



Long-term Follow-up of Patients Identified by Newborn Screening with Tandem Mass Spectrometry – Getting Started

Sara Copeland, MD

Medical Director of Newborn Screening in Iowa

Department of Pediatrics, Children's Hospital of Iowa

Tandem Mass Spectrometry in NBS

- ◆ 1996- first report of diagnosing aminoacidopathies on blood spots using MS/MS
- ◆ 1997 – population based pilot study in North Carolina for routine MS/MS screening on dried blood spots
- ◆ 2000- National Newborn Screening and Genetics Resource Center, CDC and HRSA held workshop to explore MS/MS in NBS
- ◆ 2000- Pilot study in Iowa to add MCADD
- ◆ 2001- Iowa and the Northwest region added MS/MS to routine testing

Learning from the past....

- ◆ 1960's introduced screening for galactosemia
- ◆ 20 years later start to realize that even well treated patients will have problems with dyspraxia and ovarian failure
- ◆ The underlying physiology of the problems is not understood.
- ◆ With MS/MS ability to diagnose many more disorders, want to be proactive in monitoring and detecting problems.

Establishing the need for LTFU



- “To facilitate evaluations of NBS programs, short-term and long-term performance measures should be collected.”
- “Essential long-term measures should assess whether infants with a diagnosed disorder have developmental disabilities, mental retardation, and premature mortality (5,6) (as measured by hospitalization records to assess burden of illness), and should identify adverse health outcomes associated with each disorder beyond the newborn period.”

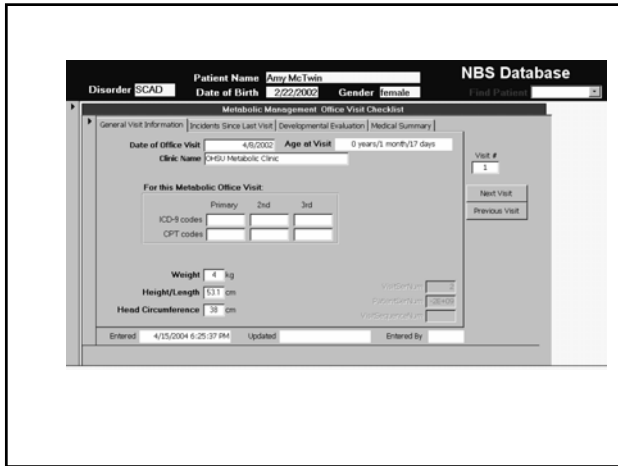
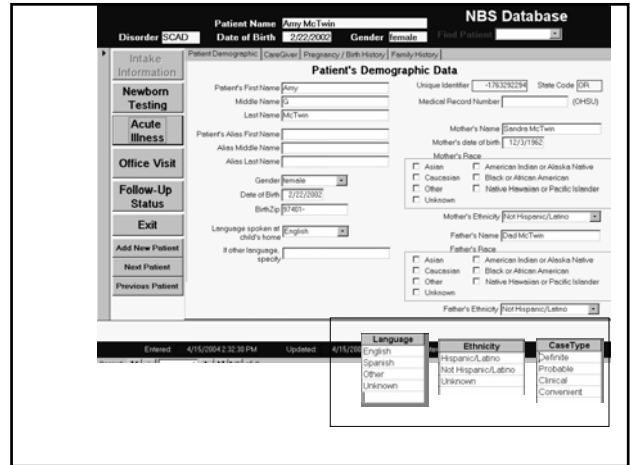
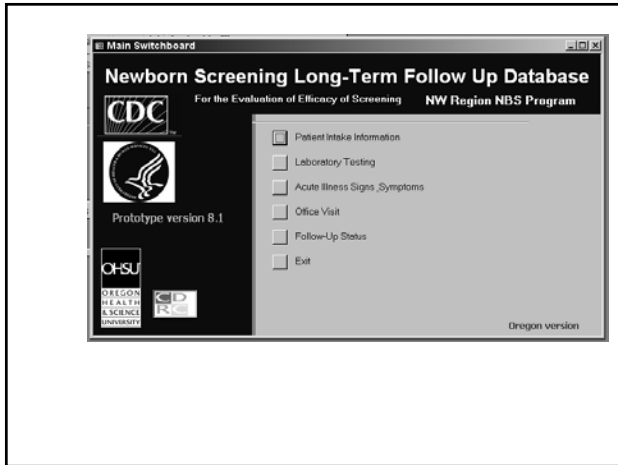
Funding Opportunity

