NBS Advisory Committee Meeting
MINUTES

Monday, August 26, 2024
1:00 p.m. – 5:00 p.m.

Attendees

Voting Advisory Committee Members Present	
Name	Position
Shelly Eagen, Chair	Nurse Practitioner, Pediatric Pulmonary, Billings Clinic
Jennifer Banna, Vice Chair	Center Coordinator, Family to Family, Parent of child with rare metabolic disorder
Kotie Dunmire	High School Business and Special Ed Teacher, Butte High School Parent of child with Cystic Fibrosis and PKU
Amanda Osborne	Licensed, Certified Professional Midwife, Helena Birth Studio
Marion Rudek	Nurse Practitioner, Blackfeet Community Hospital
Miranda McCabe	EPSDT Program Specialist, DPHHS

Voting Advisory Committee Members Absent	
Name	Position
Allison Young	Pediatrician, Western Montana Clinic
Sarah Sullivan	RN, Parent to two children with homocystinuria
Abdallah “Abe” Elias	Director of Medical Genetics and Clinical Geneticist, Shodair Children’s Hospital

Non-Voting Advisory Committee Members	
Name	Position
Amber Bell	Newborn Screening Coordinator, Children’s Special Health Services, DPHHS
Miranda Reddig	Program Specialist, Newborn Screening, DPHHS
Debbie Gibson	Lab Services Bureau Chief, Montana Public Health Laboratory, DPHHS
Jeanne Lee	Newborn Screening and Serology Supervisor, DPHHS
Jacqueline Isaly	Family and Community Health Bureau Chief, DPHHS
Dani Lindeman	Laboratory System Improvement Manager, DPHHS
Nikki Goosen	Newborn Screening Clinical Laboratory Science Lead, DPHHS
Chelsea Pugh	Nurse Consultant, Newborn Screening, DPHHS
Margaret Cook-Shimanek (Absent)	Acting State Medical Officer, DPHHS

Facilitators	
Name	Position
Anna Schmitt	Co-founder, Yarrow
Mikaela Miller	Public Health Specialist, Yarrow

Guests	
Name	Position
Aviva Rosenberg, JD	Co-Founder of Gaucher Community Alliance, Family presenter
Chris Heredia	On Gaucher Community Alliance Board, Family presenter
Dr. Ozlem Goker-Alpan	Lysosomal and Rare Disorders Treatment Center, Gaucher Subject Matter Expert

Public	
Name	Position
Ryan Colburn	Researcher, Odimm Inc.
Paloma Juarez	Pompe Advocate
James Romano	Gaucher Community Alliance
Amanda Joost	Marshall's Mountain, Pompe Advocate
Alison Breitbarth	Pompe Advocate
Joseph	[unknown]

Welcome & Roll Call

- Chair, Shelley Eagen, welcomed the group and did roll call while leading introductions so each person could introduce themselves by providing their organizations, roles, and a description of themselves.
    - Note: physical description is requested during introductions for those that might be seeing impaired.
- Yarrow provided an overview of the Agenda, Ground Rules, and the Public Comment Period.

Unfinished Business Review

- Voting meeting procedure
    - In our evaluation feedback it was requested that a vote be held within the same meeting that the condition is presented. After internal discussion it was determined to continue to vote on the condition in the subsequent meeting following the discussion. This allows for the committee members to make an informed decision and review the information prior to voting.
- Membership
    - The Montana Newborn Advisory Committee members have term limits and we have reached the first point in the existence of this committee where position turnover is required.
    - In order to stagger the terms so that all positions do not expire at once, committee members were given the opportunity to self-select to end their terms early.
    - There are 4 terms needing to be filled:
        1. A voting member who is a person affected by or a family member of a person affected by a disorder tested for pursuant to section 50-19-203, MCA
        2. A voting member who is a physician or nurse practitioner who is board-certified in obstetrics, pediatrics, family medicine, or neonatology
        3. A voting member who is a representative of a birthing center
        4. A voting member who is a representative of Medicaid or the insurance industry
    - We currently have two applications and will continue receiving applications until the positions are filled. We will begin reviewing the applications in the fall.

