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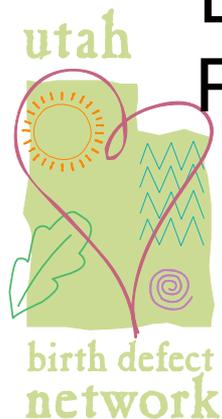
Monitoring and measuring what counts

Developing a longitudinal, sustainable program to monitor occurrence and outcomes of inherited metabolic conditions

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*Study funding from
the Centers for Disease Control and Prevention
HRSA (pilot study)*



Pilot project using the surveillance infrastructure of birth defect (BD) programs

- **Sustainability:** many BD programs have been active for years in the US, with state and federal funding
- **Quality:** High quality BD programs include clinical case review, ongoing evaluation, and active case ascertainment
- **Alignment of targets and resources:** BD programs target babies and children, visit the same hospitals and clinics, have established relations with many providers
- **Effective use of funds:** no need to build a new system, metabolic disease surveillance adds on an existing BD program.

Data needs

- ***high-quality data on the population-based cohort of children identified by screening***
 - High-quality data are essential, because the required information can be complex. For example, in many cases it will be important to characterize genotype and biochemical phenotype, both as descriptors of occurrence and as stratification variables for outcome assessment. Multiple sources of ascertainment and clinical review will also be needed.
- ***outcome data, beyond the neonatal period***
 - to assess morbidity (hospitalizations, emergency department visits, disability) and mortality, to better characterize the clinical significance of these conditions and the impact of screening.
- ***utilization of services.***
 - The goal of public health programs is effective action. Identification needs to be accompanied by sustained, cost-effective interventions. These can be evaluated, for example, by monitoring referral patterns and utilization of health care services, including those such as Medicaid that are state- or federally-funded.
- ***timely dissemination.***
 - Information for action requires timely and ongoing reports, targeted to specific stakeholders such as policy makers, the public, health care providers, and public health professionals.
- ***effective data sharing***
 - Each metabolic condition is individually rare, so data from multiple states will need to be collected and analyzed. This process will require data standardization, sharing agreements, and programs experienced in preparing and sharing data electronically.

Long-Term follow up in Utah

- **Pilot study to define parameters to be collected in long-term follow up (Mountain States Genetics Network/HRSA)**
- **Design of templates to be used in the clinical setting to collect disease-relevant information (Mountain States Genetics Network/HRSA)**
- **Incorporation of LTFU into birth defects registry (CDC/Lorenzo Botto MD): September 2008**
- **Collected data on all diseases since NB screen expansion (2006) by an abstractor using all available data (including those in other hospitals/locations).**

Demographics: identify child, family, contact information, payor at birth

Demo	Address	Family History	Previous Preg Info	Index Preg/ PN Comp	Prenatal Procs Exams	Procs Exams	Inf Info / Lab Test	Encounter	Summary	Comments
Child Information										
First Name	Joseph	Middle Name		Last Name	Wilson	Gender		Tracking Specialist Comments		
AKA First		AKA Middle		AKA Last						
DOB	9/1/2006	Delivery Hospital	Gunnison Valley Hospital	Birth Certificate Number	2006 23383					
Expire Date		Death Certificate Number		Fetal Certificate Number						
Transferred	Davis Hospital & Medical Center	Mother on Medicaid	No							
Maternal Information										
First Name		Middle Name		Last Name		Race	White	Method of Payment		
Maiden		AKA		SSN		*		Private Insurance		
DOB	3/1/1978	Age	20	Marital Status	Married	Method of Payment Comment				
Years Educ	14	Occupation	Store Manager	Country of Origin	United States	Blue Cross				
Paternal Information										
First Name	Joseph	Middle Name		Last Name	Wilson	Race	White			
DOB	6/15/1976	Years Education	15	Country of Origin	United States	*				
Occupation	Sales	Was FOB listed on birth certificate?	Yes							
Interviewer										

Note: fictitious identifying information

Pregnancy: includes prenatal complications (e.g., HELLP in LCHAD)

Demo	Address	Family History	Previous Preg Info	Index Preg/ PN Comp	Prenatal Procs Exams	Procs Exams	Inf Info / Lab Test	Encounter	Summary	Comments
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Index Pregnancy Information

Height LMP Date EDD Date EDD_Source

Preconception Weight 1st PN Weight Delivery Weight Weight Gain

Gravidity Stillbirth FullTerm Premature Abortion LiveBirth

PNC Date PNC Week

Prenatal Complications

Complication	Description/Comments	Diagnosis Date	Weeks From	Weeks To	Side Note
▶ Bladder Infection		05 / 2 / 2006			1E+09
* <input type="text"/>					

