NBS Advisory Committee Meeting
MINUTES

Thursday, April 6, 2023
11:00 a.m. – 1:30 p.m.

Attendees

Voting Advisory Committee Members Present

Committee Member	Committee Member Position
Abdallah "Abe" Elias	Director of Medical Genetics and Clinical Geneticist, Shodair Children's Hospital
Allison Young	Pediatrician, Western Montana Clinic
Amanda Osborne	Licensed, Certified Professional Midwife, Helena Birth Studio
Jennifer Banna	Center Coordinator, Family to Family Parent of child with rare metabolic disorder
Marion Rudek	Nurse Practitioner, Blackfeet Community Hospital
Sarah Sullivan	RN, Parent to two children with homocystinuria
Shelly Eagen	Nurse Practitioner, Pediatric Pulmonary, Billings Clinic
Miranda Prevel	EPSDT Program Specialist, DPHHS

Voting Advisory Committee Members Absent

Committee Member	Committee Member Position
Kotie Dunmire	High School Business and Special Ed Teacher, Butte High School Parent of child with Cystic Fibrosis and PKU

Non-Voting Advisory Committee Members

Committee Member	Committee Member Position
Amber Bell	Newborn Screening Coordinator, Children's Special Health Services, DPHHS
Crystal Fortune	NBS Follow Up Coordinator, Montana Public Health Laboratory, DPHHS
Debbie Gibson	Lab Services Bureau Chief, Montana Public Health Laboratory, DPHHS
Jeanne Lee	Newborn Screening and Serology Supervisor
Nikki Goosen	Newborn Screening Clinical Laboratory Science Lead
(Not present) Jacqueline Isaly	Family and Community Health Bureau Chief, DPHHS
(Not present) Margaret Cook-Shimanek	Acting State Medical Officer, DPHHS

Facilitators

Facilitator	Facilitator Position
Anna Schmitt	Co-founder, Yarrow
Kirsten Krane	Co-founder, Yarrow

Guests

Guest	Guest Position
Dr. Keith Van Haren	Subject Matter Expert, Stanford University
Kirsten Finn	Family Story Presenter

Public

Public in Attendance	Public in Attendance Position
Elisa Seeger	ALD Foundation, Co-Sponsor of Nomination Packet
Miranda McAuliffe	ALD Foundation
Steve Shapero	MT Advocate, Family Member, Sponsor of Nomination Packet

Welcome & Roll Call

(Yarrow Facilitators, Voting & Non Voting Committee Members, Ground Rules)

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

Unfinished Business Review

- **Internal Committee Updates**
    - All Statement by Members documents have been received
    - Chairperson Shelly Eagen has changed jobs, but will maintain her roles within the Committee
    - The nomination packet is online and available for the public
    - Meeting time concerns: the internal team understands that some meeting times are difficult for clinicians to attend, so there will be later times will be added to the Doodle Polls
        - Ultimately, the internal team will still choose the time that works best for the most people
- **Krabbe Disease Follow Up**
    - The decision memo was drafted and sent to the Director
    - The Director agreed with the Committee's recommendation to not include Krabbe to the Montana NBS panel
    - The decision has been made publicly available on the MT DPHHS website

x-ALD Nomination Packet Review and Discussion

- **Brief summary of packet responses**
    - Amber Bell led the review of the x-ALD nomination packet responses (see attached)
    - Packet was submitted by Steven Shapiro, Big Fork, MT and co-sponsored by Elisa Seeger from the x-ALD Alliance, which is a non-profit in Brooklyn, NY.
- **Nomination Packet Discussion**
    - Jennifer Banna:
        - Confirmed that the packet that we reviewed today was filled out by the nominators and that the Advisory Committee will review the selection criteria at the next meeting after having heard from the SME, Family advocate, and MT DPHHS lab.
    - Dr. Elias:
        - Gene therapy has been FDA approved, but there are on-going studies, especially around the long-term benefits. The gene therapy could be a real "game changer" in treatment of this condition.
        - From a testing perspective, there is a low false positive rate. Recommend that we consider a Two Tier based testing process that includes molecular testing.

