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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Background

- 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 2nd 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

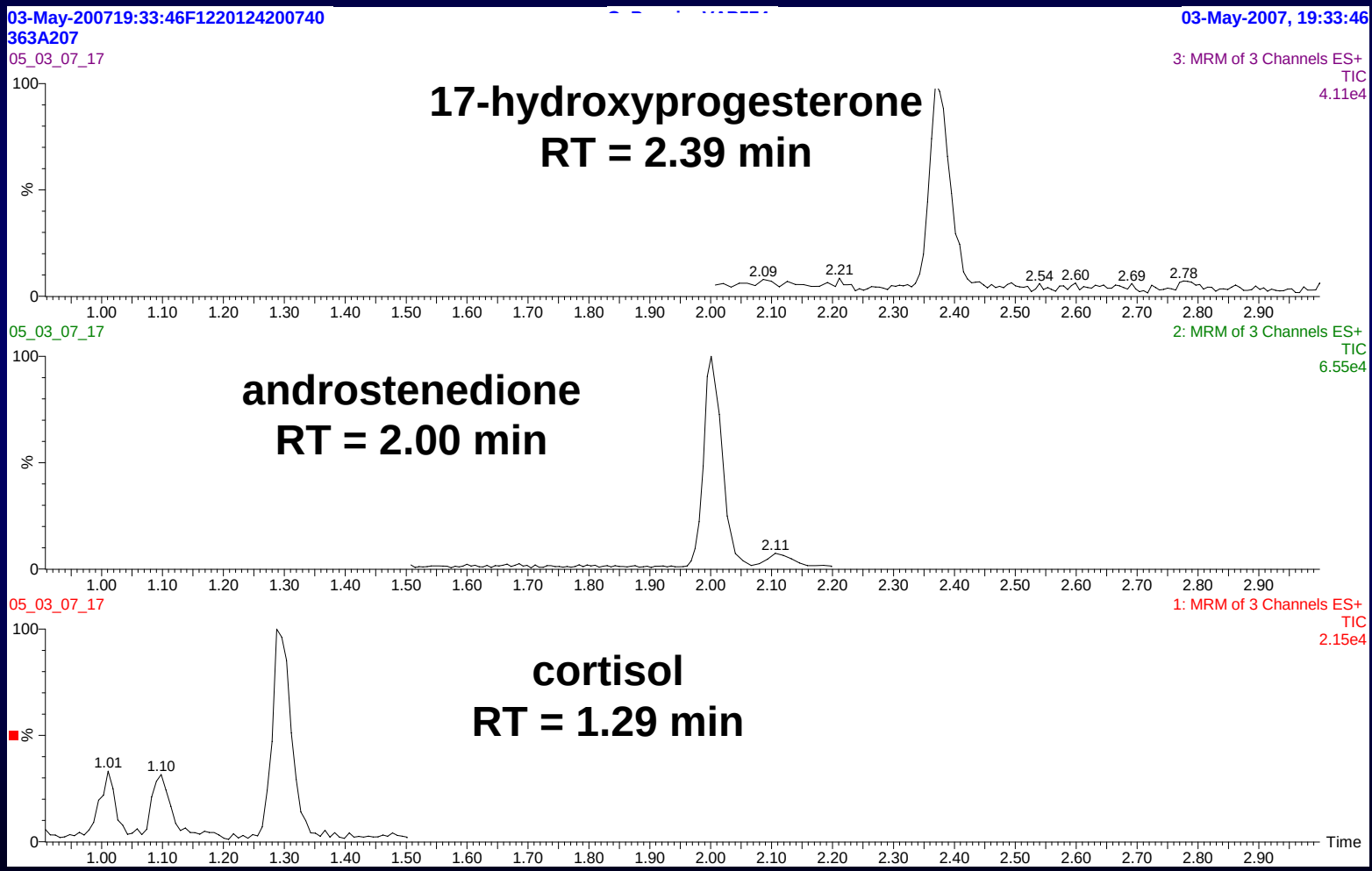
- Clinical description of the patient
- Abnormal metabolites present in the sample
- Explanation of these abnormalities
- If applicable, the importance of 2nd tier tests
- Recommendations for follow-up
- Lessons learned from different cases

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-OHP + androstenedione)/cortisol = 6.7 (Abnormal)

