ELEVATED METHIONINE
CLASSICAL HOMOCYSTINURIA / HYPERMETHIONINAEMIA

- Why does the baby need a second test?

The newborn metabolic screen result shows an increased level of methionine and a repeat blood spot is required to rule out the possibility of a metabolic disorder. It is possible for methionine to be raised in the newborn and not be significant in which case the repeat test will be normal and no further action required. However, in those cases where the methionine remains elevated (or the initial result indicates), urine and plasma samples will be required to determine whether the baby has a metabolic disorder or not.

- What can an elevated Methionine indicate?

Classical Homocystinuria due to cystathionine β synthase (CBS) deficiency
Hypermethioninaemia due to:
Methyladenosyl transferase (MAT I/III) deficiency
Glycine N-methyltransferase (GNMT) deficiency
S-Adenosylhomocysteine hydrolase deficiency
Liver Disease

In classical homocystinuria, methionine cannot be converted to cystathionine and as a result both methionine and homocysteine are elevated. In hypermethioninaemia the missing enzymes result in elevated methionine with or without homocysteine. In liver disease, phenylalanine and tyrosine would also be expected to be elevated.

- Clinical Symptoms

Classical homocystinuria is usually asymptomatic in neonates. Affected patients usually start to develop symptoms between 1 to 3 years of age. These include developmental delay, skeletal deformities, lens dislocation, thromboembolic events and psychiatric disturbances. Mat I/III is considered benign. The other causes of hypermethioninaemia are extremely rare.
- **Treatment**

Treatment for homocystinuria is effective if started early. Long term treatment includes pyridoxine (about half affected individuals are responsive to some extent to pyridoxine), folate, betaine and a methionine-restricted diet. There is no cure and treatment is life long.

- **Diagnostic Evaluation**

Plasma samples for amino acids and total homocysteine. Hypermethioninaemia conditions may require DNA analysis for confirmation.

- **What to do after receiving the elevated methionine result?**

  a) Contact the family to inform them of the screening result and ascertain the clinical status of the baby.
  b) Consult a metabolic clinician for advice if baby is unwell.
  c) Collect repeat blood spot or additional diagnostic samples as recommended in the screening report or by the metabolic clinician.
  d) If the baby develops symptoms, advise the family to go to the emergency department with the covering letter.