Homocystinuria (increased methionine) Screening Fact Sheet for Health Care Providers
Newborn Screening Program of the Oklahoma State Department of Health

What is the differential Diagnosis?
Classical homocystinuria (cystathionine beta synthase deficiency); Hypermethioninemia (due to MAT I/III deficiency); liver disease; hyperalimentation.

What are the characteristics of homocystinuria?
- Autosomal recessive genetic condition.
- Most infants are born to parents who are both unknowingly asymptomatic carriers and have NO known history of homocystinuria or hypermethioninemia in their family.
- The incidence is 1:200,000 live births worldwide.
- Methionine from ingested protein is normally converted to homocysteine. In classical homocystinuria, homocysteine cannot be converted to cystathionine. As a result, the concentration of homocysteine and its precursor, methionine, will become elevated.
- Usually asymptomatic in the neonate.
- If untreated newborns can have excess homocystiene that damages the connective tissues leading to problems in the eyes with myopia, ectopia lentis, marfanoid appearance including arachnodactyly, osteoporosis, and other skeletal deformities. Thromboembolisim is a frequent complication. Cognitive and intellectual disability and behavioral problems can also occur.
- Lifelong treatment includes management by a metabolic specialist, a special diet of low protein diet, Vitamin B6 or both.

What is the screening methodology for Homocystinuria?
1. An amino acid profile by Tandem Mass Spectrometry (MS/MS) is performed on each filter paper.
2. Methionine is the primary analyte.

What is an in-range (normal) screen result for Methionine?
Methionine less than 100 is NOT consistent with Homocystinuria. See Table 1.

What is an out-of-range (abnormal) screen for Methionine?
Methionine ≥ 100 µmol/L requires further testing.

What screen results will require a repeat filter paper?
Methionine between 100 µmol/L and 160 µmol/L requires a repeat filter paper. Consultation with a Metabolic Specialist will be left to provider discretion.

TABLE 1.
In-range Methionine Newborn Screening Results

Primary Analyte	In-Range (µmol/L)
Methionine	< 100

[1] Elevations of the secondary analytes are reported as "not consistent with an amino acid disorder" if the primary analyte is in-range.

What screen results will require diagnostic testing?
Methionine ≥ 160 µmol/L will require immediate action. The follow-up program will provide detailed guidance on required actions and a *Follow-up Management Protocol* will be provided.

The following metabolic specialists have approved all recommendations:

Integris Pediatric Specialty Clinic, Inborn Error of Metabolism (IEM) Clinic
Geneticist pager: (405) 630-3794

OU Children's Physicians – Genetics Clinic
Page Operator: (405) 271-3636

What is my role in screening?
If you are listed as the infant's planned health care provider on the filter paper requisition, you are required by the *Newborn Screening Program Regulations* to initiate follow-up activities.

Newborn Screening Program (405) 271-6617 opt 2 or 1-800-766-2223 opt 2
Metabolic Nurse Specialist (405) 271-8001, ext. 42074
http://www.ok.gov/health/