AUCD-CDC Fellowship Experience with the Developmental Disabilities Branch

AUCD Webinar Presentation
March 26, 2008

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Centers for Disease Control and Prevention

National Center on Birth Defects and Developmental Disabilities
Presentation Outline

- Background
- Overview of CDC Developmental Disabilities Branch
  - Example Data Set (MADDSP)
- AUCD Fellowship
  - Activities
  - Research Projects
    - Details of metabolic study
- Mentor Experience
  - Kim Van Naarden Braun, PhD, Epidemiologist and Surveillance Team Lead
Experience Prior to Fellowship

- BS & MS in Nutritional Sciences
- Dietetic Internship at USC University Center for Excellence in Developmental Disabilities at the Children’s Hospital of Los Angeles
- Registered Dietitian with focus on inborn errors of metabolism
- PhD in Maternal and Child Health at UNC-Chapel Hill School of Public Health
DDB Vision and Mission

- Increase the awareness of developmental disabilities by providing effective public health educational interventions to the public and to providers.

- Strengthen the national capacity to conduct population-based surveillance for developmental disabilities.

- Enhance the capability and capacity for conducting epidemiologic research on developmental disabilities.

- Increase the capacity to plan, develop, and implement developmental disabilities prevention and intervention programs.
Overview of DDB Activities

- Surveillance Systems (MADDSP, ADDM)
  - prevalence rates
  - registry of cases
  - monitor prevention

- Epidemiological Studies (SEED)
  - risk factors
  - protective factors
  - public concerns

- Prevention Programs (Learn the Signs, Act Early)
  - prevention strategies
  - public policy
  - education
Metropolitan Atlanta Developmental Disabilities Surveillance Program (MADDSP)

How common is
Autism Spectrum Disorders (ASD)?
Mental Retardation?
Hearing Loss?
Vision Impairment?
Cerebral Palsy?
Ongoing, population-based, active monitoring program based on record review.

- Intellectual disabilities, cerebral palsy, vision impairment and hearing loss; autism added for 1996 and subsequent study years

MADDSP: Program Design

- Multiple sources (educational, clinical, service)
- Five counties in metro Atlanta
- Linked to other data sets such as birth certificate data, birth defects, special education and others
MADDSP: Objectives

- To provide regular and systematic monitoring of prevalence of selected developmental disabilities (DDs) according to demographic factors such as age, sex, race/ethnicity and to examine temporal trends in the prevalence of the conditions;

- To assess the possible relationships between selected maternal and child characteristics noted on birth certificates and the occurrence of the selected DDs;
MADDSP: Objectives

- To examine the social, emotional, medical and educational consequences of DDs;
- To provide a framework for initiating special studies of children with the selected DDs through establishment of a large case series of such children.
AUCD-CDC Fellowship
AUCD-CDC Fellowship at NCBDDD

- Opportunity for graduate, post-doctoral and mid-career professionals enrolled or employed at AUCD member programs

- Epidemiologic training in developmental disabilities and child health and development

- With the Developmental Disabilities Branch of the CDC’s National Center on Birth Defects and Developmental Disabilities (NCBDDD)
  - http://www.cdc.gov/ncbddd/
Fellowship Opportunities

- Experience the CDC
- Attend lectures, seminars & conferences
  - Hear about latest research around the world
- Take CDC classes (e.g. SAS, SUDDAN)
- Interact with colleagues across disciplines
- Be involved with research studies and other branch activities
  - Many rich data sets & access for collaboration
Fellowship Activities

- Experiences at various levels of the CDC organization
  - Learned about purpose, organization and daily functioning of the CDC
  - Participated in NCBDDD activities
    - Presented at journal club and research in progress meetings
    - Attended other center meetings, speakers and celebrations
Fellowship Activities

- Experiences at various levels of the CDC organization (cont’)
  - Involvement in DD Branch Activities
    - Administrative Meeting
    - DD Scientific Meeting
      - Gave 3 presentations
    - GA SEED
      - Observed implementation of national study and assisted with staff training of nutritional materials
  - Portfolio review, retreats and other branch activities
  - Research projects
Fellowship Research Projects

- Developmental Disabilities & Special Education Enrollment Among Multiple Birth Children
  - Examine the prevalence and trends of developmental disabilities and receipt of special education among twins
  - Explore risk factors for having a developmental disability or receiving special education services among twins compared to singletons.

