Letter to the Editor

RE: MAKING DECISIONS ABOUT KRABBE DISEASE NEWBORN SCREENING

New York State began newborn screening (NBS) for Krabbe Disease (KD) in 2006. Since then, testing and screening algorithms have advanced and 9 additional states have added KD to their NBS panels. To date >6 700 000 newborns have benefited from NBS for KD and 23 newborns with infantile KD (IKD) were identified. In their article, Vergano et al[1] described the processes used by the Commonwealth of Virginia Newborn Screening Advisory Council to decide whether KD should be included in the state's NBS panel along with their decision not to include it. We believe that the Commonwealth of Virginia Newborn Screening Advisory Council failed to consider advances in screening tests and algorithms, disease definitions, and follow-up guidelines, or recent reports of efficacy of early hematopoietic stem cell transplantation for IKD.

Vergano et al highlighted, "the lack of consensus regarding the definition of EIKD and later onset forms," even among KD experts, and ambiguity surrounding the interpretation of screening and case confirmation data" and referenced the consensus guidelines developed by Stone et al.[2] However, 10 of 11 authors reached consensus for the classification of KD. Furthermore, all authors agreed to a classification based on psychosine concentrations where cases with psychosines between 2 and 10 nmol/L are at high risk for noninfantile forms and those with psychosines >10 nmol/L have IKD. Vergano et al noted a lack of genotype, phenotype correlation, which is why genotyping should not be relied upon for identification of babies with IKD through NBS.[3,4]

Vergano et al asserted that barriers exist for admission of patients to specialized centers. However, with advanced planning, the NBS program can develop roadmaps for rapid referrals to expert centers. Historically, families with newborns with IKD have been able to rapidly access treatment facilities.[5,6]

The authors state "Systemically, the minimal criteria for the implementation of a new disorder should require a stable infrastructure to conduct screening with rapid results, availability of sensitive and specific laboratory tests, the institution of equitable follow-up and effective treatment, and adequate funding for the program." We agree but know that these criteria have alretady been met in other states where the above-mentioned screening approach has been adopted.

Vergano et al refers to the use of psychosine as "still investigational," yet it has been part of routine screening of Kentucky newborns for Krabbe disease since February 2016.[4] Among more than 330 000 newborns, only 2 had positive screening results to date; both were diagnosed with IKD within days, and both were transplanted out-of-state within 30 days of life. Vergano et al states that the VA newborn screening program estimated an additional cost of "over $2 million" to add KD to their program. This seems exceedingly high and should be questioned.

Vergano et al end by emphasizing the importance of "understanding the systemic processes and challenges involved in NBS" and then "encourage pediatricians to work together with parents, legislators, and NBS advisory members to accomplish well-versed NBS decisions for their state." We couldn't agree more and hope that pediatricians and geneticists will advocate for their patients based on what NBS can be and not accept a status quo that robs newborns of a chance to survive a disease that would otherwise lead to death after suffering a relentlessly brutal neurodegenerative course.

It is not known if neurodegenerative changes occur in utero to determine available perinatal treatment outcomes.

Krabbe Disease is again being considered for addition to the Recommended Panel for Newborn Screening. When this expert review is completed and it is determined that KD meets scientific criteria for inclusion on the Recommended Panel for Newborn Screening, we trust that advocates will help problem solve with the states struggling with equity and funding concerns.

Joanne Kurtzberg
Duke University School of Medicine, Durham, North Carolina

Dietrich Matern
Mayo Clinic College of Medicine, Rochester, Minnesota

Joseph J. Orsini
New York State Department of Health, Wadsworth Center, Albany, New York

Michael Gelb
University of Washington, Seattle, Washington

Stacy Pike-Langenfeld
Krabbe Connect, Rosemount, Minnesota

Lesa Brackbill
Leukodystrophy Newborn Screening Action Network, Hershey, Pennsylvania

Anna Grantham
Hunter's Hope Foundation, Orchard Park, New York

Anthony C. Steyermark
The Legacy of Angels Foundation, Rosemount, Minnesota

REFERENCES

1. Schrier Vergano SA, Kanungo S, Arnold G. Making decisions about Krabbe disease newborn screening. *Pediatrics*. 2022;149(4):e2021053175
2. Thompson-Stone R, Ream MA, Gelb M, et al. Consensus recommendations for the classification and long-term follow up of infants who screen positive for Krabbe disease. *Mol Genet Metab*. 2021;134(1–2):53–59
3. Guenzel AJ, Turgeon CT, Nickander KK, et al. The critical role of psychosine in screening, diagnosis, and monitoring of Krabbe disease. *Genet Med*. 2020;22(6):1108–1118
4. Basheeruddin K, Shao R, Balster F, Gardley P, Ashbaugh L. Newborn screening for Krabbe disease-Illinois experience: role of psychosine in diagnosis of the disease. *Int J Neonatal Screen*. 2021;7(2):24
5. Allewelt H, Taskindoust M, Troy J, et al. Long-term functional outcomes following hematopoietic stem cell transplant for early infantile Krabbe disease. *Biol Blood Marrow Transplant*. 2018;24(11):2233–2238
6. Page KM, Ream MA, Rangarajan HG, Galindo R, Mian AY, Ho ML, Provenzale J, Gustafson KE, Rubin J, Shenoy S, Kurtzberg J. Benefits of newborn screening and hematopoietic cell transplant in infantile Krabbe disease [online ahead of print January 18, 2022]. *Blood Adv*. doi: 10.1182/bloodadvances.2021006094

doi:10.1542/peds.2022-057888

Author Response

Reply to Kurtzberg et al

Samantha A. Schrier Vergano
Medical Genetics and Metabolism, Children's Hospital of The King's Daughters
E-mail: sammyschrier@gmail.com

ACKNOWLEDGMENTS

We thank Dr Kurtzberg et al for pointing out the important differences in planning and interpretation regarding screening and outcomes for Krabbe disease. Although there are existing algorithms for follow up and management of screen positive newborns, ambiguity remains.