



# 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; **β-ketothiolase** deficiency; **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, in most of the disorders, accumulates as does its potentially toxic metabolites.

#### **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.
- 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.
- Initiate timely confirmatory/diagnostic testing as recommended by specialist.
- 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:**

(Click on the website name or X to take you to the pertinent website page. Complete URLs are listed in the Appendix)

Diagnosis	<u>Emergency Treatment Protocol</u>	STAR-G /HRSA	Gene Clinics	<u>Genetics Home Reference</u>
3-Methylcrotonyl-CoA carboxylase deficiency	<u>X</u>	<u>X</u>	<u>X</u>	<u>X</u>
Holocarboxylase deficiency	-	<u>X</u>	<u>X</u>	<u>X</u>
HMG-CoA lyase deficiency	<u>X</u>	<u>X</u>	<u>X</u>	<u>X</u>
2-Methyl-3-hydroxybutyric acidemia	-	-	<u>X</u>	-
β-Ketothiolase deficiency	-	<u>X</u>	<u>X</u>	<u>X</u>
3-Methylglutaconic aciduria type I	-	-	<u>X</u>	-
Biotinidase deficiency	-	-	<u>X</u>	<u>X</u>

**Disclaimer:** These standards and guidelines are designed primarily as an educational resource for physicians to help them provide quality medical services. Adherence to these standards and guidelines does not necessarily ensure a successful medical outcome. These standards and guidelines 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. In determining the propriety of any specific procedure or test, the healthcare provider should apply his or her own professional judgment to the specific clinical circumstances presented by the individual patient or specimen. It may be prudent, however, to document in the patient's record the rationale for any significant deviation from these standards and guidelines.

## APPENDIX: Resources with Full URL Addresses

### ***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**

**3MCC** <http://www.newbornscreening.info/Parents/organicaciddisorders/3MCC.html>

#### **Holocarboxylase synthetase deficiency**

<http://www.newbornscreening.info/Parents/organicaciddisorders/HCSd.html>

#### **HMG CoA lyase deficiency**

<http://www.newbornscreening.info/Parents/organicaciddisorders/HMGCoA.html>

**BKT** <http://www.newbornscreening.info/Parents/organicaciddisorders/BKD.html>

#### **Gene Clinics** (Click on the link below to access information on six of the seven diagnoses.)

<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>

**3MCC** (see link above)

**Holocarboxylase synthetase deficiency** (see link above)

**HMG CoA lyase deficiency** (see link above)

**2M3HBA** (see link above)

**BKT** (see link above)

**3MGA** (see link above)

#### **Biotinidase deficiency**

<http://www.genetests.org/servlet/access?db=geneclinics&site=gt&id=8888891&key=EJ4Gy2VAan2GT&gry=&fcn=y&fw=xn8V&filename=/profiles/biotin/index.html>

#### **Genetics Home Reference** <http://ghr.nlm.nih.gov/>

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

#### **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>

**Biotinidase deficiency** <http://ghr.nlm.nih.gov/condition=biotinidasedeficiency>

### ***Referral (local, state, regional and national):***

**Testing** <http://biochemgen.ucsd.edu/UCSDW3BG/Labchoose.asp>

#### **3MCC**

[http://genetests.org/servlet/access?prg=j&db=genetests&site=gt&id=8888892&fcn=c&qry=22655&res=nous&res=nointl&key=JyMZ0zRV4Za3o&show\\_flag=c](http://genetests.org/servlet/access?prg=j&db=genetests&site=gt&id=8888892&fcn=c&qry=22655&res=nous&res=nointl&key=JyMZ0zRV4Za3o&show_flag=c)

#### **Holocarboxylase synthetase deficiency**

[http://genetests.org/servlet/access?prg=j&db=genetests&site=gt&id=8888892&fcn=c&qry=53484&res=nous&res=nointl&key=JyMZ0zRV4Za3o&show\\_flag=c](http://genetests.org/servlet/access?prg=j&db=genetests&site=gt&id=8888892&fcn=c&qry=53484&res=nous&res=nointl&key=JyMZ0zRV4Za3o&show_flag=c)

#### **HMG CoA lyase deficiency**

[http://genetests.org/servlet/access?prg=j&db=genetests&site=gt&id=8888892&fcn=c&qry=22675&res=nous&res=nointl&key=JyMZ0zRV4Za3o&show\\_flag=c](http://genetests.org/servlet/access?prg=j&db=genetests&site=gt&id=8888892&fcn=c&qry=22675&res=nous&res=nointl&key=JyMZ0zRV4Za3o&show_flag=c)

#### **2M3HBA**

[http://genetests.org/servlet/access?prg=j&db=genetests&site=gt&id=8888892&fcn=c&qry=238914&res=nous&res=nointl&key=JyMZ0zRV4Za3o&show\\_flag=c](http://genetests.org/servlet/access?prg=j&db=genetests&site=gt&id=8888892&fcn=c&qry=238914&res=nous&res=nointl&key=JyMZ0zRV4Za3o&show_flag=c)

**BKT**

[http://genetests.org/servlet/access?prg=j&db=genetests&site=gt&id=8888892&fcn=c&qry=22660&res=nous&res=nointl&key=JyMZ0zRV4Za3o&show\\_flag=c](http://genetests.org/servlet/access?prg=j&db=genetests&site=gt&id=8888892&fcn=c&qry=22660&res=nous&res=nointl&key=JyMZ0zRV4Za3o&show_flag=c)

**3MGA**

[http://genetests.org/servlet/access?prg=j&db=genetests&site=gt&id=8888892&fcn=c&qry=20070&res=nous&res=nointl&key=JyMZ0zRV4Za3o&show\\_flag=c](http://genetests.org/servlet/access?prg=j&db=genetests&site=gt&id=8888892&fcn=c&qry=20070&res=nous&res=nointl&key=JyMZ0zRV4Za3o&show_flag=c)

**Biotinidase deficiency**

[http://genetests.org/servlet/access?prg=j&db=genetests&site=gt&id=8888892&fcn=c&qry=22179&res=nous&res=nointl&key=JyMZ0zRV4Za3o&show\\_flag=c](http://genetests.org/servlet/access?prg=j&db=genetests&site=gt&id=8888892&fcn=c&qry=22179&res=nous&res=nointl&key=JyMZ0zRV4Za3o&show_flag=c)

**Clinical**

<http://www.genetests.org/servlet/access?id=8888891&key=RRqZcXXEUiAx9&fcn=y&fw=zLsf&filename=/clinicsearch/searchclinic.html>

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