

Newborn Screening ACT Sheet [Increased Methionine] Homocystinuria (Cystathionine beta-synthase deficiency [CBS Deficiency])

Differential Diagnosis: Classical homocystinuria (cystathionine β -synthase (CBS) deficiency); hypermethioninemia due to methionine adenosyltransferase I/III (MAT I/III) deficiency; glycine n-methyltransferase (GNMT) deficiency; adenosylhomocysteine hydrolase deficiency; liver disease; hyperalimentation.

Condition Description: Methionine from ingested protein is normally converted to homocysteine. In classical homocystinuria due to CBS deficiency, homocysteine cannot be converted to cystathionine. As a result, the concentration of homocysteine and its precursor, methionine, will become elevated. In MAT I/III deficiency and the other hypermethioninemias, methionine is increased in the absence of or only with a slightly increased level of homocysteine.

YOU SHOULD TAKE THE FOLLOWING ACTIONS:

- Contact family to inform them of the newborn screening result and ascertain clinical status.
- Consult with pediatric metabolic specialist.
- Evaluate the newborn with attention to liver disease and refer as appropriate.
- Initiate confirmatory/diagnostic tests in consultation with metabolic specialist.
- Educate family about homocystinuria and its management, as appropriate.
- Report findings to newborn screening program.

Diagnostic Evaluation: Quantitative plasma amino acids will show increased homocystine and methionine in classical homocystinuria but only increased methionine in the other disorders. Plasma homocysteine analysis will show markedly increased homocysteine in classical homocystinuria and normal or only slightly increased homocysteine in the other disorders. Urine homocysteine is markedly increased in classical homocystinuria.

Clinical Considerations: Homocystinuria is usually asymptomatic in the neonate. If untreated, these children eventually develop mental retardation, ectopia lentis, a marfanoid appearance including arachnodactyly, osteoporosis, other skeletal deformities and thromboembolism. MAT I/III deficiency may be benign. Adenosylhomocysteine hydrolase deficiency has been associated with developmental delay and hypotonia, and both this disorder and GNMT deficiency can cause liver abnormalities.

Additional Information:

[Gene Reviews](#)

[Genetics Home Reference](#)

Referral (local, state, regional and national):

[Testing](#)

[Clinical Services](#)

[Find Genetic Services](#)

Disclaimer: This guideline is designed primarily as an educational resource for clinicians to help them provide quality medical care. It should not be considered inclusive of all proper procedures and tests or exclusive of other procedures and tests that are reasonably directed to obtaining the same results. Adherence to this guideline does not necessarily ensure a successful medical outcome. In determining the propriety of any specific procedure or test, the clinician should apply his or her own professional judgment to the specific clinical circumstances presented by the individual patient or specimen. Clinicians are encouraged to document the reasons for the use of a particular procedure or test, whether or not it is in conformance with this guideline. Clinicians also are advised to take notice of the date this guideline was adopted, and to consider other medical and scientific information that become available after that date.

LOCAL RESOURCES: Insert State newborn screening program web site links

State Resource site (insert state newborn screening program website information)

Name	<input type="text"/>
URL	<input type="text"/>
Comments	<input type="text"/>

Local Resource Site (insert local and regional newborn screening website information)

Name	<input type="text"/>
URL	<input type="text"/>
Comments	<input type="text"/>

APPENDIX: Resources with Full URL Addresses

Additional Information:

Gene Reviews

<http://www.ncbi.nlm.nih.gov/books/n/gene/homocystinuria>

Genetics Home Reference

<http://ghr.nlm.nih.gov/condition=homocystinuria>

Referral (local, state, regional and national):

Testing

http://www.ncbi.nlm.nih.gov/sites/GeneTests/lab/clinical_disease_id/2244?db=genetests&country=United%20States

Clinical Services

<http://www.ncbi.nlm.nih.gov/sites/genetests/clinic?db=genetests>

Find Genetic Services

<http://www.acmg.net/GIS/Disclaimer.aspx>

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