Mountain States Genetics
Regional Collaborative Center

Laboratory Quality Assurance

*Exchange of blood spots for educational purposes to improve quality of newborn screening by MS/MS.*

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18 May 2007
Newborn screening by tandem mass spectrometry (MS/MS) has now been implemented in most states.

Challenges with MS/MS cut-offs and interpretation of results have been addressed by the Region 4 Laboratory Quality Improvement activity.

There is still some unresolved issues on how to deal with borderline/abnormal values reflecting iatrogenic effects.
Goal of the project

- Improve recognition of abnormal patterns
- Decrease the number of unnecessary confirmatory tests
- Promote the use of 2\textsuperscript{nd} tier tests
- Decrease the number of false positives (and false negatives in some cases)
Methods

• The goal will be achieved by:
  – Encouraging all the states within Region 6 to participate in Region 4 activity and attend the training sessions
  – Sending educational challenges (blood spots from real patients with metabolic disorders or with clinical conditions resulting in abnormal amino acids or acylcarnitines)
  – Compiling a complete report that will address not just the analytical part of testing, but also the follow up/clinical aspect
Existing programs

• CDC proficiency testing
  – Quantitative assessment of several analytes, including amino acids and acylcarnitines

• ERNDIM
  – Qualitative assessment of blood spots, often from adults or patients on therapy
Newborn screening is a program
Diseases to include in the educational challenges

• Metabolic disorders detected by MS/MS

• Endocrine disorders (CAH) when either the primary screen or a 2nd tier test is performed by MS/MS

• Hyperalimentation, antibiotics, special diets, medications

• Other disorders can also be included
Educational challenges

- Markers used
- 2nd tier tests used (if applicable)
- Significance
- Recommendations for follow-up
  - Confirmatory tests
  - Metabolic referral
  - Urgency
- Involvement of Technical Supervisor/Medical Director/Metabolic consultant
Evaluation Forms

- Clinical description of the patient
- Abnormal metabolites present in the sample
- Explanation of these abnormalities
- If applicable, the importance of 2\textsuperscript{nd} tier tests
- Recommendations for follow-up
- Lessons learned from different cases
Example
Congenital Adrenal Hyperplasia (receiving corticosteroids)

- Low Birth Weight (g 2,210) with severe respiratory distress initiated on corticosteroids before collection of newborn screening sample.
- **MS/MS test results:**
  - 17-hydroxyprogesterone: 7.3 ng/mL (Normal)
  - androstenedione: 4 ng/mL (Normal)
  - cortisol: 1.7 ng/mL (LOW)
  - \((17\text{-OHP} + \text{androstenedione})/\text{cortisol} = 6.7\) (Abnormal)
Steroid profile by UPLC-MS/MS

Waters Premiere/Acquity

17-hydroxyprogesterone
RT = 2.39 min

Androstenedione
RT = 2.00 min

cortisol
RT = 1.29 min
Distribution of information

• The evaluation forms will be distributed by electronic mail
• One meeting/year will be organized to discuss the educational challenges
• Results will also be discussed at the regional meetings
• Tracking of the performance over time will determine the impact of the training sessions and the educational challenges
Challenges

• Obtaining blood from patients

  – Need for participation of many centers in order to increase the number of cases
  – Need for participation of NICUs to identify factors affecting NBS results
  – Need for consent forms that can be shared by other states
Challenges

• Consent forms
  – We will develop general consent forms and we will assist with IRB submission

• Tracking of data
  – Develop a database containing information about participating laboratories
  – Metrics to objectively evaluate results and compare them over time will be developed
Region 6

- Arizona MS/MS
- Colorado MS/MS
- Montana (No uniform panel)
- Nevada
- New Mexico
- Texas MS/MS
- Utah MS/MS (ARUP)
- Wyoming

- Wisconsin MS/MS
- Oregon MS/MS
Enrollment

• Although this project will start as a regional effort, enrollment will be open to every laboratory performing NBS by MS/MS
• There will be no cost for laboratories to participate
Requirements

• Participating laboratories will be asked to:
  – Analyze 2-3 sets of blood spots twice per year
  – Fill the results form
  – E-mail the results
  – Attend one meeting/year
Summary

• This project will:
  – Improve the quality of screening
  – Increase awareness and education about metabolic disorders
  – Complement the activities of Region 4 collaborative project and the existing proficiency testing run by the CDC