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LETTER TO THE EDITORS

A brief overview of galactosemia newborn screening in the United States

Brook M. Pyhtila · Kelly A. Shaw · Samantha E. Neumann · Judith L. Fridovich-Keil

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Dear Editor,

In the United States in the past 50 years an estimated >2500 infants with classic galactosemia (CG) (Fridovich-Keil and Walter 2008) have been identified by newborn screening (NBS). Most of these babies were spared the trauma of potentially lethal acute disease by early diagnosis and intervention; many are alive today because of NBS. Newborn screening for galactosemia is a success story, but continuing disparities between states in their approach to NBS, follow-up testing, and intervention for variant forms of galactosemia reveal gaps in our knowledge and highlight opportunities for improvement. To characterize existing disparities we recently collected and compared data from 39 state NBS programs (Pyhtila et al 2014 in press).

On some matters the programs we surveyed agreed. All identified CG in close to 1/50,000 newborns and recommended immediate and life-long dietary restriction of galactose for affected infants. On other matters the programs disagreed. For example, median detection rates for Duarte galactosemia (DG), a common and ostensibly mild form of transferase deficiency, varied from 0.4 to 34.7 per 100,000 births; this range largely reflected differences in screening approach. Similarly, NBS in some states was sufficient to detect epimerase or kinase deficiency in addition to transferase deficiency; in other states it was not. Median false positive rates for galactosemia NBS also varied markedly, from as low as 2.0 to as high as 575.5 per 100,000 births. High false positive rates were particularly troubling in some states due to the associated healthcare costs of follow-up testing for so many presumably healthy infants (Fernhoff 2010), and the worry and potential breastfeeding interruption imposed on the families involved.

The factor most clearly associated with differential DG and false positive rates was the NBS GALT activity cut-off level. Longitudinal data provided by one state demonstrated that lowering the cut-off from 3.5 to 3.0 U/g Hb did not change the detection rate for CG but lowered the DG detection rate by close to six-fold and the false positive rate by close to ten-fold. This was a striking result.

Whether galactosemia NBS *should* be designed to detect DG and what *should* be done with those DG infants identified are issues that remain controversial (Fernhoff 2010). A study of 28 children with DG of mean age <4 years found no evidence of developmental delay (Ficicioglu et al 2008). In contrast, a study of elementary school records noted that children with DG were significantly over-represented in a cohort of students receiving special educational services (Powell et al 2009). Whether these apparently contradictory results reflect statistics of small numbers, or whether they indicate that DG children are at increased risk of developmental difficulties in mid- but not early childhood, remains unclear.

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This study was approved by both the Emory University Institutional Review Board (IRB# 00024933, PI: Fridovich-Keil) and the Georgia Department of Public Health Institutional Review Board (GA PDH IRB# 130306, PI: Fridovich-Keil). Data accessed from the Emory Genetics Lab MEDGIS database were ascertained through a HIPAA waiver granted by the Emory IRB (under IRB# 00024933).

B. M. Pyhtila · J. L. Fridovich-Keil (✉)
Department of Human Genetics, Emory University School of Medicine, Rm. 325.2 Whitehead Bldg., 615 Michael St, Atlanta, GA 30322, USA
e-mail: jfridov@emory.edu

K. A. Shaw
Graduate Program in Genetics and Molecular Biology, Graduate Division of Biological and Biomedical Sciences, Atlanta, GA, USA

S. E. Neumann
Emory College, Emory University, Atlanta, GA 30322, USA

At the time of this study and in the states surveyed, follow-up caregivers associated with ~80 % of the NBS programs recommended complete or partial dietary galactose restriction for DG infants in the first year of life, or gave mixed recommendations, and ~20 % recommended no intervention. Until a sensitive and statistically powerful case–control study of diet and long-term developmental outcome in DG children recruited from across the intervention spectrum is conducted and published, NBS programs, healthcare providers, and the families they serve will not be able to make truly evidence-based decisions regarding what to do about Duarte galactosemia.

Conflict of interest None.

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