- Socio-demographic Factors & ASD Diagnosis
  - Investigates the relationship between age of first ASD diagnosis with socioeconomic and demographic factors

- Long-term Developmental Outcomes of Children with Inborn Errors of Metabolism: An Update Study
Long-Term Developmental Outcomes of Children with an Inborn Error of Metabolism: Update Study
Study Collaborators

- CDC Developmental Disabilities Branch
  - Kim Van Naarden Braun, PhD
  - Marshalyn Yeargin-Allsopp, MD
  - Lori Plummer

- CDC Pediatric Genetics Team
  - Richard Olney, MD
  - Stuart Shapira, PhD

- Emory University, Division of Medical Genetics
  - Rani Singh, PhD RD
Inborn Errors of Metabolism (IEM) or Metabolic Disorders
- Genetic mutations that interrupt some aspect of metabolism
  - Usually affecting breakdown of amino, organic or fatty acids
  - Example: phe $\xrightarrow{PAH}$ tyr
- Consequences if untreated
  - Metabolic decompensation, behavioral difficulties, poor growth, neurological problems, intellectual disabilities and/or death
- Treatment (medication and/or strict dietary modifications) starting in early infancy can prevent neurologic sequelae
  - However, the success of a treatment’s ability to prevent neurological impairment is dependent on the timeliness of detection and initiation of treatment, patient compliance with treatment protocol and severity/type of IEM
Identifying IEM

- Newborn Screening (NBS)
  - GA NBS until January 1, 2007:
    • Galactosemia, homocystinuria, maple syrup urine disease, phenylketonuria, and tyrosinemia

- Clinical Identification
  - Delayed identification, more symptoms and complications, more likely to have significant deficits in communication, daily living skills, socialization and motor skills
Previous Study

Among children with a metabolic or endocrine disorder identified through GA NBS who were born in Metropolitan Atlanta during 1981-1995:

- Of 147 children with positive NBS for metabolic or endocrine disorder, 3 identified with ID (MADDSP linkage birth cohort 1981-1991)
- Of 216 children with positive NBS for metabolic or endocrine disorder, 9 identified with developmental disability less severe than ID (SEDMA linkage birth cohort 1981-1995)
The current study plans to update the work by Van Naarden Braun et al. and expand the analysis to include children identified clinically with an IEM in order to examine the magnitude of selected developmental disabilities attributable to IEM in Metropolitan Atlanta.
Specific Aims

- **Specific Aim 1**: Determine the number of children with an IEM who have a developmental disability or receive special education services.

- **Specific Aim 2**: Examine different factors that may play a role in the developmental outcomes of children diagnosed with an IEM such as type of IEM/genotype of IEM, clinical vs. newborn screen identification, age at screen, age at intervention, baseline level of metabolite at treatment initiation and compliance to treatment.
Study Population

- **Inclusion Criteria**
  - Born during 1988-2001
  - Diagnosed with an inborn error of metabolism
    - Children were confirmed with a diagnosis either after identification through newborn screening or clinical symptoms.
  - Mother resided in the five-county area of metropolitan Atlanta which included Clayton, Cobb, DeKalb, Fulton and Gwinnett counties.
Data Sources

- Georgia Newborn Screening Program
  - Newborn blood-spot screening for metabolic disorders
    - galactosemia (classical and variant), homocystinuria, maple syrup urine disorder, phenylketonuria, and tyrosinemia

- Emory Clinical Genetics Records
  - Used to identify children diagnosed with metabolic disorder following clinical identification of symptoms
  - Genetic medical history and treatment information reviewed
Data Sources

- Metropolitan Atlanta Developmental Disability Surveillance Program (MADDSP)
  - Methods described earlier
  - Study uses surveillance years 1996, 2000, 2002, 2004 (8 year olds) and conducted separate MADDSP review of records for cases not born in surveillance year cohorts

- Special Education Database of Metropolitan Atlanta (SEDMA)
  - Electronic files from all nine school systems in metropolitan Atlanta which identify children who received special education services and were 3-10 years old
  - For multiple records, used child’s most recent age / exceptionality
Data Linkages

- Data Linkage
  - Children who were identified with an metabolic disorder born from 1988-1996 were linked to MADDSP data (surveillance years 1996, 2000, 2002, 2004) to determine the number children who have a metabolic disorder and a developmental disability.

