

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 synthetase 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. In most of the disorders, the substrate, for which the enzyme is named, accumulates as do its potentially toxic metabolites.

YOU SHOULD TAKE THE FOLLOWING 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 synthetase deficiency and biotinidase deficiency (the latter clarified by biotinidase assay).

Clinical Considerations: The neonate is usually asymptomatic in 3MCC deficiency. In 3MCC deficiency, the undiagnosed condition in the mother can result in an elevation of 3-methylcrotonyl-CoA carboxylase in the neonate. 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 specific to each condition.

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

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 and Genomics, 2012 (Funded in part through MCHB/HRSA/AHHS grant #U22MC03957)

American College of Medical Genetics *ACT SHEET*

LOCAL/STATE RESOURCES: Insert State newborn screening program web site links

Local/State Resource site (insert state newborn screening program website information)

| | |
|----------|----------------------|
| Name | <input type="text"/> |
| URL | <input type="text"/> |
| Comments | <input type="text"/> |

APPENDIX: Resources with Full URL Addresses

Additional Information:

Emergency Treatment Protocol <http://newenglandconsortium.org/for-professionals/acute-illness-protocols/organic-acid-disorders/>

3MCC <http://newenglandconsortium.org/for-professionals/acute-illness-protocols/organic-acid-disorders/3-methylcrotonyl-coa-3-mcc-dehydrogenase-deficiency/>

HMG CoA lyase deficiency <http://newenglandconsortium.org/for-professionals/acute-illness-protocols/organic-acid-disorders/3-hydroxymethylglutaryl-coa-3-hmg-coa-lyase-deficiency/>

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

<http://www.ncbi.nlm.nih.gov/sites/genetests/clinic?db=genetests>

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=&fnc=y&fw=xn8V&filename=/pr/ofiles/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

3MCC

http://genetests.org/servlet/access?prg=j&db=genetests&site=gt&id=8888892&fnc=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&fnc=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&fnc=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&fnc=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&fnc=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&fnc=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&fnc=c&qry=22179&res=nous&res=nointl&key=JyMZ0zRV4Za3o&show_flag=c

Clinical Services

<http://www.ncbi.nlm.nih.gov/sites/genetests/clinic?db=genetests>

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.