Prenatal Exposures

Prenatal Exposure	Exposure Amount	Start Date	Stop Date	Weeks From	Weeks To	Side Note
▶ PNV						1E+09
Antibiotics						1E+09
Zantac						1E+09
* <input type="text"/>						

Confirmation of diagnosis

- **Metabolic results**
- **Enzyme assay**
- **Molecular studies**

Encounters: information on clinical findings, morbidity, use of services

Demo	Address	Family History	Previous Preg Info	Index Preg/ PN Comp	Prenatal Procs Exams	Procs Exams	Inf Info / Lab Test	Encounter	Summary	Comments																					
Encounter Type Metabolic Visit		Method of Payment Medicaid		IDUBDN: 999000003		Health Assessment normal neonatal exam, macrocephaly																									
Encounter Date 9/6/2006		Discharge Date		Place of Hospitalization PCMC		Reviewer Assessment																									
Morbidity		Comments		Number ICU Days		GROWTH MEASURES																									
* normal neurologic exam						<table border="1"> <thead> <tr> <th></th> <th>>/<</th> <th>Percentile</th> </tr> </thead> <tbody> <tr> <td>Weight</td> <td>3570</td> <td>70</td> </tr> <tr> <td>Length</td> <td>50</td> <td>75</td> </tr> <tr> <td>OFC</td> <td>38</td> <td>99</td> </tr> <tr> <td>Wt/Height ratio</td> <td></td> <td>1</td> </tr> <tr> <td>BMI</td> <td></td> <td></td> </tr> <tr> <td>Notes</td> <td colspan="2">Macrocephaly</td> </tr> </tbody> </table>						>/<	Percentile	Weight	3570	70	Length	50	75	OFC	38	99	Wt/Height ratio		1	BMI			Notes	Macrocephaly	
	>/<	Percentile																													
Weight	3570	70																													
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OFC	38	99																													
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BMI																															
Notes	Macrocephaly																														
Diagnosis		Primary/Secondary		Comment		Services																									
Glutaric aciduria I		Primary		classic clinical and biochemical findings, DN		<input checked="" type="checkbox"/> Genetic Counseling <input checked="" type="checkbox"/> Medical Nutrition Therapy <input checked="" type="checkbox"/> Social Services <input checked="" type="checkbox"/> Physician case Management <input checked="" type="checkbox"/> Health Education <input checked="" type="checkbox"/> Interpretation lab tests <input checked="" type="checkbox"/> Labs ordered <input type="checkbox"/> Neuropsychology <input checked="" type="checkbox"/> Dietician Consultation																									
Prescribed Med/Food/Vitamins/Enzymes		Dose		Comment		Development Neurologic Assessment																									
Carnitine		100 mg/kg		2 ml BID Carnitor (100mg/ml)		Notes																									
Glutarex 1		17g/4oz		lysine prescription = 100mg/kg		Overall, normal neurologic exam, with normal tone, strength, neonatal reflexes																									
Record: 7 of 8																															

Common and disease-specific elements

- **Medical treatment**
- **Metabolic results reflecting adequacy of treatment and compliance**
- **Functional outcome: growth, development, IQ, occupation**

Encounters (2): hospitalizations, metabolic visits, consultations

Demo	Address	Family History	Previous Preg Info	Index Preg/ PN Comp	Prenatal Procs Exams	Procs Exams	Inf Info / Lab Test	Encounter	Summary	Comments
Encounter Type Hospital		Method of Payment Medicaid		IDUBDN:		Health Assessment Hypotonia, vomiting, diarrhea. Emergency protocol started at Emergency Department				
Encounter Date 1/21/2007		Discharge Date 1/28/2007		Place of Hospitalization PCMC		Reviewer Assessment				
Morbidity		Comments		Number ICU Days 1		GROWTH MEASURES				
Hypotonia/weakness		present also at discharge				Weight 5965 80				
Lethargy		resolved on day 2				Length 52 75				
Poor feeding		resolved by discharge				OFC 39 99				
Vomiting		resolved by discharge				Wt/Height ratio 1				
						BMI				
						Notes Macrocephaly				
Diagnosis		Primary/Secondary		Comment		Development Neurologic Assessment				
Glutaric aciduria I		Primary		classic clinical and biochemical findings, DN		Notes Hypotonia				
Prescribed Med/Food/Vitamins/Enzymes		Dose		Comment						
Carnitine		100 mg/kg		3 ml BID Carnitor (100mg/ml)						
Glutarex 1		17g/4oz		lysine prescription = 100mg/kg						
*										
Record: 9 of 9										