Federal Register 2002 May 31; 67(105):38115-8

- ◆ DEPARTMENT OF HEALTH AND HUMAN SERVICES Centers for Disease Control and Prevention [Program Announcement 02172]
 - Surveillance and Epidemiologic Research of Duchenne and Becker Muscular Dystrophy and Other Single Gene Disorders; Notice of Availability of Funds
 - Type II: Surveillance and Tracking of Conditions With Universal Screening Programs

What got funded...

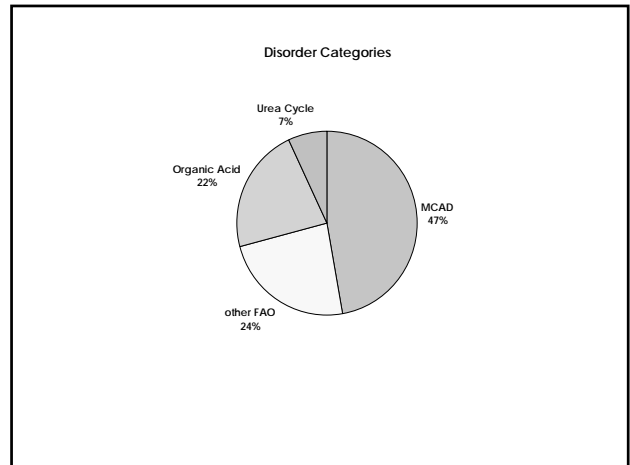
- ◆ Iowa and Oregon were co-awardees for the CDC sponsored research- starting Oct 2002
- ◆ The PIs decided to limit the study to organic acidurias, fatty acid oxidation defects and urea cycle defects- new disorders for newborn screening
- ◆ Observational data points were established
- ◆ Comprehensive and flexible database was created

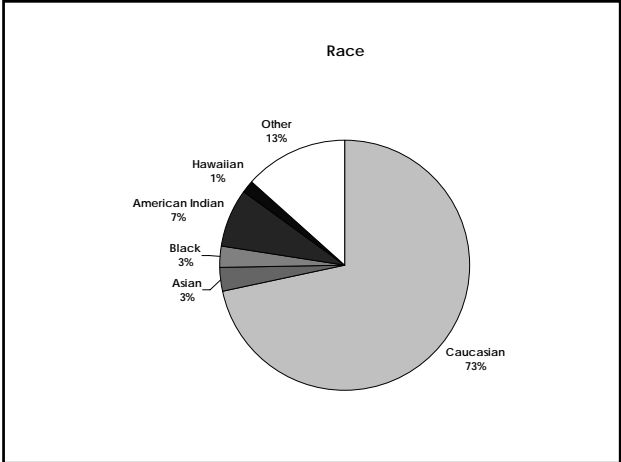
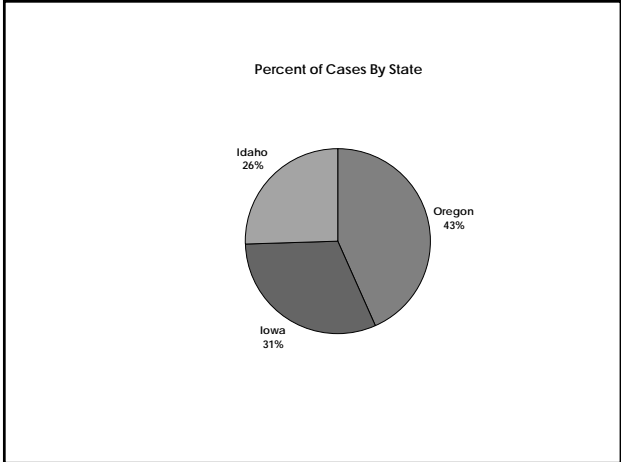


- ### What is it?
- ◆ Observational database written in Microsoft Access
 - ◆ Password protected
 - ◆ Data collected in 3 states for about 3 years time
 - ◆ Portable, standardized and flexible
 - Add different disorders
 - Add various data points
 - Combine data for statistical significance

Who is in the database?