- Children who were identified with an metabolic disorder born from 1988-2001 were linked to SEDMA data (school years 1998-2004) to determine the number of children who have a metabolic disorder and receive special education services.
Clinical Genetics Record Review

- Physician Review
  - Two pediatric geneticists and a developmental pediatrician assessed the clinical genetics medical records to determine whether the developmental disability could have been attributable to a cause not related to the inborn error of metabolism
  - Degree of certainty will be assigned
    - Based on guidelines for MADDSP ASD Clinician Review
    - scale of 1-5 from (not sure to very sure)
    - indicating reason for unsure response (1-3)
Clinical Genetics Record Review

- **Dietitian Review**
  - Two registered dietitians reviewed laboratory results for ages 0-3 years or 3 years after diagnosis to assign level of metabolic control
  - Consensus was made to define metabolic control by disorder based on clinical care
  - 4pt scale – fair, poor, good, excellent
Data Analysis

- Calculate the number of children with an IEM who have a developmental disability or receive special education services (noting exceptionality).

- Calculate the number of children expected to have intellectual disabilities using annual and cumulative incidence rates from each disorder screened for in Georgia and the number of live-births for the corresponding area of Metropolitan Atlanta.

- Summarize factors that may have contributed to the developmental outcomes such as newborn versus clinical identification.
Preliminary Results
Flow Chart Illustrating the Number of Children Identified by Newborn Screening Test with Metabolic Disorders who have a Developmental Disability or Receive Special Education Services

580,192
Live Births
1988-2001
5 County Metro Atlanta

127
Diagnosed with Metabolic Disorders Following a Positive Newborn Screen

115
No DD or Special Ed

11 GG Gal
75 Gal
7 DD Gal
1 HCY
2 MSUD
13 Hyperphe
11 PKU

11
Special Education

2 GG Gal
5 DG Gal
2 MSUD
2 PKU

1
MADDSP

1 MSUD

Abbreviations: MADDSP= Developmental Disability per MADDSP surveillance, Ed= Education, GAL= Galactosemia, GG= Classical Galactosemia, DG= Duarte Galactosemia, DD= Duarte Homozygote, HCY= Homocystinuria, MSUD= Maple Syrup Urine Disorder, PHE= Phenylalanine test, PKU= Phenylketonuria, Hyperphe= Hyper Phenylalanine
Characteristics of children who were identified by newborn screening and diagnosed with a metabolic disorder and were identified in MADDSP (1988, 1992, 1994, or 1996) or SEDMA (1989-2003)

<table>
<thead>
<tr>
<th>ID Number†</th>
<th>Year of Birth</th>
<th>Type of Metabolic Disorder</th>
<th>Age at Initiation of Treatment</th>
<th>Metabolic Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>MADDSP</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cerebral Palsy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1*</td>
<td>1992</td>
<td>Maple Syrup Urine Disorder</td>
<td>15 days</td>
<td>excellent</td>
</tr>
<tr>
<td>Mental Retardation / Intellectual Disability</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1*</td>
<td>1992</td>
<td>Maple Syrup Urine Disorder</td>
<td>15 days</td>
<td>excellent</td>
</tr>
<tr>
<td>SEDMA</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Autism</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>2000</td>
<td>Phenylketonuria</td>
<td>3 days</td>
<td>excellent</td>
</tr>
<tr>
<td>Behavior Disorder</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>1995</td>
<td>Duarte Galactosemia</td>
<td>29 days</td>
<td>unknown</td>
</tr>
<tr>
<td>Learning Disorder</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>1992</td>
<td>Duarte Galactosemia</td>
<td>17 days</td>
<td>fair</td>
</tr>
<tr>
<td>5</td>
<td>1990</td>
<td>Duarte Galactosemia</td>
<td>19 days</td>
<td>excellent</td>
</tr>
<tr>
<td>6</td>
<td>1995</td>
<td>Phenylketonuria</td>
<td>12 days</td>
<td>poor</td>
</tr>
<tr>
<td>Mild Intellectual Disability</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7*</td>
<td>1999</td>
<td>Classical Galactosemia</td>
<td>10 days</td>
<td>fair</td>
</tr>
<tr>
<td>Moderate Intellectual Disability</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>1991</td>
<td>Classical Galactosemia</td>
<td>7 days</td>
<td>fair</td>
</tr>
<tr>
<td>Other Health Impairment</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>1995</td>
<td>Maple Syrup Urine Disorder</td>
<td>6 days</td>
<td>excellent</td>
</tr>
<tr>
<td>10</td>
<td>1991</td>
<td>Maple Syrup Urine Disorder</td>
<td>12 days</td>
<td>excellent</td>
</tr>
<tr>
<td>Significant Developmental Delay ‡</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>11*</td>
<td>1999</td>
<td>Galactosemia</td>
<td>10 days</td>
<td>fair</td>
</tr>
<tr>
<td>Speech/Language Disorder</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>1992</td>
<td>Duarte Galactosemia</td>
<td>34 days</td>
<td>excellent</td>
</tr>
<tr>
<td>13</td>
<td>1988</td>
<td>Duarte Galactosemia</td>
<td>16 days</td>
<td>excellent</td>
</tr>
</tbody>
</table>