Newborn Screening Advisory Committee Vote on Pompe

- Voting members were asked *"Do you recommend including Pompe on the Montana Newborn Screening Panel?"* with the following voting options:
    - *Yes, recommend*
    - *No, do not recommend*
    - *I do not have enough information to make a decision at this time*

- Vote Count
    - Jenn Banna
    - Shelly Eagen
    - Miranda McCabe
    - Amanda Osborne
    - Marion Rudek
    - Kotie Dunmire

All 6 of the committee members present at the time of vote voted: "Yes, recommend" to include Pompe on the Montana Newborn Screening Panel. This passed with a quorum.

Gaucher Nomination Packet Review

- Symptoms and age of onset:
    - There are often diagnostic delays and misdiagnoses
    - Low platelet count (thrombocytopenia) and enlarged spleen
    - Complications include avascular necrosis, severe bleeding, chronic bone pain, sepsis, pathologic fractures, growth failure, and chronic liver disease
- How is this disorder currently identified?:
    - Symptomatic presentation followed by a blood test
- Why should it be screened at birth?:
    - Early detection and management can help mitigate some of these serious health risks and improve the quality of life for individuals with Gaucher disease.
- How is this disorder treated?:
    - Is there a treatment available?
        - Yes - FDA approved
    - Is the treatment in the experimental phase?
        - No
- Proposed screening test method:
    - Dried blood spot
- Status of condition in the United States:
    - States currently screening for the condition: 6 (IL, MO, NJ, NM, TN, OR)
    - Registries or databases currently established for the condition: 2
    - Condition has been reviewed by RUSP: No
- 1. It can be identified at a period of time (24 to 48 hours after birth) at which it would not ordinarily be clinically detected. - True
- 2. A test with appropriate sensitivity and specificity is available. - True
- 3. There is a significant risk of illness, disability, or death if babies are not treated promptly (within the recommended time frame for the condition). - True
- 4. Effective treatment is available and access to follow-up care and counseling is generally available. - True

- 5. There are demonstrated benefits of early detection, timely intervention, and efficacious treatment. - True
- 6. The benefits to babies and to society outweigh the risks and burdens of screening and treatment. - True
- 7. There are minimal financial impacts on the family. - True
- 8. There is a public health benefit to conducting the test. - True
- 9. There exist responsible parties who will follow up with families and implement necessary interventions. - True
- 10. The condition's case definition and spectrum are well described. - True

Gaucher Packet Discussion

- No Committee members had questions or commentary to provide at this time.

Gaucher Presentation and Background Information

- **SME Presentation**
    - Dr. Ozlem Goker-Alpan - Dr. Goker-Alpan is a world-renowned authority in lysosomal and other rare genetic disorders for her work over 20 years. She coordinated the NIH Gaucher Clinic at the Medical Genetics Branch of the National Human Genome Research Institute (NHGRI). She also established the Lysosomal and Rare Disorders Treatment Center and is a translational scientist in rare genetic and lysosomal storage disorders.
        - Presentation slides are attached. See slides for additional details.
    - This presentation will focus on Gaucher disease in the early stages.
    - Gaucher Disease (GD) Background
        - GD is the most commonly occuring lysosomal disease in developing countries.
        - Adults diagnosed with GD are rare.
        - After early treatment children with GD can obtain normal growth and development
        - Gaucher cells are activated macrophages
            - When they engulf the red blood cells that store the substrate they begin releasing molecules that act as markers for GD
    - Natural history
        - GD presents in varying signs and symptoms, including in families that have multiple siblings with GD
            - Often the first born child with GD is the most severely affected because later siblings born with GD are treated earlier
    - Clinical subtypes
        - Uses a classical clinical subtype identification procedure
            - There are 3 types
                - Type 1: Symptoms can range from asymptomatic to patients with childhood-onset of the disease

