Approaches to Developmental Delay in Neonatal Diabetes: A Framework for Understanding CNS Functioning

Michael E. Msall, MD
University of Chicago Comer Children’s Hospital
Kennedy Research Center on Intellectual and Developmental Disabilities
Center for Developmental and Behavioral Pediatrics
Advances in Monogenic Diabetes and Care
July 20, 2013
Tradition of Developmental Pediatrics

- Builds on Gesell, Illingworth, and Capute
- Examines multidimensional aspects of developmental processes in motor, communicative, cognitive, adaptive, and regulatory behaviors
- Uses a biopsychosocial lifecourse human developmental framework
Measuring Child Developmental and Behavioral Outcomes in an Era of Fragmentation and Scarcity

• Biopsychosocial Model: Integration of Health, Developmental, Social & Community Context
  – Increased Survival of Preterm Infants, Children with I Genetic Disorders and Children with Technology Dependency
  – Increased recognition in early childhood of Autistic Spectrum Disorders as well as communicative and behavioral disorders
  – Increased high stakes educational test.
  – Misinformed zero tolerance.
  – Increasing indicators of family social and economic adversity.
  – Fragmentation in Family Support, Care Coordination, and Comprehensive Medical Homes
  – Tendency to ignore vulnerable children and not prioritize sustainable community prevention efforts
BORN TOO SOON
The high-tech, high-risk drama of keeping the tiniest babies alive

Jason Michael Waldmann Jr., who weighed only 1.6 pounds at birth.
Measuring Quality of Life in Child Neurodisability

Medical Management, Developmental Interventions, Family Supports

Family Values, Beliefs, Judgment

- Health, Growth, Neurological Integrity
- Developmental Skills
  - Functional Skills
  - Behavioral Competencies

- Social Interactions and Community Participation

- Educational and Vocational Successes

-Adapted from Spilker
Parental Concerns About Function

- Will my child be healthy?
- Will my child walk?
- Will my child talk?
- Will my child learn self care?
- Will my child learn at school?
When time is critical in severe neonatal RDS...

INFASURF effectively treats and prevents RDS

INFASURF contains an SP-B level close to that of natural surfactant

Infasurf (calfactant) Intratracheal Suspension

For complete details about contraindications, warnings, precautions, adverse reactions, and dosage and administration, please see brief summary of prescribing information on last page of this advertisement.
1983-86 RCT + Open Infasurfer

24-28 weeks
n=194

50 Betamethasone
55 Neither
89 Surfactant

Neurodevelopmental morbidty among survivors (N=149). CP = cerebral palsy; ID = intellectual disability
Functional Status at Kindergarten Entry

- Walks 150 Feet: 97.3%
- Talks in Sentences: 96.6%
- Toilets Self: 95.9%
- Self-Care/ADL: 95.9%
- Tech Dependent: 2.0%

Predictors of NDD

Cerebral Palsy:
- Ventriculomegaly RR7 (3-18)
- IVH3/4 RR 5 (2-13)

Intellectual Disability:
- Ventriculomegaly RR4 (2-10)
- Sepsis RR4 (2-8)
- Seizures RR3 (1.2-8)
- Minority RR3 (1.3-6)
# Functional Outcomes and Neurodevelopmental Disability

<table>
<thead>
<tr>
<th>Activity</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Walks 150 Feet</td>
<td>87%</td>
</tr>
<tr>
<td>Talks in Sentences</td>
<td>84%</td>
</tr>
<tr>
<td>Toilets Self</td>
<td>81%</td>
</tr>
<tr>
<td>Self-Care/ADL</td>
<td>81%</td>
</tr>
<tr>
<td>Understands Request</td>
<td>94%</td>
</tr>
</tbody>
</table>

Requirements for special education resources among survivors of extreme prematurity (N=149)
## Predictors of Special Education Resources at Kindergarten Entry

<table>
<thead>
<tr>
<th>Predictor</th>
<th>RR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Poverty</td>
<td>7.3</td>
<td>2.5 - 21.4</td>
</tr>
<tr>
<td>Minority status</td>
<td>2.5</td>
<td>1.2 – 5.3</td>
</tr>
<tr>
<td>Male gender</td>
<td>2.4</td>
<td>1.1 – 5.0</td>
</tr>
</tbody>
</table>

Msall et al. AJDC 1992; 146:1371-1375
Skill Formation and the Economics of Investing in Disadvantaged Children

- Brain and skill formation are influenced by interaction of genetics and individual experience.
- Mastery of skills essential for economic success follow hierarchical rules.
- Cognitive, linguistic, social, and emotional competencies are interdependent.