† Case definition of MADDSP takes priority over SEDMA exceptionality
‡ Significant developmental delay used until age 5 and then must be replaced with more specific exceptionality

*MADDSP developmental disabilities are not mutually exclusive
Flow Chart Illustrating the Number of Children Clinically Identified with a Metabolic Disorders who have a Developmental Disability or Receive Special Education Services

- **42** Clinically Identified IEM 1988-2003
  - 5 County Metro Atlanta

- **33** No DD or Special Ed
  - 1 3-Methylcrotonyl-CoA Carboxylase
  - 2 Carnitine / Aycilcarnitine Translocase Deficiency
  - 1 Citrullinemia
  - 1 Carnitine Uptake Deficiency
  - 2 Glutaric Aciduria
  - 6 Glycogen Storage Disease
  - 4 Isovaleric Aciduria
  - 3 Long Chain 3-Hydroxyacyl CoA Dehydrogenase

- **8** Special Education
  - 2 Arginosuccinic Acidemia
  - 2 Methylmalonic Aciduria
  - 2 Ornithine Transcarbamylase Deficiency
  - 2 Pyruvate Dehydrogenase Deficiency
  - 2 Short Chain Acyl-CoA Dehydrogenase Deficiency
  - 3 Tyrosinemia

- **1** MADDSP
  - 1 Citrullinemia

Preliminary data
**Characteristics of children who were clinically identified and diagnosed with a metabolic disorder and were identified in MADDSP (born 1988, 1992, 1994, or 1996) or SEDMA (1989-2003)**

<table>
<thead>
<tr>
<th>ID Number†</th>
<th>Year of Birth</th>
<th>Type of Metabolic Disorder</th>
<th>Type of Diagnosis</th>
<th>Age at Initiation of Treatment</th>
<th>Metabolic Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>MADDSP</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mental Retardation / Intellectual Disability</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>1994</td>
<td>Citrullinemia</td>
<td>Prenatal Dx</td>
<td>birth</td>
<td>good</td>
</tr>
<tr>
<td>15</td>
<td>1994</td>
<td>MCADD</td>
<td>Prev Sib Death</td>
<td>birth</td>
<td>good</td>
</tr>
<tr>
<td>SEDMA</td>
<td></td>
<td>Learning Disorder</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>1991</td>
<td>Methylmalonic acidemia</td>
<td>Clinical ID</td>
<td>infancy</td>
<td>pending</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Moderate Intellectual Disability</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>17</td>
<td>1997</td>
<td>Mevalonic aciduria</td>
<td>Clinical ID</td>
<td>2 years</td>
<td>pending</td>
</tr>
<tr>
<td>18</td>
<td>1994</td>
<td>Homocystinuria</td>
<td>Clinical ID</td>
<td>9 years</td>
<td>poor</td>
</tr>
<tr>
<td>19</td>
<td>1990</td>
<td>ASA</td>
<td>Clinical ID</td>
<td>3 days</td>
<td>excellent</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Significant Developmentally Delay</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20</td>
<td>1993</td>
<td>ASA</td>
<td>Clinical ID</td>
<td>7 years 6 months</td>
<td>excellent</td>
</tr>
<tr>
<td>21</td>
<td>1998</td>
<td>OTC</td>
<td>Clinical ID, no NBS born out of country</td>
<td>3 years 5 month</td>
<td>unknown</td>
</tr>
<tr>
<td>22</td>
<td>1995</td>
<td>Propionic Acidemia</td>
<td>Clinical ID</td>
<td>3 days</td>
<td>excellent</td>
</tr>
</tbody>
</table>