        - Type 2: This is the acute neuropathic form with a severe prognosis with limited survival (2-3 years)
        - Type 3: This type includes neurological involvement, which generally appears later in life than in Type 2 GD. There may be severe systemic involvement (Type 3b). Patients may survive until their fifth decade.
- Phenotypic variation
    - Since publication, N370 is the most common variant in the Ashkenazi Jewish peoples and often presents as a mild form of Type I.
- Global presentation and prevalence
    - In the U.S. GD Type 1 is more prevalent when you compare with other subtypes in Asian countries, where GD Type 3 is more prevalent. This could also be due to lack of diagnosis in GD Type 1 patients since it is more mildly symptomatic and less recognizable than GD Type 3.
    - In sum, there are more common Gaucher disease presentations in different populations and ethnicities.
- Phenotypic spectrum
    - Why does this spectrum occur?
        - Type 1, or adult onset, is often due to enzymatic activity
            - This enzymatic activity does not describe the clinical type that will be predicted and varies between individuals.
        - There may also be other epigenetic factors, therefore, cellular, genetic, and epigenetic factors may all play a role in phenotypic presentation of the disease.
- Clinical spectrum
    - Residual enzyme activity did not correlate with the clinical course.
    - As a general rule, two null variants are not compatible with life.
    - There is a positive linear relationship between severity of phenotypic presentation and enzymatic activity.
- Cell Biology of GD
    - GD leads to cellular dysfunction and death and leads to downstream immune and inflammatory responses.
- Preclinical diagnosis of GD
    - Direct sequencing is the gold standard to avoid missing cases
    - Large deletions may go missed at prenatal screening panels
- Two videos were shown of children who present with Gaucher disease:
    - Child one began treatment at 3-4 weeks of age.
    - Child two has Type 2 but would defy the typical description of GD Type 2.
- Definition of Neuronopathic Gaucher Disease
    - Two eye movement videos were shown to demonstrate rapid blinking and strabismus or “crossed eyes”.
- Definition of GD Type 2

        - This type often includes rapid neurological deterioration, severe apnea, feeding difficulties, epilepsy, and failure to achieve independent gait. Death often occurs by age 4.
    - Non-neurological aspects of GD
        - These often include chest cavity abnormalities, lung disease, eye symptoms, and immune dysfunction.
    - Neurological Spectrum in GD
        - Video of patient with tremor
    - Non-neurological aspects of the disease
        - These are more common
    - Clinical Manifestations of Type 1
        - This often presents as a bone disease if treated late
        - This can be presented at any age
    - Levels of Lyso-GB1 and GD severity
        - The highest levels were observed in patients with untreated GD Types 2 and 3.
    - Management Plan
        - Literature on treatment guidelines were established in 2004. They are working on publishing new data.
    - Treatment of infants and young children with nGD
        - On the right hand side the table depicts how fast you can reach normal Lyso levels.
        - You can control the level of severity of the disease if the treatment is administered early enough.
    - Current and emerging treatments for Gaucher disease
        - There are several treatments in various stages including, FDA-Approved treatments that are approved for home infusions, Human Trials, treatments in preclinical stages, and “Off-label” treatments.
- **Family Presentation**
    - Chris Heredia -Chris is here today to present as the family representative as the father of a child who was diagnosed with Type 3 Gaucher Disease shortly after birth. Chris acts as a Gaucher advocate and is on the Board of Directors with the Gaucher Community Alliance.
        - Presentation slides are attached. See slides for additional details.
        - Chris is a lawyer by trade, a father of 3, and ives outside the suburbs of Chicago
        - His son Mateo is a twin and is nearly 5. Matero was diagnosed with GD Type 3 shortly after birth through Newborn Screening.
        - Neither Chris nor his wife’s family has any presentation of the disease.
        - Seeing the information about GD on the internet was very overwhelming for him.
        - Photo 1: Mateo at 4 months of age on a plane headed to receive his very first ERT treatment.

        - Photo 2: Mateo in April of 2020 at 5 months old when they began completing his ERT infusion treatments closer to Chicago.
        - Photo 3 and 4: Mateo sees many specialists but is able to live a normal life now that he can do infusions at home.
            - The backpacks were designed to allow him to roam the house freely during the infusion.
        - Photo 5 depicts what Mateo's infusions typically look like, comfortable on the couch at home with his cat and family.
        - Photo 6 depicts Mateo thriving and developing interests, such as airplanes.
            - He wishes to be a pilot one day.
        - Photo 7 shows that Mateo is able to travel and enjoy each trip to his doctors appointments by treating them as an opportunity to experience new things and places.
        - Photos 8 and 9 shows Mateo with his siblings traveling, including a 3 mile walk in a cave in the national parks in New Mexico.
        - Photo 10 shows Mateo with his Father and brothers living a normal life.
        - Photos 11 and 12 show Mateo living a normal life doing things that other kids are able to do like swimming and learning to ride a bike.
        - Photo 13 shows Mateo smiling with his stuffed duck.
        - The primary point of this presentation is to highlight how the NBS test was able to give Mateo the best chance at a normal childhood and success in life.
        - Placing GD on the NBS panel may give other children the opportunities that Mateo received from early treatment.
    - Aviva Rosenberg, JD - Aviva is here to share as a family presenter. She is a healthcare attorney and taught as an adjunct professor at several universities. Aviva was diagnosed with Gaucher disease at age 27 and is the mother to a son with Type I Gaucher disease. She is the co-founder and co-president of Gaucher Community Alliance.
        - Presentation slides are attached. See slides for additional details.
        - Aviva has Type 1 and also has a son with Type 1 GD.
            - Her son has been able to lead a different life than her due to treatment opportunities.
        - It is not fair that quality of life with GD differs depending on what state you are born.
        - Montana is one of 12 states that has a procedure to be able to add conditions to the NBS panel.
        - Case for NBS
            - It is well documented that the treatment therapies show great outcomes for the non-neurological types of GD.
            - They have also shown improvement for the neurological forms as well, but there is no current scientific explanation for this.
        - There are currently 6 states that have GD on their NBS panel
            - Some states have been screening for it for over 10 years.

