Meeting Minutes: Advisory Committee on Heritable and Congenital Disorders (Newborn Screening Advisory Committee) Spring 2025 Meeting

April 15, 2025

Minutes prepared by: Samantha Colston and Amy Dahle
Location: The Wilder Foundation, Saint Paul

Attendance

- Jennifer Arveson
- Sue Berry
- Alex Boucher
- Christen Ebens
- Kaitlin Campbell
- Tricia Hall
- Bob Jacobson
- Courtney Jarboe
- Dietrich Matern
- Brooke Moore
- Katie Pfister (attended virtually)
- Randal Richard
- Theresa Rink
- Emelia Rogers
- Annamarie Saarinen
- Kali Schreiner
- Kathy Stagni
- Queenie Tan
- Renee Temme (attended virtually)

Absent: Rae Blaylark

Decisions Made

MLD

- Christen Ebens: motioned to close the MLD discussion
    - Kathy Stagni: seconded the motion
- Dieter Matern: motioned to recommend the addition of MLD to the Minnesota Newborn Screening Panel
    - Sue Berry: seconded the motion
- Vote: 16:2 in favor to move forward with the recommendation to add MLD to the Newborn Screening Panel

Gaucher disease

- Christen Ebens: motioned to close the Gaucher discussion
    - Kaitlin Campbell: seconded the motion
- Sue Berry motioned: "We will delay moving forward with this readiness work group until, we have the new format in process. When the new format is ready, we will ask that it be prepared and shared with the condition readiness workgroup, for review."
    - Christen Ebens: seconded the motion
- Vote: 16:3 in favor to delay evidence review vote on Gaucher disease until revised Readiness Criteria is adopted by the committee passes

Fabry

- Sue Berry: Motioned to close the discussion on Fabry
    - Dieter Matern: Seconded the motion
- Sue Berry motioned: "We delay moving forward with this readiness workgroup, in fashion that was in parallel with our previous decision, for the same reasons."
    - Bob Jacobson: seconded the motion
- Vote: 13:5 in favor to delay evidence review vote on Fabry disease until revised Readiness Criteria is adopted by the committee passes

Action Items

- Move forward with the recommendation to **add MLD to the Newborn Screening Panel.**
- **Delay evidence review vote on Gaucher disease** until the Condition Nomination Improvement Workgroup reconvenes. Revised process will need to be approved by the committee members.
- **Delay evidence review vote on Fabry** until the Condition Nomination Improvement Workgroup reconvenes. Revised process will need to be approved by the committee members.

Agenda

1. Welcome, Roll Call, and Updates
2. Revisit MLD Evidence
3. MLD Public Comment
4. Discussion and Vote
5. Break
6. Gaucher Public Comment
7. Gaucher Presentation
8. Discussion and Vote
9. Fabry Public Comment
10. Fabry Presentation
11. Discussion and Vote
12. Advisor Updates and Closures

Meeting Notes

1. Welcome, Roll Call and Program Updates

a. Change in coordinator
    i. McKayla has left MDH
    ii. Carrie will be the new co-coordinator
b. Advisory Committee on Heritable Disorders in Newborn and Children (ACHDNC) has been disbanded effective on 4/5/25
    i. New conditions will not be added to the panel through the Federal route
    ii. Minnesota has its own process and will continue to review NBS conditions
    iii. Work on MLD and DMD were under review by the Federal Committee for which the work has stopped.
c. Presumptive eligibility for infants with a positive newborn screening result
    i. Immediate insurance coverage so diagnosis and treatment are not delayed

2. Revisit MLD Evidence
    a. Dieter Matern, committee member and Co-Director of the Biochemical Genetics Lab at Mayo spoke.
        i. MLD was voted down last fall, the nominators were sent a letter.
        ii. The evidence review workgroup was reconvened to review new information/data
        iii. MLD is an autosomal recessive condition. Sulfatides can be measured in urine but can be done in blood. MLD has four groups
            1. Late infantile
            2. Early juvenile
            3. Late juvenile
            4. Adult
        iv. Symptoms are nonspecific, takes on average 6 months to diagnosis.
        v. There is an FDA approved gene therapy for late infantile and early juvenile
            1. If older than 7 years old, no gene therapy but a bone marrow transplant.
        vi. Concerns made by the committee last time.
            1. Limited US data
                a. However, sulfatides do not appear to be age dependent!
            2. 2nd tier testing options
                a. However, an ARSA enzyme in DBS will be available at Mayo by June 2025.
            3. Target of screening
                a. However, there have been consensus guidelines for diagnosis and follow-up published recently.
            4. Diagnostic ambiguity
                a. Enzyme assays in leukocytes using LC-MS/MS will likely improve specificity.
                b. Interpretations of genotypes is improving
                c. Consensus guidelines on diagnosis and follow-up exist.
            5. Access to treatment/follow-up care.
                a. Legislations that may provide for access to timely treatments of NBS conditions has been introduced.
    b. Carrie Wolf, NSAC Co-coordinator and NBS Manger spoke
        i. Conditions could still be added without the ACHDNC Committee, but the MLD review is on hold at this time.
        ii. Current MLD legislation in MN
        iii. Access and cost
            1. Cost is like that of other conditions on our panel
        iv. Christen Eben said that they have successfully transplanted two MLD patients, who are MN Medicaid. There is some evidence that access is getting better.

