Suggested Follow-up for Elevated C3: Propionyl Carnitine

Possible Causes: Elevated C3 is the primary marker for **propionic acidemia (PA) and methylmalonic acidemia (MMA).** Both are disorders of isoleucine (ILE), methionine (MET), threonine (THR), valine (VAL) and odd chain fatty acid metabolism. If C5-OH, 3-OH isovaleryl carnitine, is also elevated, the infant may have **holocarboxylase synthetase deficiency** (multiple carboxylase deficiency), an enzyme necessary for activation of four carboxylases involved in amino acid metabolism, gluconeogenesis and fatty acid synthesis.

Next Steps if Abnormal: **Potential medical emergency if C3 is over 10 uM with elevated C3/C2 or if C3 is over 15 uM with normal C3/C2.** See infant as soon as possible to ascertain health status. Consult pediatric metabolic specialist and initiate diagnostic evaluation and treatment as recommended. Common diagnostic studies include plasma total and free carnitines, plasma acylcarnitines and urine organic acids. In addition, repeat acyl carnitine profile on filter paper and send to the DHEC laboratory.

Neonatal Presentation: Poor feeding, vomiting, tachypnea, lethargy, metabolic acidosis, ketosis, hyperammonemia. Infants are at risk for metabolic decompensation/crisis.

Emergency Treatment: Treatment of metabolic crisis includes provision of sufficient nonprotein calories (concentrated dextrose infusion with appropriate electrolytes) to correct catabolic state and biochemical abnormalities if needed.

Standard Treatment: PA or MMA—Protein restricted diet with use of metabolic formula without ILE, MET, THR, VAL. Carnitine supplementation.

Holocarboxylase synthetase deficiency—Biotin supplementation.

Advice for Family: **Elevated C3's are the most common false positive test result on the acyl carnitine profile.** Provide basic information about organic acid disorders. The handout, *When Baby Needs a Second Test for an Organic Acid Disorder (Elevated C3)*, may be used for this purpose. Stress the importance of seeking immediate medical attention if the infant shows any signs of illness.

Internet Resources:

http://oregon.gov/DHS/ph/nbs/expand.shtml

http://web1.tch.harvard.edu/newenglandconsortium/scientists_physicians2.html

http://ghr.nlm.nih.gov/condition=propionicacidemia

http://www.genetests.org/query?dz=mma

http://ghr.nlm.nih.gov/condition=holocarboxylasesynthetasedeficiency

http://www.acmg.net/resources/policies/ACT/condition-analyte-links.htm