            - There is ample data that shows how to screen for this.
        - This slide depicts the cases for Illinois and shows the differences between states like New York that may have higher Ashkenazi Jewish populations.
        - In Tennessee, over an 18 month period, 1 Gaucher disease was detected. This may be ethnically similar to MT.
            - This can mean the world for that one family.
        - In New Jersey over a 2 year period, 7 cases were detected.
        - New York pilot program is currently screening at 8 hospitals in Manhattan and detected 17 cases over a 4 year period, 2 of those were determined to be negative.
- **Lab Presentation**
    - Jeanne Lee, Newborn Screening and Serology Supervisor (DPHHS), joined us today to provide the Montana State Laboratory Presentation component.
        - Presentation slides are attached. See slides for additional details.
    - Gaucher Cost
        - This cost is similar for the Montana Public Health Lab to Pompe because it can be multiplexed with Pompe. This means that one punch can detect both tests.
        - Although Wisconsin does not have GD on their panel, they would be able to do the testing for MT.
        - It would cost around $11 per screen plus staff time, so around $15 per screen
        - A reagent rental can also occur and cost about $16.50 per screen
        - Who incurs this cost?
            - The cost to add the test to the screen is added to the total NBS panel cost. This panel is around $145. This cost is passed to the patient to pay out of pocket or bill to their health insurance.
            - However, since it would be added to multiplex with Pompe (if Pompe is added to the MT NBS panel), cost would actually be less (less than $1 per condition plus staff time of the 6 conditions testable with the multiplex).

Gaucher Discussion

- Jenn Banna question - does this catch infantile version only or late-onset too?
    - The tests will catch everyone with GD through the enzymatic analysis of the test.
    - Adult onset is a misnomer because it can occur earlier with a milder phenotypic presentation.
- Jenn Banna wanted to clarify that Pompe is strictly just a recommendation for the State.
    - Have we given guidelines to the state for how long they process our recommendations?
        - As far as we are aware the only timelines for responsibilities on informing others is on the end of the Advisory Committee.
- Thank you to the presenters. End of presentation discussion.

Public Comment Period

- Ryan Colburn
    - Congratulations to the Committee on the recommendation for Pompe. Multiplexing allows tests to be packaged and processed together so that you may test multiple conditions for little additional cost. This may be worth noting to the Director and to keep in mind for future condition considerations. Ryan noted the difference in quality of life between children with GD who were able to achieve an early diagnosis and receive testing.
- Dr. Goker-Alpan
    - Dr. Goker-Alpan wanted to stress the importance of pre-symptomatic treatment. Differences between diagnoses in ages result in differences of quality of life.
    - The patient in the middle of the GD types photos was not diagnosed until 2 and has the same type as Mateo and is crippled now due to delayed treatment.
- Additional comments via email were accepted up to 04:15 pm MT on August 26th.
    - No additional comments were sent.

Thanks and Next Steps

- Follow up email will be sent soon and will include:
    - Meeting minutes
    - Recording
    - Transcription
    - Presentation slides
    - Feedback survey
- A doodle poll will be sent out to Committee members to schedule the next meeting.
    - The next meeting will occur in the fall.
- Please email if you have questions, comments, or need anything.

This meeting was concluded by Anna Schmitt at 03:15 pm on August 26, 2024.