Removing Short-chain Acyl-CoA Dehydrogenase (SCAD) Deficiency and Isobutyryl-CoA Dehydrogenase Deficiency (IBD) from the Newborn Screening Panel: Michigan's Experience

2017 Newborn Screening and Genetic Testing Symposium

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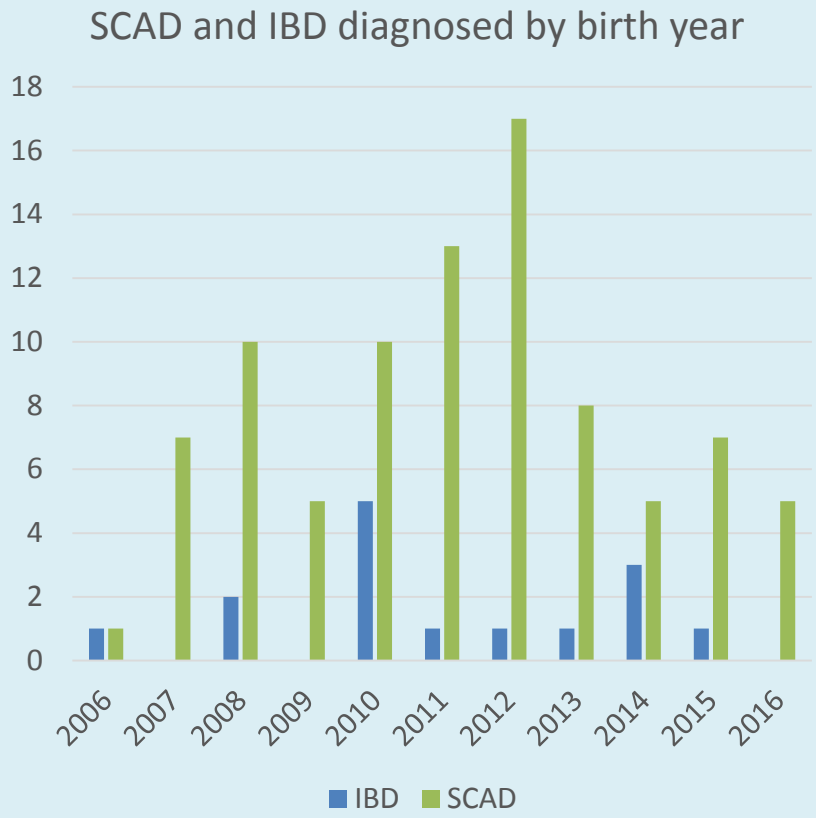
RICK SNYDER, GOVERNOR | NICK LYON, DIRECTOR

The start of SCAD and IBD

- Expansion of tandem mass spectrometry (MS/MS)
- American College of Medical Genetics determines Recommended Uniform Screening Panel for newborn screening
  - 29 primary target disorders
  - 25 secondary target disorders
    - Including SCAD and IBD
- 2005 - Michigan adds 31 metabolic disorders identifiable by MS/MS, including SCAD and IBD

Michigan's SCAD and IBD population

- Children's Hospital of Michigan Metabolic Clinic (CHMMC) in Detroit is the designated medical management coordinating center for metabolic disorders on Michigan's newborn screening panel
- All positive screens for metabolic disorders are referred to CHMMC for diagnosis, follow-up and medical management
- CHMMC SCAD cohort = 77 cases
- CHMMC IBD cohort = 13 cases



First look at SCAD and IBD…

- Dr. Robert Conway, CHMMC clinic director, reviewed data and information from Dr. Bill Rhead, clinical geneticist and biochemical geneticist in Wisconsin, who promotes the removal of SCAD from NBS panels
- Dr. Conway reviewed cohort of Michigan cases and from the Inborn Errors of Metabolism Registry
  - Continues to follow individuals with true mutations but asymptomatic and no treatment in place except avoiding unnecessary fasting and ER protocol
  - Discharged SCAD patients with 625A>G mutation, either in homozygous or heterozygous form
  - IBD patients had no developmental concerns and continue to follow with no treatment in place except avoiding unnecessary fasting and ER protocol
- Dr. Conway began conversations related to removing SCAD and IBD with NBS staff
- NBS lab had already adjusted cut-offs to reduce SCAD referrals

Why remove SCAD and IBD?

- SCAD and IBD appear to be largely benign

- No apparent increased risk of:
  - Hypoglycemia
  - Liver disease
  - Seizures
  - Developmental delay/Autism
  - Acidosis, hyperammonemia, or “metabolic decompensation”
- Risk of secondary carnitine deficiency?
  - Very low to none for SCAD
  - Low for IBD; observed only in context of illness; mild and self-corrected

Possible Adverse Effects of Making a SCAD/IBD Diagnosis

- Increasing medical costs for undetermined benefit
- Utilization of medical resources (clinic visits) for child who does not need it
  - Impact on family's finances and time
- Increased risk of unnecessary parental worry/bonding in the newborn period
- Promoting risk of vulnerable child syndrome
  - Increases likelihood of hospitalizations, ER or MD visits
  - Increased ordering of unnecessary tests during routine childhood illnesses
  - Altered child behaviors or activities because of perceived medical risk
  - Risk of parental driven interventions (diet/etc) independent of medical recommendations