Steroid profile by UPLC-MS/MS

Waters Premiere/Acquity



Distribution of information

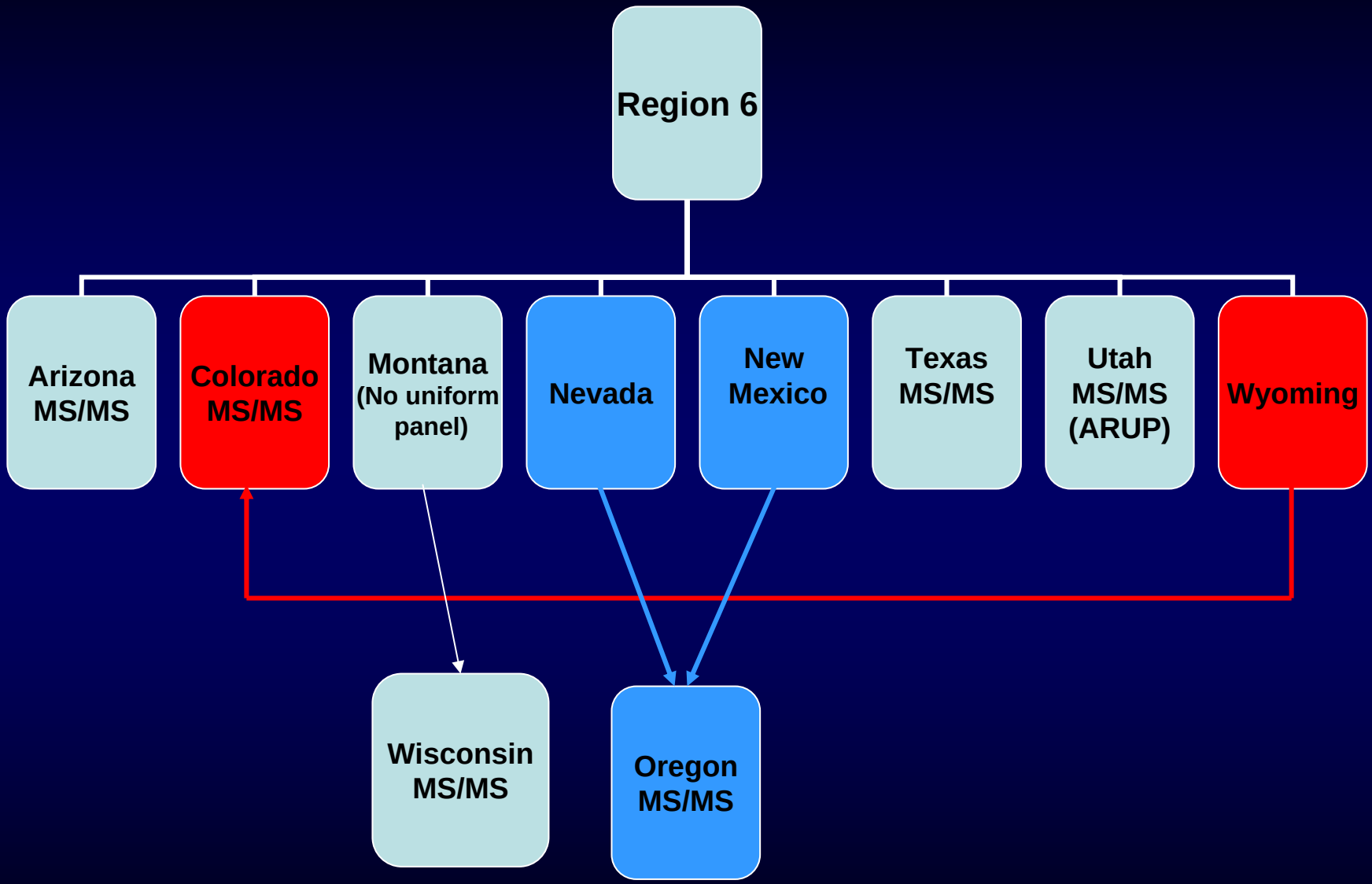
- The evaluation forms will be distributed by electronic mail
- One meeting/year will be organized to discuss the educational challenges
- Results will also be discussed at the regional meetings
- Tracking of the performance over time will determine the impact of the training sessions and the educational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