v. Sue Berry said that the legislation is making progress.

3. MLD Public Comment
    a. None was given
4. MLD Discussion and Vote
    a. Sue Berry asked Dieter to explain the ARSA enzyme a bit more.
        i. He said currently they have a leukocyte assay, which is not the best.
            1. But they are moving to LC-MS/MS
            2. “Might have more false positives or more needs for sequencing because of the stability issue”
    b. Sue Berry asked about sequencing.
        i. Carrie said that we will likely contact that testing out, but that we would figure out more during implementation.
    c. Tricia asked how we are considering this nomination again?
        i. Per Carrie, we didn't have an explicit statement saying if the vote didn't go forward what direction it would take other than to reconvene the evidence workgroup.
            1. Tricia expressed her concerns about the precedent we have set and how it’s a slippery slope.
            2. Carrie acknowledged it, said we can make it clear when going through the new evidence review process.
    d. Annamarie Saarinen commented that the voting at the last meeting was slipper slope.
        i. She said that she appreciated the MLD overview and asked Dieter to talk about the breakdown of which babies will end up in each category.
            1. Dieter said that the early form is the most common form. Which is what we assume, but once you start screening you find things different.
    e. Dieter asked Christen how the two transplanted babies are doing.
        i. Christen didn’t have those details.
    f. Christen Ebens motioned to close the discussion.
        i. Kathy Stagni seconded the motion.
    g. Dieter Matern made a motion to have MLD added to the Newborn Screening Panel.
        i. Sue Berry seconded the motion.
    h. **Vote: 16:2 in favor to move forward with the recommendation to add MLD to the Newborn Screening Panel**
5. Break
6. Gaucher Public Comment
    a. Cyndi Frank the cofounder and copresident of the Gaucher Community Alliance spoke.
        i. Gaucher Disease is a multi-system disease that leads to a spectrum severity.
        ii. There is an FDA treatment.
        iii. For those with Type 1, still has complications such as osteonecrosis.
        iv. For those with Type 3, who have received ERT, had prolong lives.
        v. States currently screening for Gaucher include IL, MO, NJ, TN, OR and NM
    b. Chris Heredia, a board member and father of a child living with Type 3 Gaucher disease.
        i. Chris has three boys, a 7-year-old and 5-year-old twins.
            1. One of the twins was picked on newborn screening in IL.
            2. Confirmed through genetic testing and started ERT at 4 months of age.
        ii. In 2020 switched to in home infusions and having the treatment has allowed him to have a childhood.

iii. Mateo has more doctor's appointment than most of his friends, but he still has some normalcy to his life.
iv. Early diagnosis, early detection is important.

