**C3 Elevated (Isolated)**

Elevated C3 (isolated)

- **Assay:**
  - Urine OA
  - Plasma AC
  - Plasma Homocysteine

- **‡Routine labs:**
  - Glucose, electrolytes, blood gas, ammonia, CBC

Plasma C3 – Normal
- Urine OA – Normal
- Plasma Homocysteine - Normal

Plasma C3 – High
- Urine OA – MMA
- Plasma Homocysteine - Normal

Plasma C3 – High
- Urine OA – Propionic acid
- Plasma Homocysteine - Normal

Plasma C3 – High
- Urine OA – Propionic acid
- Plasma Homocysteine - Normal

Plasma C3 – High
- Urine OA – MMA
- Plasma Homocysteine - Normal

Plasma C3 and C4DC – High
- Urine OA – MMA
- Plasma Homocysteine - Normal

Plasma C3 – High
- Urine OA – MMA
- Plasma Homocysteine - High

Plasma C3 – High
- Urine OA – Propionic acid
- Plasma Homocysteine - Normal

Plasma C3 – High
- Urine OA – MMA
- Plasma Homocysteine - Normal

Plasma C3 – Normal
- Urine OA – Normal
- Plasma Homocysteine - Normal

Plasma C3 and C4DC – High
- Urine OA – MMA
- Plasma Homocysteine - Normal

Plasma C3 – High
- Urine OA – MMA
- Plasma Homocysteine - High

Succinyl-CoA synthetase (SUCLA2) deficiency

- **Optional Confirmatory Testing:**
  - SUCLA2 sequencing

Methylmalonyl-CoA mutase (Mut*, Mut†), CblA or CblB deficiency

- **Optional Confirmatory Testing:**
  - Mut assay/Cbl Complement studies (fibroblasts)

CblC, CblD, CblF, TC-II, or vitamin B12 deficiency

- **Optional Confirmatory Testing:**
  - Cbl Complement studies (fibroblasts)

Propionyl CoA carboxylase deficiency (Propionic acidemia; PA)

- **False positive**

Consider maternal vitamin B12 deficiency

Methylmalonyl-CoA mutase (Mut*, Mut†), CblA or CblB deficiency

- **Optional Confirmatory Testing:**
  - Mut assay/Cbl Complement studies (fibroblasts)

Succinyl-CoA synthetase (SUCLA2) deficiency

- **Optional Confirmatory Testing:**
  - SUCLA2 sequencing

Propionyl-CoA carboxylase assay (fibroblasts)

**Abbreviations/Key:**
- AC = acylcarnitine
- CBC = Complete blood count
- Cbl = cobalamin
- MMA = methylmalonic acidemia
- Mut = mutase
- OA = organic acid
- TC-II = transcobalamin II

‡ - When the positive predictive value of screening is sufficiently high and the risk to the infant is high, some initiate diagnostic studies that are locally available at the same time as confirmation of the screening result is done.

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

**Disclaimer:** This guideline is designed primarily as an educational resource for clinicians to help them provide quality medical care. It 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. Adherence to this guideline does not necessarily ensure a successful medical outcome. In determining the propriety of any specific procedure or test, the clinician should apply his or her own professional judgment to the specific clinical circumstances presented by the individual patient or specimen. Clinicians are encouraged to document the reasons for the use of a particular procedure or test, whether or not it is in conformance with this guideline. Clinicians also are advised to take notice of the date this guideline was adopted, and to consider other medical and scientific information that become available after that date.

© American College of Medical Genetics, 2009 (Funded in part through MCHB/HRSA/HHS grant #U22MC03957)