Newborn Screening ACT Sheet
[Increased methionine]
Homocystinuria (CBS Deficiency)

Differential Diagnosis:
- Classical homocystinuria (cystathionine ß-synthase (CBS) deficiency);
- Hypermethioninemia due to MAT I/III deficiency;
- 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 hyper-methioninemias, methionine is increased in the absence of or only with a slightly increased level of homocysteine

MEDICAL EMERGENCY: TAKE THE FOLLOWING IMMEDIATE 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.

(See flowchart for information concerning the specific actions)

You Should Take the Following Actions:

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.

Disclaimer: These standards and guidelines are designed primarily as an educational resource for physicians to help them provide quality medical services. In determining the propriety of any specific procedure or test, the healthcare provider should apply his or her own professional judgment to the specific clinical circumstances presented by the individual patient or specimen

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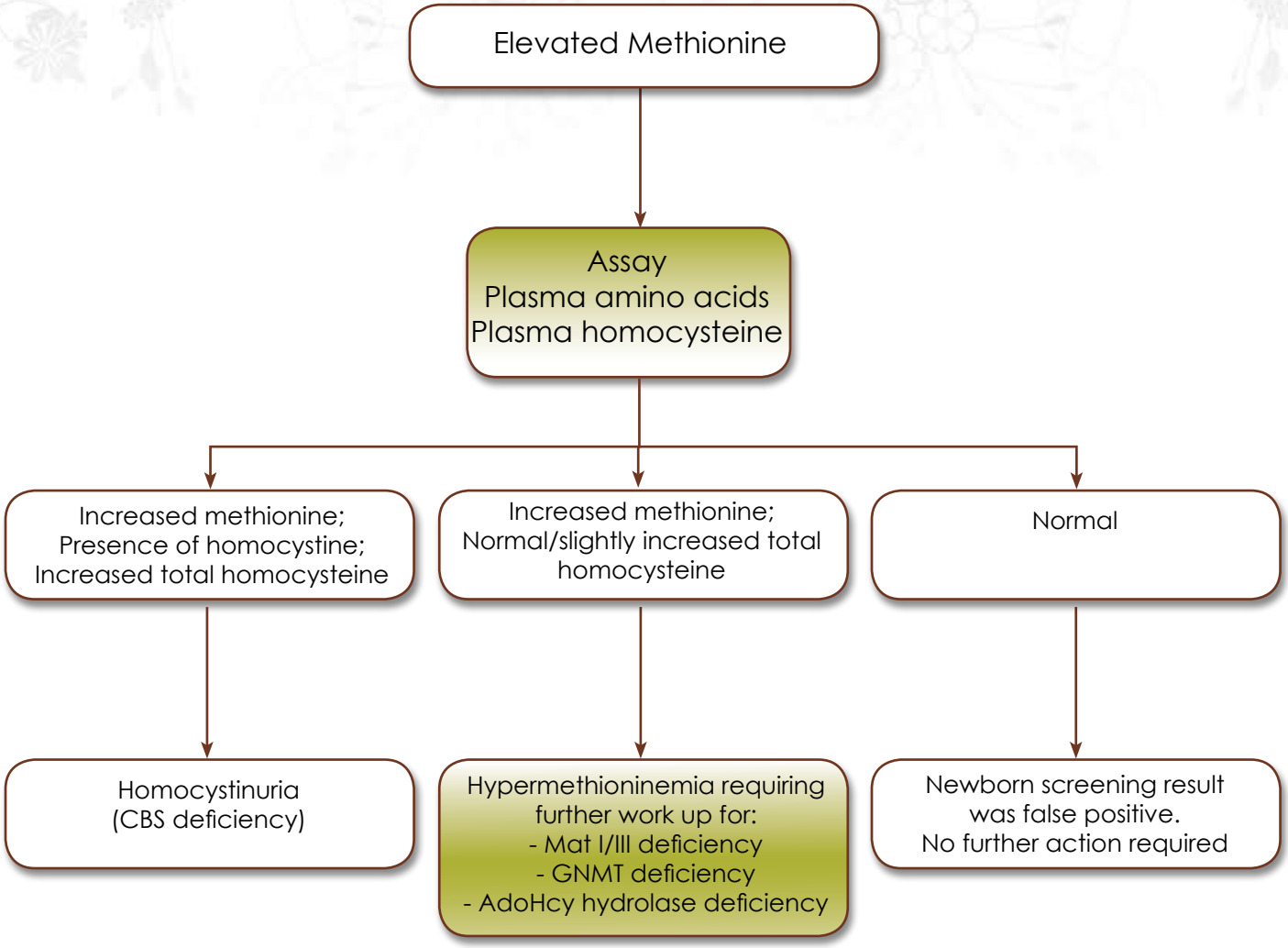
Methionine Elevated



Actions are shown in shaded boxes; results are in the unshaded boxes.

Abbreviations / Key:

Mat = Methyladenosyltransferase
CBS = Cystathionine β-synthase
AdoHcy hydrolase = Adenosylhomocysteine hydrolase
GNMT = guanidinoacetate methyltransferase

Disclaimer: These standards and guidelines are designed primarily as an educational resource for physicians to help them provide quality clinical services. Adherence to these standards and guidelines does not necessarily ensure a successful medical outcome. These standards and guidelines 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. In determining the propriety of any specific procedure or test, the healthcare provider should apply his or her own professional judgment to the specific clinical circumstances presented by the individual patient or specimen. It may be prudent, however, to document in the patient record the rationale for any significant deviation from these standards and guidelines.

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