



## HCU Network America

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*For more information, please watch our webinar, 'Classical Homocystinuria: A Journey to Improve Outcomes Through Newborn Screening Methodology' by scanning below*



<sup>1</sup> Morris A, Kozich V, Santra S et al. Guidelines for the diagnosis and management of cystathionine beta-synthase deficiency. *J Inherit Metab Dis.* 2016; Page 9, 1, 9.

<https://onlinelibrary.wiley.com/doi/10.1007/s10545-016-9979-0> <sup>2</sup>Keller R, Chrastina P, Pavlíková M et al. Newborn screening for homocystinurias: Recent recommendations versus current practice. *J Inherit Metab Dis.* 2019; 42: 128–139. Pages, 9-10, 9, 3.

<https://doi.org/10.1002/jimd.12034> <sup>3</sup>Matern D, Tortorelli S, Oglesbee D et al. Reduction of false-positive rate in newborn screening by implementation of MS/MS-based second-tier tests: The Mayo Clinic experience (2004-2007). *J Inherit Metab Dis.* 2007; 30: 585-592

<sup>4</sup>Chace D, Hannon W. Impact of Second-Tier Testing on the Effectiveness of Newborn Screening. *Clin Chem.* 2010; 56: 1653-1655 <https://doi.org/10.1373/clinchem.2010.153494>

### Dear Newborn Screening Stakeholders,

As states across the U.S. continue to work diligently to ensure newborns are optimally screened for serious genetic disorders, I would like to share with you recent and troubling data calling out the urgent need to revise newborn screening protocols for Classical Homocystinuria (HCU). **This new data suggests that, currently, up to 50% of babies born with HCU are being missed, receiving false negative results that can have a devastating impact on them<sup>1</sup>.**

HCU is a genetic disorder of the metabolism in which individuals are born with abnormalities in both copies of the Cystathionine Beta Synthase (CBS) gene. A rare and potentially serious inherited condition, HCU prevents the body from breaking down certain amino acids (the building blocks of proteins) causing a harmful build-up of substances in the blood and urine that can have severe and potentially life-threatening consequences. Thankfully, because of newborn screening, we have been able to identify many individuals and provide preventive treatment early in life when it is most effective and before symptoms develop. However, as science has advanced since the first newborns were screened for HCU, we now know that some are now being missed at birth due to outdated screening protocols. **We urge you to consider the latest recommendations by experts to revise current protocols and prevent more serious HCU consequences for patients in your state.**

Although HCU officially became part of the Recommended Uniform Screening Panel in 2009, issues with screening protocols continue to result in missed cases. For example:

- The biomarker used to screen for HCU, Methionine (MET), is not as sensitive as another biomarker called total plasma homocysteine (tHCY) – yet many newborns are only being tested for MET.
- The window of time when the screening blood specimen is collected (24-48 hours after birth) is too soon to detect HCU in many affected newborns, who typically do not have positive bloodwork for or show signs of increased MET until after this period<sup>2</sup>.

**US and international experts in newborn screening for HCU have recommended a revised process that includes a lower cut-off for MET and/or a corresponding ratio of MET to Phenylalanine (PHE).**

The lower cutoff for MET can range from 39 to 50  $\mu\text{mol/L}$ , depending on lab median<sup>1</sup>. Additionally, experts recommend a second-tier test for tHCY using the same dried blood spot<sup>2</sup>. The CDC is finalizing a second-tier assay for tHCY that will be made available to the state labs.

By taking these steps, your state would both significantly lower the number of false negatives and increase the likelihood of identifying HCU in newborns<sup>3,4</sup>. People with HCU need and deserve to be diagnosed as newborns so that they have a better chance at living healthier, happier lives!

***Will you help us in the fight to vastly improve newborn screening for babies with HCU?*** If you have any questions, please feel free to contact me at [dbartke@hcunetworkamerica.org](mailto:dbartke@hcunetworkamerica.org) or at 630-360-2087.

Sincerely,  
Danae' Bartke  
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