ELEVATED CITRULLINE
UREA CYCLE DISORDERS / AMINO ACID DISORDERS

- Why does the baby need a second test?

The newborn metabolic screen result shows an increased level of citrulline and a repeat blood spot is required to rule out the possibility of a metabolic disorder. It is possible for citrulline 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 citrulline 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 citrulline indicate?

Citrullinaemia type I
Arginosuccinic aciduria (ASA)
Citrin deficiency / Citrullinaemia type II
Pyruvate carboxylase deficiency

Citrullinaemia I and ASA are urea cycle disorders. Deficiencies in urea cycle enzymes prevent removal of waste nitrogen from the body and lead to an accumulation of ammonia. Citrullinaemia type II arises due to deficiency of the mitochondrial aspartate-glutamate carrier. Pyruvate carboxylase deficiency is extremely rare.

- Clinical Symptoms

Citrullinaemia I and ASA can present acutely in the newborn with hyperammonaemia, seizures, failure to thrive and coma. Citrin deficiency may present with cholestatic liver disease. Pyruvate carboxylase deficiency may present with severe neonatal lactic acidosis, encephalopathy, hypotonia and coma.
Treatment

Symptomatic Citrullinaemia type I and ASA need urgent treatment during episodes of acute decompensation. This consists of intravenous hydration, correction of blood gas abnormalities, use of ammonia scavenging drugs and even dialysis in severe cases. Long term treatment for Citrullinaemia I and ASA includes a low protein diet and ammonia-scavengers such as sodium benzoate. Citrin deficiency with neonatal cholestasis needs management of liver disease. After the neonatal period, a high protein/lipid low carbohydrate diet may be recommended. There is no cure for these conditions and treatment is life long.

Diagnostic Evaluation

The diagnosis of these disorders is confirmed through the analysis of urine organic acids and plasma amino acids and ammonia which reveal the abnormalities associated with these conditions.

What to do after receiving the elevated citrulline 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.