Clinical Background: SME

- **x-ALD clinical background presentation by SME, Dr. Keith Van Haren, Stanford University**
    - Please see Dr. Van Haren's presentation
    - Follows about 100 x-ALD boys currently. About ⅔ of them were identified through newborn screening, the other ⅓ were identified through other affected family members.
    - ALD produces symptoms in some parts of the body, and not others as opposed to other disorders, where you might see a disease in many parts of the body.
    - It specifically affects most prominently the brain, spinal cord and the adrenal glands.
    - One of the challenges and one of the opportunities of ALD at newborn screening is that when children are born with an ALD mutation, whether they're boys or girls, they look totally healthy. You cannot tell they have ALD, and they develop normally. They can develop normally for 40 years, potentially before they have symptoms. We can go a long time without being identified. This is good, and it's dangerous.
    - Adrenal insufficiency happens over time and steroids are the primary treatment method for adrenal insufficiency.
        - When sick, may need "stress dose" steroids
        - Sometimes children need only the "stress dose" steroids without the ongoing, daily steroids before adrenal insufficiency becomes severe
        - Adrenal screening begins very early (earlier than the MRI for brain lesions)
    - Signs and Symptoms include things such as signs of severe illness, including low blood sugar, low blood pressure. Coma and seizures can develop.
    - Signs and symptoms can develop in the late teenage years, but could be as late as thirties or forties.
    - Signs and symptoms that appear in women happen much later in life and may include peripheral and spinal cord issues.
    - Treatment - available for the adrenal portion of the condition using steroids.
    - Brain Lesions - treatment is much more complicated for the brain lesions that can develop as a result of the condition. These may appear as early as 4-10 years old. Brain lesions do not appear in about ⅓ of cases.
        - Showed brain MRI of brain with lesions
        - Brain lesions can be treated before there are even any symptoms, and gene therapy and marrow transplant can provide good therapy at this point if we know to look for it
        - If brain lesions are detected too late, then treatments are not as effective
        - Lesions begin small and grow slowly
    - Survival rate is vastly improved if we identify lesions early and can know to monitor and provide treatment as necessary in real time.
    - Bone Marrow Transplant Treatment for Brain Lesions
        - Works well – with caveats

        - Requires either a bone marrow donor (sibling or unrelated who is matched with immune markers)
        - New gene therapy products allow for boys to be their own bone marrow donor if a good bone marrow match cannot be identified
        - So far, this gene therapy and bone marrow transplant looks very promising. Have seen about 50 patients go through this treatment.
        - Gene vectors seem stable so far, but we don't know the long-term effects
        - Safety - in about 3 children the gene therapy products create a type of cancer and then need to go through a new transplant, ideally with a bone marrow donor this time.
        - This is a definitive therapy for the brain lesions.
        - Caveats:
            - Must treat the lesions early to stop their progression. The larger the lesions, the more likely they are to continue growing.
    - x-ALD newborn screening is very common among most states. Only HI, NV, MT are not screening.
    - Screening:
        - In California there are 3 Tiers to screening. (See powerpoint)
    - There is a group of researchers out of the Netherlands that map gene mutations.
    - Treatment Interventions:
        - Begin brain MRIs every 6 months starting around the age of 2-12 years old.
        - See powerpoint for treatment algorithm
    - Among the rare diseases that we see, x-ALD is one of the most common
    - The newborn screening process has revolutionized treatment and lives of children with x-ALD
    - This does increase the "worry" among families, but that is because before the screening they had no idea of the condition in their child and therefore didn't know they needed to be concerned.

x-ALD Family Story

- **Family story presentation by Kirsten Finn**
    - Originally from Canada, but now lives in Overland Park, KS.
    - Seven year old son was diagnosed with x-ALD. Her son was able to be identified because of a different family member – who, tragically, died within 3 months of diagnosis.
    - Kirsten provided a basic overview of the physiology and presentation of the disease.
    - Her son was 4 years old when diagnosed with a large lesion in his brain. Their family was in Canada when they identified the lesion and were forced to the US to find adequate treatment. She and her husband were forced to liquidate retirement savings to be able to obtain treatment in Minnesota for therapy. Her son responded well to bone marrow and gene therapy treatments and is doing well now.

- Told about Jayden DeSousa, who is another child who was diagnosed too late and misdiagnosed as ADHD for almost two years. Jayden passed away from x-ALD. She told of the devastating deterioration of Jayden's health including blindness, inability to walk, seizures, vegetative state and death.
- Over 500 boys have been identified in NY since they began their NBS process.
- Not only does it identify the boys early, but helps families plan and identify x-ALD earlier.
- Un-diagnosed or too late diagnosed, x-ALD leads to a cruel and excruciating death among these children.
- This mimics other diseases and is commonly missed until it is too late to provide treatment.

Laboratory Background

- **Montana Public Health Laboratory Screening Methods by Crystal Fortune**
  - MT Laboratory does not currently have the expertise in-house to perform the test, but the Wisconsin laboratory that is used by Montana will start to test for this in May 2023. The cost to send out to Wisconsin is approximately $5 per test.
  - If we were to do this in-house in Montana's Public Lab, the additional test would require an additional FTE, training, equipment such as Tandem Mass Spectrometry, raise fee of each screening test by $15
  - See powerpoint slide for more information
  - Crystal Fortune will also provide a newspaper article with additional information about the laboratory options

Discussion Period

- Yarrow opened the floor for questions and discussion
- Family Story
  - Screening women is overall beneficial and have not found the burden of this knowledge to be unwanted. Have found this to be empowering for women.
- Clinical Background
  - How many years of data do we currently have on gene therapy/transplantation?
    - About 7 years
  - The label restriction to provide the gene therapy, what is this based on? Age?
    - Unsure if it is age or therapeutic need. There are specific centers across the nation that can provide this treatment. Minnesota would be the closest Transplant Center to Montana.
  - The implementation of a robust follow up and surveillance of the boys identified - where it may become difficult to implement locally are the standardized MRI studies. Often with rare disorders, the radiologists in Montana may have some difficulty in being able to accurately read these MRIs. How do other states handle issues like this?