Organic Acidurias		Fatty Acid Oxidation Disorders		Urea Cycle Disorders	
Glutaric acidemia, Type 1 (GAI)	3	Carnitine transport defect	3	Arginase Deficiency	1
Methylmalonic acidemia (MMA) (1 death)	5	Long chain hydroxyacyl CoA dehydrogenase deficiency (LCHAD)	2* (1 death)	Argininosuccinic aciduria (ASA)	1 (death)
Isovaleric acidemia (IVA)	1	Medium chain acyl CoA dehydrogenase deficiency (MCAD)	36	Citrullinemia	3 (2 mild)
3-Methylcrotonyl carboxylase deficiency (3MCC)	9	Short chain acyl-CoA dehydrogenase deficiency (SCAD)	5		
		Very long chain acyl CoA dehydrogenase deficiency (VLCAD)	6 (1 death)		
		Carnitine palmitoyl transferase deficiency (CPT1)	1		
Total Number	17		53		5
Incidence (95% CI)	1-18,700 (1:11,600 to 1:29,400)		1:6,000 (1:4,600 to 1:7,800)		1:63,600 (1:27,000 to 1:143,000)





Can we draw conclusions?

- ◆ OR, IA and ID make up about 2.6% of all births in the US
 - 46,000/year OR
 - 40,000/year IA
 - 24,000/year ID
- ◆ Oldest patient is just 4 years old- if include those identified in pilot study
 - No info on school performance
 - Puberty
 - Fertility
 - Longevity/morbidity

Info we do have on outcomes:

OR	ID	IA	Total	
Follow-up Status				
3	1	2	6	Moved out of state
3	1		4	Deceased
2			2	Closed
21	15	21	57	Active
Acute Illness - Metabolic Episodes				
8	4	1	13	patients with hospital admissions
9	2	2	13	patients with ER visits (4 admitted to hospital)
12			12	patients without Metabolic Episodes
Visit Reason: Metabolic Related				
6		3	9	patients
				4 Hospital
				2 ER

3 years later...

- ◆ Have a database that is searchable, flexible and easy to interface
- ◆ Continuing data on 57 children, with the oldest child 4 years old

Maternal and Child Health Bureau

Newborn Screening: Toward a Uniform Screening Panel and System > Report for Public Comment > Executive Summary

- printer-friendly Newborn Screening executive summary (Acrobatpdf)

Introduction
 In the United States, newborn screening is a highly visible and important state-based public health program that began over 40 years ago. States and territories mandate newborn screening of all infants born within their jurisdiction for certain disorders that may not otherwise be detected before developmental disability or death occurs. Newborns with these disorders typically appear normal at birth. Appropriate compliance with the medical management prescribed can allow most affected newborns to develop normally. As the model for public health-based population genetic screening, newborn screening is nationally recognized as an essential program that aims to ensure the best outcome for the nation's newborn population.

What's Next....

- ◆ Web-enable the database
- ◆ Disseminate to other states
- ◆ Continue to collect data
- ◆ Add measurements
 - Cost of care etc.
 - Parental stress and other psychological indicators
- ◆ Add more diseases- all disorders screened for on NBS
 - Thyroid
 - CAH
 - Etc.

Next steps

- ◆ Let people know what we are doing
- ◆ Share the database
- ◆ Collaborate to share data
- ◆ Provide some evidence and real long-term follow-up that is significant and evidence based.

Acknowledgements

- ◆ CDC
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