Response to van Rijt *et al.*

To the Editor: We appreciate the insightful letter "Neonates at Risk of Medium-Chain Acyl-CoA Dehydrogenase Deficiency: A Perinatal Protocol for use Before Population Neonatal Screening Test Results Become Available," by van Rijt et al.,[1] commenting on our article.[2] We strongly agree with their proposal to implement a uniform perinatal protocol for neonates at risk for this deficiency.

After delivery, our center provides a letter detailing the initial management protocol for all infants with a known risk factor (usually a positive family history) for an inborn error of metabolism that may present in early infancy. In the case of medium-chain acyl-CoA dehydrogenase deficiency, we provide a letter to the family that contains details of the diagnosis and suggestions for initial management. We ask the delivery hospital to send a newborn screen to the state laboratory immediately after birth and again at the standard time (36–48 h after birth). We provide our contact information and ask the outside provider to call us to inform of us of the birth and discuss the infant's condition. Once we are notified of the birth, we arrange to have the newborn screening results expedited. In Pennsylvania, the state laboratory can provide rapid genetic analysis for the *ACADM* c.A985G and c.T199C mutations. Using this strategy, if a family carries one of these common mutations, we can provide both biochemical and genetic confirmation of a diagnosis by the second day of life.

As with acylcarnitine profile analysis of umbilical-cord samples, very early blood acylcarnitine profile norms are not as well established as those for traditionally timed samples. The idea of using the sequential ratio analysis is an intriguing way to overcome this limitation. We have not used this technique at our center because we have access to rapid mutation testing for the specific mutations that have presented at an early age in our population.

Genetic confirmation of the diagnosis is greatly appreciated by the families we have managed and meets two additional goals of genetic clinical care: offering emotional reassurance of a definitive diagnosis and providing tools for future family planning. Ideally, in the future, rapid genotyping in conjunction with biochemical testing (rather than targeted mutation or acylcarnitine ratio analysis alone) using an early newborn screen blood spot will become available. Complete genotyping would provide families who harbor known, clinically significant *ACADM* mutations with a rapid answer as to whether their newborn is affected with the disease.

DISCLOSURE

The authors declare no conflict of interest.

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REFERENCES

1. van Rijt WJ, Jager EA, van Spronsen FJ, et al. Neonates at risk of medium-chain acyl-CoA dehydrogenase deficiency: a perinatal protocol for use before population neonatal screening test results become available. *Genet Med* e-pub ahead of print 22 September, 2016.
2. Ahrens-Nicklas RC, Pyle LC, Ficicioglu C. Morbidity and mortality among exclusively breastfed neonates with medium-chain acyl-CoA dehydrogenase deficiency. *Genet Med*; e-pub ahead of print 5 May 2016.

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