        - Pediatric MRIs often look like there are abnormalities and these need to be read by specialists who really understand this. There is not a comprehensive guide for radiologists, but Stanford is working on this. Still need to figure out this barrier.
        - Dr. Van Haren generally recommends that families stay close to home for care and MRIs.
        - Can send MRIs to specialists in other places in the nation if necessary.
    - There can be a lot of psychological trauma for families if there are incorrect diagnoses.
    - Will the screening also catch some of the children who will encounter x-ALD later in life?
        - Yes. About 80% of women who have the x-ALD gene will have fatty acid abnormalities. In the past, this has been one of the ethical burdens of providing girls with this knowledge.
        - In the Netherlands, they only screen boys for x-ALD. Unaware of any place in the US that only screens boys.
        - A secondary benefit of screening girls is that it might help identify other family members who are at risk or are carriers. Dr. Van Haren feels like most of these families with girls who have this knowledge are not overly burdened.
    - Why do we not treat women with transplant treatment even later in life?
        - Transplant only treats brain lesions, which are not typically the way that x-ALD presents in women.
        - Women's genes are different and experience slower aging of CNS. Symptoms include bowel and bladder dysfunction, stiff joints, generally mild. The symptoms are much later in life and milder.

- Laboratory Background
    - Will the screening be done on all children or just boys?
        - All children will be screened if we screen in MT
    - The cost analysis may need to include other costs that weren't at first put in the powerpoint that was presented. For example, what is the cost of not identifying this early?
        - What are the testing related costs? MRI every 6 months, bone marrow transplant.
        - What are the costs associated with not testing?
            - It is very difficult to study and consider all of the costs associated with each condition that we look at
        - Assume that the MRI and endocrine follow up will happen in state.
        - Unsure if there are other treatments that would need to happen out of state (transplant/gene therapy).
        - Could Medicaid afford these costs?
        - **Cost of a lost life of a child, family, society must be considered.** Otherwise, you will find that it is more cost effective to diagnose late, offer palliative care until the child passes away. It is very different for a child to pass away when there is

no treatment rather than when a child misses the opportunity to receive treatment.
        - There is no way to prevent some mis-diagnosis, or late diagnosis that require multiple transplant treatments and these will become costly.
    - A lot of the screening in state costs would be the upfront costs of the new equipment. Once that equipment is purchased, estimate that the annual lab costs would be closer to $150k per year.
        - At this point, it would be cheaper to send out of state until that equipment is purchased.

Newborn Screening Advisory Committee Next Steps, Comment Period, & Wrap Up

Public Comment Period

- **Elisa Seeger:** Lost her son in 2012 to x-ALD. Was eligible for bone marrow transplant and this cost almost $5 million when they traveled to Duke in North Carolina from NY. Cost about $500,000 to add ALD to NBS in NY. Many families live for 10, 20, 30 years and these costs are staggering. Must be under 18 years to treat with gene therapy transplant.
    - Cost of treatment isn't usually an issue. Families generally figure out a way to make this work and use insurance to get the care covered.
    - Women being tested is not a general burden for the families. Has seen this as being helpful in many instances, especially in family planning and diagnosing other family members. May decide not to have children, or consider it IVF.
- **Steve Shapero:** Thank you for having this meeting today. 10 year old grandson has this condition and is receiving consistent screening and good treatment. Newborn screening is the best way to catch this disease early and get treatment started at the right time. Would love to see this screening in MT. It shouldn't matter where you live whether you are screened.
- **Miranda McAuliffe:** She is one of the first mothers in the country to have her son screened and identified with x-ALD. Her son is 7 years old and doing well, but there are a lot of doctor's visits and critical information and treatments that happen consistently. She is a carrier and experiencing symptoms as she is getting close to 40 years old. Her family used this information to inform their family planning. Has many resources available that would be useful to families who are diagnosed with x-ALD. The ALD Foundation has many resources and are happy to support families. They also help bring other state leaders together to share resources and information to support patients and families.

Next Meeting

- Date to be determined: Committee will vote to add x-ALD to the MT NBS panel
- Only required to have 2 meetings per year, but would recommend that we have another meeting in 1-2 months to discuss and vote on x-ALD sometime this summer.
    - Dr. Elias is quite busy, unsure if will be able to meet before the fall for a vote

    - Marion Rudek would like to attend an additional meeting, but it is difficult to get away from clinical responsibilities
    - Allison Young, would like to participate in an additional meeting, but difficult to get away from clinical responsibilities
    - Amber Bell supports an additional meeting
    - Jennifer Banna supports an additional meeting
    - Shelly Eagan supports an additional meeting
- Prior to next meeting, it would be helpful for Crystal Fortune to present a more comprehensive financial plan to ensure that we are able to implement this in an orderly fashion and notify endocrinology and radiology professionals around the state.

Thanks and Next Steps

- Follow up email will be sent soon and will include:
    - Meeting minutes
    - Recording
    - Transcription
    - Presentation slides
    - Shared resources on x-ALD

- Please email if you have questions, comments, or need anything

This meeting was concluded by Anna Schmitt at 1:22 pm on April 6, 2023, via Zoom.