



## Newborn Screening ACT Sheet

### Elevated C5-OH Acylcarnitine Organic Acidemias

**Differential Diagnosis:** Most likely 3-methylcrotonyl-CoA carboxylase (3MCC) deficiency (infant or mother); may be 3-hydroxy-3-methylglutaryl (HMG)-CoA lyase deficiency;  $\beta$ -ketothiolase deficiency (BKT); multiple carboxylase deficiency (MCD), including biotinidase deficiency and holocarboxylase deficiency, 2-methyl-3-hydroxybutyric acidemia (2M3HBA), 3-methylglutaconic aciduria (3MGA).

**Condition Description:** Each of the disorders is caused by a deficiency of the relevant enzyme. The substrate, for which the enzyme is named, accumulates as does its potentially toxic metabolites in most of the disorders.

#### Medical Emergency: Take the Following Immediate Actions

- Contact family to inform them of the newborn screening result and ascertain clinical status (poor feeding, vomiting, lethargy).
- Consult with pediatric metabolic specialist. (See attached list.)
- Evaluate the newborn (hypoglycemia, ketonuria, metabolic acidosis).
- If any of these parameters are abnormal or the infant is ill, initiate emergency treatment as indicated by metabolic specialist and transport IMMEDIATELY to tertiary center with metabolic specialist.
- Initial testing: urine organic acids, plasma acylcarnitine analysis. Acylcarnitine profile on mother.
- Repeat newborn screen if second screen has not been done.
- Educate family about signs, symptoms, and need for urgent treatment of metabolic acidosis (poor feeding, vomiting, lethargy).
- Report findings to newborn screening program.

**Diagnostic Evaluation:** Confirmatory tests include urine organic acids on infant and mother, plasma acylcarnitine analysis, and serum biotinidase assay. The organic acids analysis on infant and mother should clarify the differential, except for holocarboxylase deficiency and biotinidase deficiency (the latter clarified by biotinidase assay).

**Clinical Considerations:** The neonate is usually asymptomatic in 3MCC deficiency. However, episodic hypoglycemia, lethargy, hypotonia, and mild developmental delay can occur at any time from the neonatal period through childhood for any of these disorders. There is beneficial treatment that is specialized to each condition.

#### Additional Information:

##### Emergency Treatment Protocol

[http://www.childrenshospital.org/newenglandconsortium/NBS/Emergency\\_Protocols.html](http://www.childrenshospital.org/newenglandconsortium/NBS/Emergency_Protocols.html)

##### 3MCC

<http://www.childrenshospital.org/newenglandconsortium/NBS/MMC.html>

##### HMG CoA lyase deficiency

<http://www.childrenshospital.org/newenglandconsortium/NBS/HMG.html>

##### STAR-G/HRSA

<http://www.newbornscreening.info/Parents/facts.html>  
<http://www.newbornscreening.info/Pro/facts.html>

**Gene Clinics** <http://www.genetests.org/servlet/access?db=geneclinics&site=gt&id=8888892&key=yedaWhvZIR6qb&gry=&fcn=y&fw=dns7&filename=/profiles/oa-overview/index.html>

##### Genetics Home Reference

**3MCC** <http://ghr.nlm.nih.gov/condition=3methylcrotonylcoacarbonylasedeficiency>

**Holocarboxylase synthetase deficiency** <http://ghr.nlm.nih.gov/condition=holocarboxylasesynthetasedeficiency>

**HMG CoA lyase deficiency** <http://ghr.nlm.nih.gov/condition=3hydroxy3methylglutarylcoalyasedeficiency>

**BKT** <http://ghr.nlm.nih.gov/condition=betaketothiolasedeficiency>