Title: Glutaric Acidemia Type 1 *GeneReview* – False Positive and False Negative Results on Newborn Screening
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Initial posting: August 2019

**False positive newborn screening (NBS) results** (elevated C5DC levels in an infant who does not have glutaric acidemia type 1 [GA-1]) can result from any one of the following in descending order of likelihood:

- Regional laboratory-specific variations in cutoff levels for C5DC
- Renal insufficiency [Hennermann et al 2009]
- Elevations in hydroxydecanoylcarnitine (C10-OH) due to multiple acyl-CoA dehydrogenase (MADD) deficiency or medium-chain acyl-CoA dehydrogenase (MCAD) deficiency. Note: C10-OH and C5DC have almost identical molecular weights and are indistinguishable on plasma acylcarnitine profiling (when the esters are usually butylated) in contrast to the dried blood spots used in NBS [Chace et al 2003]. Note that the addition of multiple analyte monitoring to tandem mass spectrometry (MS/MS) has increased the sensitivity of C5DC on NBS and reduced the rate of false-positive results [German Society for Newborn Screening 2015].
- Maternal GA-1 is a consideration when both NBS and initial follow-up testing show increased C5DC and/or depleted free carnitine, but subsequent biochemical testing is normal. Note: When the mother has GA-1, the infant's C5DC is expected to normalize in the first few weeks of life [Crombez et al 2008]. Confirmatory testing (*GCDH* molecular genetic testing or glutaryl-CoA dehydrogenase analysis) is normal in the infant and abnormal (diagnostic) in the mother.

**False negative NBS results** (i.e., normal or only slightly increased C5DC levels in an infant who has GA-1) can result when:

- Infants have substantial residual enzyme activity (see Genotype-Phenotype Correlations);
- Infants have extremely depleted carnitine reserves, such as in maternal or infantile carnitine transporter deficiency.

## References


Chace DH, Kalas TA, Naylor EW. Use of tandem mass spectrometry for multianalyte screening of dried blood specimens from newborns. Clin Chem. 2003;40:1797–817.

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Hennermann JB, Roloff S, Gellerman J, et al. False-positive newborn screening mimicking glutaric aciduria type I in infants with renal insufficiency. J Inherit Metab Dis. 2009;32(S1):S355-9.