

Developing Diagnostic Guidelines for Conditions in the Newborn Screening Panel

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NYMAC



NEW YORK-MID-ATLANTIC CONSORTIUM
FOR GENETIC AND NEWBORN SCREENING SERVICES

Delaware, District of Columbia, Maryland, New Jersey
New York, Pennsylvania, Virginia and West Virginia

NYMAC's goal is to ensure that individuals with heritable disorders and their families have access to quality care and appropriate genetic expertise and information in the context of a medical home.

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Newborn Screening Standardization Workgroup

- **Vision:** To ensure that all newborns receive screening for all recommended analytes and conditions; that infants who screen positive receive appropriate clinical evaluation and diagnosis; that infants who diagnose positive are entered into appropriate clinical management; and that the state newborn screening program is able to ensure that the child receives appropriate care over the short-term to diagnosis and over the long-term through adulthood.

Goal 1: To standardize the clinical evaluation and laboratory analyses, including reimbursement, necessary to achieve confirmation of a diagnosis by:

- Improving the diagnostic process including confirmation of diagnosis, specificity of the screen and reduction of false positives by developing and disseminating a diagnostic evaluation tool.
- Supporting improvements in reimbursement for testing and evaluation by identifying reimbursement issues and strategies to address them.
- Evaluating NBS lab cut-off values
- Standardization of metabolic lab screening
- Examining NBS follow-up protocols

Goal 2: To develop screening criteria for premature and sick infants, including timing of initial screening and subsequent samples and follow-up of screen-positive results by:

- Identifying the number of premature and sick infants in region
- Identifying existing practices in screening premature infants
- Developing pilot projects to address follow-up issues for premature infants
- Monitoring deliberations of Clinical Laboratory Standards Institute (CLSI) committee that is developing guidelines to identify areas for coordination with NYMAC efforts

Goal 3: To develop guidelines to deal with infants who are identified as carriers as a by-product of screening.

- Projects will be developed in future years to address the range of issues involved

Development of the Diagnostic Table

- First project of newborn screening standardization
- Consider specifically the diagnostic criteria for each disorder detected by newborn screening
- Initially presented at the SSIEM meeting in March 2008
- Workshop held at the Maria Fareri Children's Hospital at Westchester Medical Center to review and further refine the table
- Table was reworked based on the workshop and then sent out for comment
- Presented at SERRG meeting in Charleston, SC and APHL Meeting, San Antonio, TX
- Plan to publish manuscript on the development and rationale for defining each diagnosis

Confirming Diagnoses on abnormal Newborn Screening Results

- Concerns about how diagnoses are confirmed
 - Patients not being fully worked up
 - Inadequate insurance coverage
 - Clinically stable patients not being fully worked up
 - Patients being diagnosed with inadequate work ups – “metabolite diagnoses”

Why is it important to confirm the diagnosis on an abnormal screening test?

- Make sure you are treating the right disorder
- Allows for prognostication
- Unconfirmed diagnoses have a negative consequence on the screening process and keep cutoffs lower
- Long term follow up studies with unclear starting points

What are the Criteria to Accept a Diagnosis is Confirmed?

- An abnormal newborn screening result
- Consistent test results abnormalities on follow up testing
- An enzymatic or molecular test result consistent with the diagnosis

NYMAC Diagnostic Table Workshop

- Disorders divided into six groups and four participants reviewed their assigned disorders.
- Answer the questions for each disorder
- Come to a consensus or at least a set of minimal criteria for diagnosis
- The KEY concern for this workgroup was really on what constitutes a **CONFIRMED DIAGNOSIS**
- Metabolite and probable diagnoses are ultimately unacceptable for the **SYSTEM**

Now lets take a look at the Table!

NYMAC Newborn Screening Guidelines for Evaluation of Infants Who Screen Positive:

Conclusions

- Why did we develop the table?
 - Concerns about high levels of false positives. Asymptomatic patients being carried with metabolite diagnoses.
- How was it developed?
 - Initial draft developed by NYMAC newborn screening standardization workgroup. Subsequent workshop at Westchester Medical Center with metabolic specialists from around the country
- What role has the table?
 - Set out the minimum set of tests and expected results for patient being tested for presumed inborn errors of metabolism detected by newborn screening
- Ultimately newborn screening is a state mandate, but the diagnosis and follow up of these patients goes often unfunded!

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