



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
- 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.

(See flowchart for information concerning the specific actions)

You Should Take the Following Actions:

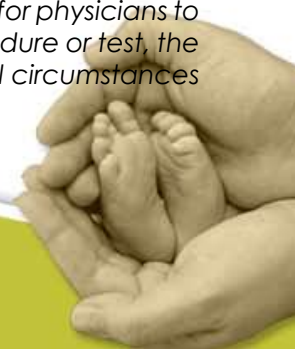
Diagnostic Evaluation:

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.

Disclaimer: These standards and guidelines are designed primarily as an educational resource for physicians to help them provide quality medical services. 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





Screening Today for a Safer Tomorrow

C5-OH Elevated

Elevated C5-OH

****Routine Labs:**
Glucose, electrolytes,
blood gas, ammonia

Assay:
Urine OA
Plasma AC

Plasma C5-OH: high
Urine OA: MCC

Plasma C5-OH: high
Urine OA: BKT

Plasma C5-OH: high
Urine OA: MGA

Plasma AC: normal
Urine OA: normal

Plasma C5-OH: high
Urine OA: HMG-CoA
lyase

Plasma C5-OH: high
Urine OA: MHBD

Plasma C5-OH: high
Urine OA: MCD

3-MCC

HMG-CoA
Lyase
deficiency

Beta-
ketothiolase
deficiency

2M3HBA/
(MHBD)
deficiency

3-methyl-
glutaconic
aciduria type 1

Biotinidase
assay

Activity
deficient

Activity
normal

Holocarboxylase
synthase assay

Activity
deficient

Activity
normal

Holocar-
boxylase
deficiency

Infant healthy.
Rule out ma-
ternal IEM*

Biotinidase
deficiency

Biotin
deficiency

Optional
confirmatory testing:
DNA analysis and/or
enzyme assay



NEWBORN



SCREENING

Screening Today for a Safer Tomorrow

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

Abbreviations / Key:

OA = organic acid

AC = acylcarnitine

MCC = methylcrotonyl-CoA carboxylase

MCD = multiple carboxylase deficiency

HMG-CoA = 3-hydroxy-3-methylglutaryl-CoA

BKT = