low birth weight at age 8 years
  • Weakness in this study—lack of true incidence of diagnosis data

http://looneytunes.wikia.com/wiki/Tasmanian_Devil
Adolescent and Adult Functioning

- More likely to repeat one or more grades
- More likely to require special education
- More likely to leave school early
- 74%-82% graduate from high school
- 30-32% matriculate to college

http://www.francis.edu/Commencement.htm
Adolescent and Adult functioning: Self Perception

- Do not perceive themselves as different from their peers behaviorally or emotionally
- Rate themselves lower in scholastic, athletic, romantic and job competency measures
- Women: more difficulty with relationships, mental health
- Parent report: more difficulty with behavior, social skills, attention, scholastic competency
  - To be interpreted with caution SES and other potential confounders exist

[Image]

Future Research and Medical Trajectories

- Recent developmental outcome studies involved children born in the early to mid 1990s
- New technology
- Improved outcome?

http://www.zazzle.com/vintage_science_fiction_rocket_over_the_moon_earth_poster-228067567993836359
Life Course Application

- Adverse developmental outcomes can lead to difficulties in social, employment, and health realms in adults who are born premature
- This could lead to continued economic and social disparity
- Increasing risks for future progeny
Enter department name here

LBW, Premature?

Risk Factors

Protective Factors

Reproductive Potential

0 5ys Puberty Pregnancy Life Course
In Summary

• Studies suggest that a life course model applies to intergenerational disparity in birth outcome
• Low birth weight children are at increased risk themselves of having infants that are low birth weight
• Premature and low birth weight infants have persistent disabilities
• Disabilities that are precipitated by being premature or low birth weight contribute to the perpetuation of low birth weight outcomes in communities
• More research in area needed!