7. Gaucher presentation by Carrie Wolf, Reena Kartha and Chet Whitley
    a. Carrie Wolf, MDH NBS Manager, spoke about MDH having the ability to do screening via the NeoLSD kit.
        i. We currently use the NeoLSD kit for Pompe, MPS1 and Krabbe screening.
    b. Renna Kartha, a faculty member in the College of Pharmacy at UMN, presented a clinical overview of Gaucher.
        i. Gaucher disease is an autosomal recessive disease, that leads to a deficiency in a key enzyme (glucocerebrosidase). Without the enzyme, toxic fatty acids accumulate in the organs like the liver, spleen, bone marrow and lungs.
        ii. GBA1 gene.
        iii. Muti-system manifestations (organ enlargement, bone disorders and neurological involvement)
        iv. The natural history is complex
            1. Onset age varies, the severity and rate of progression varies
            2. "it's not possible to correlate the genotype with the phenotype"
        v. Age on set depends on the type
            1. Type 1 – childhood and adulthood (>95% prevalence)
                a. Symptoms range from asymptomatic to patient with childhood onset
            2. Type 2- prenatally and newborn (~ 1% prevalence)
                a. Acute neuronopathic form with severe prognosis; limited survival (2-3 years)
            3. Type 3- late infancy/childhood (~5% prevalence)
                a. Neurological involvement, which general appears later in life
                b. Seizures are common in type 3A
        vi. There is a published Gaucher disease diagnostic algorithm. It mostly about ruling out symptoms.
        vii. Genetic testing is not straightforward. Direct sequencing is the gold standard.
    c. Treatment: Enzyme Replacement Therapy
        i. Life-prolonging treatment (oral (SRT) or infusions (ERT)).
        ii. Gene therapy is on trial.
    d. Case Study: Two siblings
        i. Sibling 1 – seizure free, had no change in neurological status
        ii. Sibling 2 - at age 7 no signs or symptoms of GD. Overall cognitive function was better
    e. Chet Whitely, lysomal disease specialist at UMN,
        i. He sees 3 to 6 lysomal disease patients a week.
        ii. There are three companies making IV enzymes
        iii. Two oral medications
        iv. Gene therapy in trail.
        v. We have very good care here in MN.
8. Gaucher Discussion and vote
    a. Sue Berry asked what the target of screening was, so the committee can judge "if this is an appropriate strategy for support for this condition." She also expressed the importance of needed to know what we are looking for, given this disorder has a high rate of adult onset.
        i. We don't have good information when to start therapy
    b. Dieter Matern agreed with Sue's question. He mentioned "it was nice to hear about all these programs and they identify cases, but there was no word about false positives."
        i. There is not much in the literature to that effect.
        ii. The last data he saw out of Taiwan suggests that everything, but the brain is treatable with ERT.

iii. "How babies have low activity but don't have Gaucher disease and will never have Gaucher disease?" You can do a second-tier test.

c. Kaitlin Campbell had questions about the clinical subtypes and what the target would be.
    i. She asked Carrie if the kit would be able to pick up all the subtypes and what are other states doing.
        1. Carrie said that she wasn't sure, but some states are doing two different testing methods. We likely would need some type of second tier testing.

ci. Christen Ebens motioned to close discussion.
    i. Kaitlin Campbell seconded it.

cii. Three options were presented: delay, recommend moving forward or decline
    i. Tricia Hall asked if we could delay until our new structured approach was finished.
    ii. Sue Berry made a motion to delay moving forward with evidence review until we have our new format.
        1. Christen Ebens asked if this means it would be delayed until October
            a. Carrie confirmed that we would meet in-between.
        2. Dieter Matern reassured nominators that this not meant to be an administrative hurdle, but that there are questions that need to be addressed. We need to know things how it's going in other states, false positives and how do you decide when to treat?
        3. Renna spoke to the committee and said that they were not focusing on a particular type because she thinks treatment is beneficial for all three types. In addition, she said that they can't distinguish which subtype. If there is the common variant, it's going to be one type or the other.
    iii. Tricia clarified that we delay and then at that time we move forward
    iv. Christen offered a suggestion to update the motion to delay at that time it moves to evidence review
    v. Sue motioned that we delay moving forward with the readiness workgroup until we have the new format and process. When the new format is ready, we will ask that be prepared and shared with the condition readiness workgroup for review.
        1. Christen Eben seconded it.

ciii. **Vote: 16:3 in favor to delay evidence moving Gaucher forward until the Condition Nomination Improvement Workgroup reconvenes. Revised process will need to be approved by the committee members.**

9. Fabry Public comment
    a. Jessica Weaver is a MN resident who was diagnosed with Fabry disease 6 years ago.
        i. Looking back, she had the following symptoms, stomach pain, fatigue, burning and tingling in feet.
        ii. Frustrating to tell doctors what she was experiencing but none of them had answers.
        iii. Her sister is a genetic counselor who encouraged family members to get tested.
        iv. She thought she passed it on to her son, which made her sad. It can be very painful for men. Luckily, he tested negative.
        v. She feels better on medication. When she is off, she forgets words.
        vi. Early screening and treatment will help kids have a normal life.
    b. Shaina Elfert-Halverson is a MN resident with Fabry disease.
        i. Her second cousin informed the family about Fabry, 22 members did genetic testing, 17 were found to have it.
        ii. It was difficult for Shaina to get testing despite having a family history.
        iii. The males in her family had more severe symptoms and organ damage.
        iv. She is now on medication that makes her symptoms manageable.
    c. Rachelen Varghese, with Testing for Tots, read a letter on behalf of Tim Falencik.

i. As teen he experienced symptoms and learned to hide them.
ii. In his early 50's he was diagnosed. The treatment journey just began.
iii. ERT has improved his quality of life.
iv. He attends Fabry Camp, help kids navigate the disease.

