

Collaborative use of a long-term follow-up database after newborn screening: initial outcomes for medium-chain acyl CoA dehydrogenase deficiency



Region 4 Genetics Collaborative
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Region 4 Collaborators: our Priority 2 Project Workgroup

Metabolic Clinicians and State Health Department NBS Specialists

- ♦ Illinois
- ♦ Indiana
- ♦ Kentucky
- ♦ Michigan
- ♦ Minnesota
- ♦ Ohio
- ♦ Wisconsin



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♦ Heartland Centers (Missouri, Oklahoma, Arkansas)

Use a condition registry as a research platform

- ♦ Document interventions that can be assessed with data in IBEM-IS
- ♦ Plan initial projects should examine
 - "Natural" history
 - Short term outcomes

At enrollment we request registry subjects to consider consent to allow continuing contact, anticipating engaging them as participants in future research trials.

MCAD deficiency: a place to start

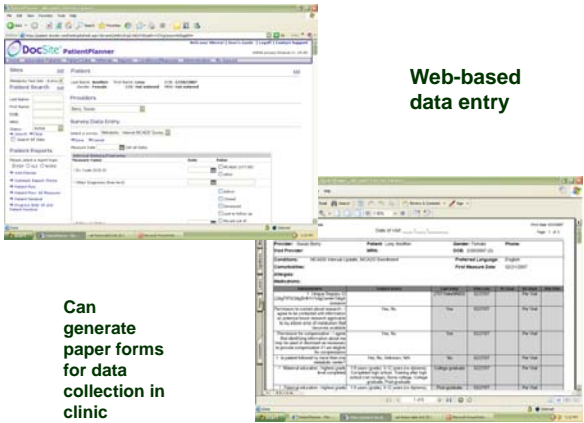
- ♦ Sufficiently rare that no one practitioner sees enough
- ♦ Sufficiently common that cooperation in data gathering can yield relatively rapid meaningful data
- ♦ Some, but not complete agreement about treatment strategies

Hypotheses developed to assess initial data collection on MCAD deficiency patients

- ◆ Children with the highest C8 screening values will be most symptomatic
- ◆ The highest C8 values will be found in children who are 985 A>G homozygotes

Methods for collecting project data using the IBEM-IS

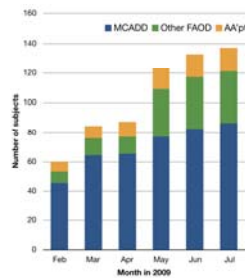
- ◆ Obtain prospective informed consent
- ◆ Ascertain data as clinic visits begin
- ◆ Gather data elements for initial presentation “enrollment” and at each visit “interval”
- ◆ Enter data at each clinic visit via web-based entry forms



Web-based data entry

Can generate paper forms for data collection in clinic

Region 4 cumulative enrollment Feb-Jul 2009



- ◆ 42 infants with MCAD deficiency ascertained by NBS: C8 as informative value
 - Report from system sought data about lab abnormalities or other symptoms at the time of initial metabolic presentation.
 - Many had genotype done; data sought in report.
- ◆ Stratified by C8 values
 - Bottom half “lo” range 0.4-8.69 $\mu\text{Mo}/\text{mL}$
 - Top half “hi” range 8.97-38.8 $\mu\text{Mo}/\text{mL}$

Higher C8 values on NBS are associated with more symptoms/laboratory findings

- ◆ “Lo” range patients: 18 had no labs done, no abnormal labs and/or had no symptoms
 - 1 - abnormal liver function tests; dehydration
 - 1 - respiratory distress due to prematurity
 - 1 - admitted for possible apnea but apnea was not confirmed, poor feeding.
- ◆ “Hi” range patients: 14 had no labs done, no abnormal labs and/or had no symptoms
 - 1 - loose stools
 - 1 - dehydration and irritability
 - 1 - fever, irritability and hypoglycemia
 - 1 - pallor, limp, poor feeding, hypoglycemia
 - 1 - poor breast feeding, lethargy, hypoglycemia, uric acid elevated
 - 1 - hypoglycemia
 - 1 - jaundice

Infants with “Hi” C8 value on NBS are more likely to be 985 A>G homozygotes

- ◆ “Lo” range infants
 - 17 with two mutations
 - 5 were 985 A>G homozygotes
- ◆ “Hi” range infants
 - 16 with two mutations
 - 11 were 985 A>G homozygotes

Conclusions

- ◆ Higher C8 values on NBS are associated with an increased risk for symptoms for affected newborns
- ◆ Infants with higher C8 values are more likely to be 985 A>G homozygotes
- ◆ IBEM-IS provided a successful platform for investigating hypotheses
- ◆ *Collaboration in data gathering may help us improve outcomes after newborn screening*

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<http://region4genetics.org/>

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