What do we know?

• Early learning confers value on acquired skills, which leads to self-reinforcing motivation to learn more.
• Early mastery of cognitive, social, and emotional competencies makes learning at later ages more efficient and more likely to continue.
• Early family environments are major predictors of cognitive and non-cognitive abilities.

Data from the Abecedarian Program collected when the individuals were 21 Y

### Economic benefits and costs to Perry Preschool Program

<table>
<thead>
<tr>
<th>Category</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Childcare</td>
<td>$986</td>
</tr>
<tr>
<td>Earnings</td>
<td>$40,537</td>
</tr>
<tr>
<td>K-12</td>
<td>$9,184</td>
</tr>
<tr>
<td>College/adult</td>
<td>-$782</td>
</tr>
<tr>
<td>Crime</td>
<td>$94,065</td>
</tr>
<tr>
<td>Welfare</td>
<td>$355</td>
</tr>
<tr>
<td>Abuse/neglect</td>
<td>$0</td>
</tr>
<tr>
<td><strong>Total benefits</strong></td>
<td><strong>$144,345</strong></td>
</tr>
<tr>
<td><strong>Total costs</strong></td>
<td><strong>$16,514</strong></td>
</tr>
<tr>
<td><strong>Net present value</strong></td>
<td><strong>$127,831</strong></td>
</tr>
<tr>
<td><strong>Benefits to cost ratio</strong></td>
<td><strong>8.74</strong></td>
</tr>
</tbody>
</table>

17 Year Outcomes in Functioning and Participation after Prematurity: Applications of the International Classification of Functioning Model

Michael E. Msall¹, Robin J. Miller², Mary C. Sullivan ²,³

¹ Developmental and Behavioral Pediatrics, Kennedy Research Center on Intellectual and Developmental Disability, Comer Children’s Hospital, University of Chicago, Chicago, IL; ² Brown Center for the Study of Children at Risk, Brown University, Providence, RI; and ³ College of Nursing, University of Rhode Island, Kingston, RI
Research Opportunities in Monogenic Diabetes I

• What are the mechanisms by which KCN channels lead to refractory seizures
• What is it about these channels compared to SCN channels.
• What brain systems contribute to a spectrum of developmental coordination disorders?
Research Opportunities in Monogenic Diabetes II

• Are there specific functional neuroimaging correlates of children with motor and speech apraxia?

• How do KCN channels relate to diverse brain networks underlying verbal, performance, and executive function skills?

• How do KCN channels relate to the social brain, mood stability, and regulatory behaviors
What does this tell us?

• Understanding factors that promote and restrict developmental processes in monogenic diabetes can help inform neurobiological mechanisms.

• Early intervention for vulnerable children (minority, genetic, developmental) have higher returns than later interventions (e.g., reduced teacher-student ratio, public job training, convict rehabilitation programs, etc.)

DBP Chicago Model

Examine sequential outcomes after implementing translational science and community interventions so that disability is prevented, function optimized, and we create systems of care that strive to eliminate health care disparities for vulnerable children.
Lifecourse Developmental Medicine

A partnership between health professionals, children, families, and community supports.

A biopsychosocial framework of coordination and collaboration

Investing in children, science and community supports that optimize health, functioning, and well being.
Prevalence of Big 3: Middle Childhood

- Language Disabilities: 5%
- Reading Disabilities: 15%
- ADHD: 10%
ADHD: A Paradigm of Executive Function and CNS Dynamic Connectivity

- ADHD is a multisystem disorder leading to academic, social, and psychological disruption
- Historically, it was viewed as a benign, although intense, transient behavioral disturbance of prepubescent children
- It is a life long neurodevelopmental disorder that is neither benign or transient and has major public health implications
Neurobehavioral Impact

- 50% of ADHD have LD
- 25% of children with math disability have attention problems
- Many children with ADHD have challenging behaviors at home and school.
- Children with combined and inattentive ADHD have more social problems
- Families with ADHD & CD have high rates of depression, anxiety, alcoholism, substance use
Mental Health Impact