10. Fabry presentation by Carrie Wolf, Chet Whitley and Linda Hasadsri
    a. Carrie Wolf, MDH NBS Manager, spoke about MDH having the ability to do screening via the NeoLSD kit.
        i. We currently use the NeoLSD kit for Pompe, MPS1 and Krabbe screening.
        ii. Currently 8 states screening for Fabry Disease
    b. Chet Whitely, gave a clinical overview
        i. There are people here in MN that can take care of these patients.
        ii. X-linked disease. Males and females have different trajectories.
            1. In childhood, people have pain, stomach issues, sweating, organ damage and heat intolerance
        iii. Stokes and heart attacks occur early
        iv. Delayed diagnosis is common because its misdiagnosed.
        v. Mutation analysis does not determine severity!
        vi. symptoms have been described in 8–11-month-olds.
            1. Infancy is the target population
        vii. The pain is hard to manage
        viii. Accumulation of GL-3 increases over time.
    c. Treatment: Enzyme Replacement Therapy
        i. ERT is the standard of care
        ii. Gene therapy is in approval.
        iii. There are management and treatment guidelines available.
    d. Linda Hasadsri, Director of Molecular Laboratory at Mayo
        i. 8 states that are screening, 1 state screening via pilot study, 4 states have a bill in progress and 4 states are in progress with Newborn Screening Committees.
        ii. There is an FDA approved kit. Most labs are using tandem mass spec.
            1. Reflex to molecular testing
        iii. Families often not feel burdened by knowing that their baby was identified with a partial deficiency allele.
            1. Instead, they felt empowered. It allowed them to be monitored and to have conversations with a provider when to start therapy.
                a. And it allowed the opportunity to have additional family member identified.
            2. The goal is to find the males, as they will benefit for early enzyme replacement therapy.
            3. Predicated incidence ~32 screen positives/year in MN
                a. 3 severely affected males
                b. 10 or more to have the partial deficiency allele
            4. Second tier testing – molecular
            5. Multiple Fabry specialists here in MN
            6. Presented a slide comparing the RUSP and MN criteria = met

11. Fabry Discussion and vote
    a. Dieter Matern was concerned about the positive predictive value of 10%, especially for a condition where you don't know when to start treatment.
    b. Sue Berry questioned what the target is and stated, "I don't know that we should handle it any differently than we did the other one."

c. Courtney Jarboe asked if we could review the slide again from when the federal committee reviewed the nomination back in 2008. Can those at highest risk of serious symptoms be found in newborns?
d. Carrie went back to the "relevant position statements" slide and allowed member to review it.
e. Christen Ebens pointed out that there was a bit of difference in the confirmed positive from those that screened positive from state to state.
    i. Dieter said that there are different cut off being used and whether states are reporting out variants of unknown significance.
    ii. Dieter also stated "I don't like false positive results, and this is a lot of false positive results for the for condition where we don't know what to do with them. For some time, also relying on free testing which can go away any day.
f. Chet Whitley spoke and asked "What is the state's role to screen or diagnose and treat?
g. Tricia Hall stated that it's the state's role to "screen well" and that is where the concerns are coming from. She too has concerns about the high positive predictive value.
h. Sue Berry motioned to close the discussion.
    i. Dieter Matern seconded the motion.
i. Sue Berry made a motion to delay moving forward with this readiness work group in a fashion that was parallel with our previous decision.
    i. Bob Jacobson seconded the motion.
j. **Vote: 13:5 in favor to delay evidence moving Fabry forward until the Condition Nomination Improvement Workgroup reconvenes. Revised process will need to be approved by the committee members.**

12. Advisory Updates and Closures
    a. Sue Berry informed the committee that after Krabbe was implemented, we diagnosed a baby shortly after that.
        i. Baby was transplanted at 28 days of life
    b. Brooke Moore talked about changes that will be coming for the CF screening.
        i. Sequencing
    c. Sue Berry encouraged members to contact their congressional representatives about how important the Advisory Committee on Heritable Disorders in Newborns and Children.
    d. Annamarie Saarinen mentioned about the new CCHD screening protocol for the AAP.
    e. Carrie informed the committee that we will meet sometime before October to go over the new process.

Newborn Screening Advisory Committee
Minnesota Department of Health
PO Box 64899
St. Paul, MN 55164
651-201-5466
health.nsac@state.mn.us
www.health.state.mn.us

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