- Services**
- Genetic Counseling
 - Medical Nutrition Therapy
 - Social Services
 - Physician case Management
 - Health Education
 - Interpretation lab tests
 - Labs ordered
 - Neuropsychology
 - Dietician Consultation

Procedures: evaluating management and use of services (GA-1 = MRI, G-tube, etc)

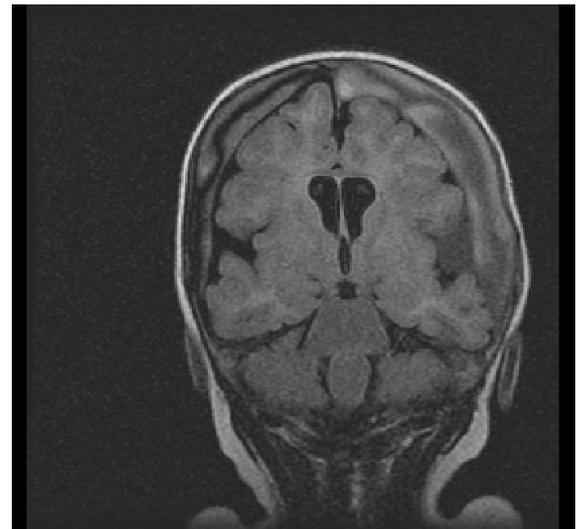
Postnatal / Metabolic Procedures/Exams											
Exam	Date	Date Order	Examiner	Location	Outcome	Results	Post Pre	Contact Mode	Side Note (Referral Hospital)		
▶	12	10	8	2006	35	2	5	Brain MRI: macrocephaly, widening of perisylvian fissures, normal t	Post	F2F	normal basal ganglia
*									Post		

GLUTARIC ACIDEMIA TYPE 1 (GA-1)

Outcome?

Patients with GA-1 can appear normal at birth. Many have or develop macrocephaly, can be mildly hypotonic. They can develop acute dystonia with the first episode of fever/vomiting/fasting. This is irreversible. Patients without decompensation can have normal mentality. About 90% of patients will become spastic and wheel-chair bound without treatment.

Patients identified by newborn screening can develop dystonia even without decompensation.



GA-1 IN UTAH

12 Patients

5 Males

7 Females

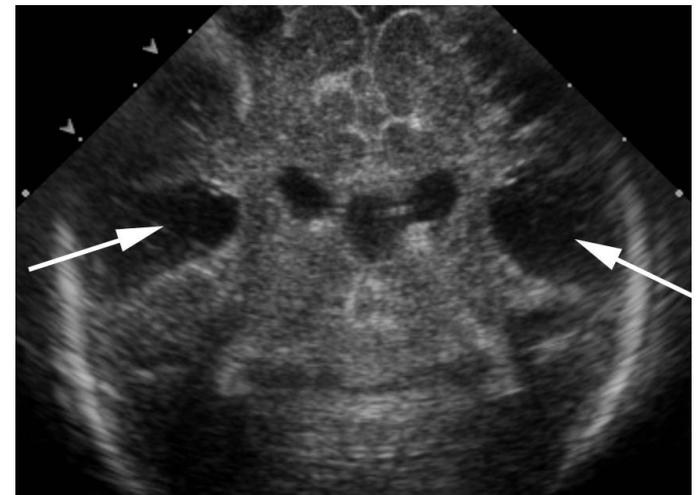
Diagnosis confirmed in all by DNA testing/enzyme assay.

All with different mutations (Genetic heterogeneity)

4 NB Screen / 7 Symptomatic / 1 affected sibling

Among other data, we are entering data on brain imaging in our patients to determine whether brain atrophy and caudatum or putamen degeneration are present.

Our hypothesis is that patients who develop dystonia without decompensation have damage of caudatum and putamen at birth or shortly after.



CONCLUSIONS

Long-term follow-up is essential for understanding the natural course of rare diseases and the effects of screening and treatment.

Different models can be used for this activity. Incorporation into birth defect surveillance programs, where present, can build on an ongoing infrastructure with public health and research capabilities.

Data from multiple centers need to be combined to obtain statistically significant results. Longitudinal data (multiple years) are needed to truly define outcome.

ACKNOWLEDGEMENTS



LTFU Project University of Utah



Utah Birth Defect Registry

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