Michigan's Options

1) Do nothing and continue status quo
   - 5-10 new cases of SCAD will be identified each year, most with inactivating mutations
   - The clinic will follow these patients in accordance with current care plan
2) Continue to identify, confirm cases to "explain" NBS results to parents, but do not treat
   - Treats the result as an incidental finding
   - Diagnostic costs will remain unchanged
3) Do not report SCAD cases, but continue to attempt to find and report IBD cases
   - An alternative or 2nd tier method would likely be required to differentiate cases at the level of the lab
4) Stop reporting isolated C4 acylcarnitine
   - Disorders appear to be benign, and neonatal screening is not justified

Metabolic Quality Improvement Committee (MetQIC)

- Provides quality assurance oversight to Michigan's NBS Program
  - Each subset of conditions on Michigan's NBS panel has its own quality improvement committee
- Reviews lab and clinical services, proposed strategies and policies related to inborn errors of metabolism that may be detected in Michigan newborns
- Committee comprised of a variety of specialists
  - Biochemical geneticists, medical geneticists, neonatologist, pediatrician, nurse, pediatrician, metabolic dietitians, Medicaid representative, MDHHS NBS follow-up and laboratory representatives

May 2015 – Metabolic Quality Improvement Committee (MetQIC)

- Preliminary discussion on removing SCAD from NBS panel
  - Dr. Conway presented on SCAD and IBD
  - Review of CHMMC SCAD and IBD patient populations and protocol

MetQIC requested additional information on how other states removed SCAD from their NBS panels, more data on Michigan population and cases, and to consider the question, "Is it useful to continue to follow patients with 2 inactivating mutations?"

Technical Advisory Committee (TAC)

- Provides expert review and input to the NBS Program
  - Final review & commentary on NBS program procedure and policy changes forwarded to the committee from the disease-specific subcommittees
  - Serve as the department's technical expert committee for recommending new disorders to be added to the NBS panel. Recommendations are forwarded annually to the legislatively-mandated NBS Quality Assurance Advisory Committee for review and approval
- Committee comprised of variety of specialists
  - Chair of disease subcommittees, neonatologists, families of children w/ NBS disorders, PCP, nurses, Michigan Health & Hospital Association rep, midwife, Medicaid/CSHCS rep, MDHHS NBS follow-up and laboratory reps
- Meets twice annually

March 2016 –TAC

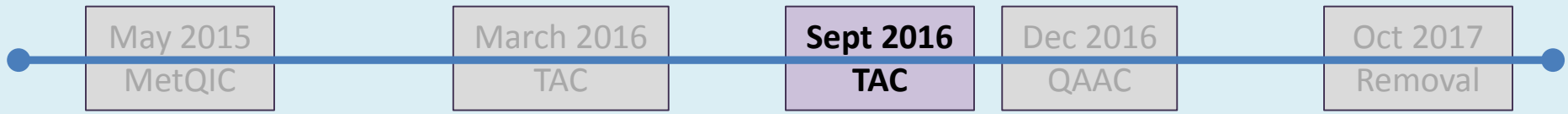
- Detailed presentation on SCAD and IBD
  - How SCAD made it as secondary condition on RUSP
  - Potential clinical signs
  - Recent concerns regarding necessity of treatment
  - Implications of removal of C4 analyte: IBD review
  - Review of Michigan patient cohort for SCAD and IBD
  - Review of IBEM and Region 4 data
  - Discussion on how Wisconsin and Iowa removed it from panels

TAC agreed that there was no additional information needed to make a decision at the September meeting.

September 2016 –TAC

- Vote on Removal of SCAD/IBD

TAC unanimously approved the removal of SCAD and IBD with no objections. This was forwarded to the QAAC.



Quality Assurance Advisory Committee (QAAC)

- Legislatively-mandated committee
  - Reviews the list of disorders for NBS
  - Submits written report on recommendations to revise NBS panel
  - Financial review of recommended changes to NBS panel and recommendations for increase or decrease in the fee charged for NBS
- Ten member committee
  - Representatives include: Michigan nonprofit health care corporation, Michigan Health and Hospital Association, Michigan State Medical Society, Michigan Osteopathic Association, two MDHHS representatives, neonatologist with NBS experience, health maintenance organization, two members of general public
- Meets once annually

December 2016 – QAAC

- Short review and discussion on SCAD and IBD
- Vote on Removal of SCAD and IBD

Recommendation from QAAC: *Whereas short-chain acyl-CoA dehydrogenase deficiency (SCAD) and isobutyryl-CoA dehydrogenase deficiency (IBD) were added to the Michigan NBS Panel as secondary targets of tandem mass spectrometry in 2005, but the conditions have now been found, after expert review, to have minimal to no clinical consequences, the MDHHS should remove them from the screening panel immediately.*

QAAC Report

- Recommendations supported by the QAAC are compiled into a report to be reviewed by:
  1. MDHHS Director: 30 days to approve or reject recommendations, if no action is taken the recommendations are forwarded to…
  2. Legislature: approximately 45 days (time period must include a sufficient number of legislative session days) to approve or reject recommendations, if not rejected, the recommendations are considered approved and adopted by the department to take effect 6 months after adoption

February 7, 2017	**February 10, 2017**	**March 31, 2017**	**September 30, 2017**
MDHHS Director sent report to Legislature	Agents of Legislature accept report	End of 45 day voting window for Legislature	Cease SCAD and IBD testing

Lessons Learned

- Willingness to re-evaluate secondary target conditions
- Removal process allows for multiple levels of review before being adopted
- Public Health Code legal review
- Clarified timelines defined in Code

Acknowledgments

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  - Dr. Mary Seeterlin, NBS Laboratory Scientist
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