† Case definition of MADDSP takes priority over SEDMA exceptionality
# Observed and Expected Number of Children who have a Developmental Disability or Receive Special Education Services after a Positive Newborn Screen and Confirmatory Diagnosis for a Metabolic Disorder, 1988-2001

<table>
<thead>
<tr>
<th>Metabolic Disorder</th>
<th>Birth Prevalence per 100,000*</th>
<th>Expected number of affected children with DD, in untreated†</th>
<th>Observed number of children with DD (MADDSP)</th>
<th>Observed number of children receiving special education (SEDMA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phenylketonuria</td>
<td>3.9</td>
<td>22</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Homocystinuria</td>
<td>0.2</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Maple Syrup Urine Disorder</td>
<td>0.6</td>
<td>4</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Tyrosinemia</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prolonged Neonatal</td>
<td>0.1</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Type II</td>
<td>0.2</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Galactosemia</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Classic</td>
<td>2.7</td>
<td>16</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Variant</td>
<td>14.6</td>
<td>85</td>
<td>0</td>
<td>5</td>
</tr>
</tbody>
</table>

*Birth prevalence rate in Georgia for 1988-2001
†Based on the birth prevalence in Georgia and the number of live-born infants of metropolitan Atlanta residents, 1988-2001
Next Steps

- Finish Review of off-MADDSP surveillance year cases
- Finalize Physician Review of cases
- Confirm residency during study ages in metropolitan Atlanta to be eligible for data linkages
- Prepare manuscript for publication
Acknowledgements

Developmental Disabilities Branch
- Marshalyn Yeargin-Allsopp, MD, Branch Chief, Developmental Disabilities Surveillance and Epidemiology
- Kim Van Naarden Braun, PhD, Epidemiologist
- Developmental Disabilities Branch

AUCD
- George Jesien, PhD, Executive Director
- Sue Lin, MS, Project Director, CDC Cooperative Agreement
- AUCD Staff
THANK YOU!
Mentor Experience
Presentation Outline

- Background
- Overview of CDC Developmental Disabilities Branch
  - Example Data Set (MADDSP)
- AUCD Fellowship
  - Activities
  - Research Projects
    - Details of metabolic study
- Mentor Experience –
  - Kim Van Naarden Braun, PhD,
    Epidemiologist and Surveillance Team Lead
Mentor Experience

Kim Van Naarden Braun, PhD, Epidemiologist and Surveillance Team Lead
Process of AUCD fellowship with the Developmental Disabilities Branch

- Prior to acceptance of fellow
  - Project Lead brainstorming for analytic projects and identification of multiple options

- Orientation:
  - Multiple modules addressing all aspects of Branch-wide activities and specific aspects of fellow’s project.
Process of AUCD fellowship with the Developmental Disabilities Branch

- Meet with technical monitor at least once a week to discuss progress and troubleshoot issues.

- Technical monitor is responsible for scientific and programmatic support.

- Technical monitor facilitates and encourages presentations of works-in-progress at DD Scientific meetings (Branch-wide), journal clubs and research in progress meetings (Division-wide).
Scope of AUCD fellowship with the Developmental Disabilities Branch

- Exposure to numerous intramural and extramural programs both those in existence and those in beginning implementation phases.

- Participate in CDC offered courses and seminars.

- Encourage and assist in submission of projects for poster and oral presentations to national scientific meetings.
Scope of AUCD fellowship with the Developmental Disabilities Branch

- In addition to other learning opportunities, the goal of AUCD fellowship is to complete at least 1 analytic project for publication.

- Potential for remaining with DDB after fellowship.
2006-2008 AUCD fellowship experience

- Great match between DDB goals and activities and fellow’s training and experiences.
- Strong analytic and writing skills
- Willingness to participate in wide variety of activities and assist on smaller projects
- Positive team player