- ADHD-I have more learning problems and are at greater risk for depression
- Indicators of depression in ADHD include changes in functioning, family history of mood disorders, and initial diagnosis in adolescence
- Children with ADHD and depression are at increased risk for challenging behaviors and adolescent/adult risk taking behaviors.
- Appropriate multimodal treatment of early elementary school children with ADHD would probably avoid many adverse trajectories.
Genetics

• Genetic factors are important
• Dopamine transporter was the first gene identified in influencing development of ADHD
• ADHD is probably an AD disorder with reduced penetrance
• LD and ADHD may be transmitted independently
• Advances occurring in functional neuroimaging
ADHD is a Neurodevelopmental Disorder

- The severity, not the presence, of symptoms may relate to parenting skills
- Diagnosis and management requires collaboration
- Although there may be some over diagnosis, there is more underdiagnosis, misdiagnosis, and incomplete diagnosis
- Variability in performance eludes a checklist approach
Initial Screening

• How is your child doing in school?
• Are there any problems with learning that you or the teacher has seen?
• Are you concerned with any behavioral problems in school, at home, or when your child is playing with friends?
• Is your child having problems completing classwork or homework?

Typical Pre-School Presentation (3-5 Years)

- Motor restlessness (always on the go)
- Aggressive (hits others)
- Spills things
- “Dangerously Daring”
- Vigorous and destructive play
- Demanding, argumentative
- Noisy, interrupts
- Excessive temper tantrums
- Low levels of compliance
Typical Presentation of a School Age Child (6-12 Years)

- Easily distracted
- Homework poorly organized, contains careless errors, often not completed
- Blurts out answers before question is completed (often disruptive in class)
- Often interrupts or intrudes on others and displays aggression (difficulties in peer relationships)
- Fails to wait turn in games
- Often out of seat, fidgety
- Perception of immaturity (not completing chores at home)
Myths About Medication

- Medication is dangerous
- Medication is addictive
- Medications are a sedative or “chemical straightjacket” for children
- Medication will affect my child’s sleep
- Medication will affect my child’s appetite and eating habits
- Medication will reduce my child’s growth
- Some children are too young for medication
- Medication will make my child smarter
- If medication is to be used, let it be the least possible dosage
- “Mother Nature” on the internet
Medication Management

- Stimulants exhibit some of highest therapeutic indices of any drugs in pediatrics
- Effective in 75-80% of cases of ADHD
- Mood elevation and euphoria do not occur in children with ADHD on stimulants
- Anxiety and dysphoria may occur in preschoolers on stimulants
- Stimulants do not cause tic disorder but may accelerate expression
- Many children with ADHD have sleep disorders
- Stimulant medication is the subject of many urban myths
- Never use medication as the only mode of intervention
- Use caution in evaluating web information
Principles and Perspectives on Referrals for Assessment

- A child should not be treated for ADHD unless there is an evaluation of academic skills.
- ADHD-I and ADHD-C are associated with greater levels of school problems.
- ADHD-HI is associated with impaired peer socialization and presence of externalizing disorders.
- ADHD-HI is least common form of ADHD but youngest in age of referral.
- ADHD-I is oldest in age of clinic referral but highest in percentage of referrals.
Section 504 of Rehabilitation Act and IDEA 1997 (PL 105-17)

• School must provide reasonable accommodations and necessary related services and special education supports. Helpful tools include
  – Peer tutoring
  – Cooperative learning
  – Graphic organizers
  – Study guides
  – Organizational routines
  – Learning strategies instruction

Lerner & Yasutaki, pg 476.
Principals of Accommodation

- Recognize individual differences in pacing and cognitive style and promote full inclusion
- ADHD is not an excuse for threatening, noxious, or counterproductive behavior in school or employment

Hinchlaw in Accardo & Whitman, 2000. Pg XV
Long Term Outcome of ADHD

- 70% do not have serious negative outcomes but do less well than siblings or controls
- Long term psychostimulant mediation combined with counseling appears to play a critical role
- Psychiatric and substance abuse, legal difficulties, interpersonal failures, and occupational underachievement occur in 30%

Whitman, pg 697.
Conclusion

• Common sense holism
• Be careful about grade repetition
• Time on task matters
• Promote prevention, resiliency, and community participation