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

Differential Diagnosis: Classical homocystinuria (cystathionine ß-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:

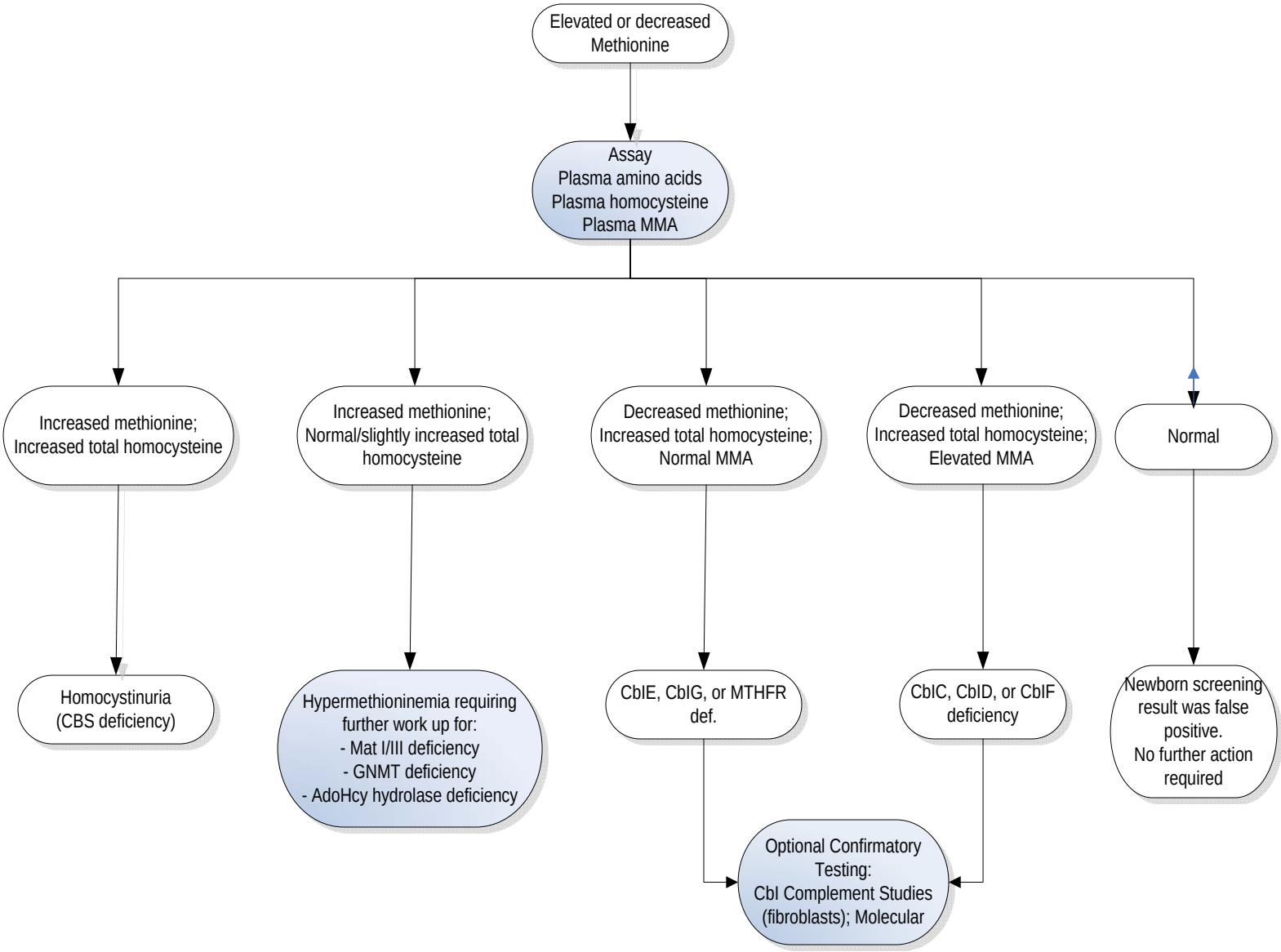
Gene Reviews
Genetics Home Reference

Referral (local, state, regional and national):

Testing
Clinical Services
Find Genetic Services

ACMG
American College of Medical Genetics and Genomics
Translating Genes Into Health®

Methionine Elevated or Decreased



Action steps are shown in shaded boxes; results are in the unshaded boxes.

Abbreviations/Key

AdoHcy hydrolase = Adenosylhomocysteine hydrolase
CBI = cobalamin
CBS = Cystathionine β-synthase
GNMT = glycine N-methyltransferase
Mat = Methyladenosyltransferase
MMA = Methylmalonic Acidemia
MTHFR def = Methylene Tetrahydrofolate Reductase Deficiency

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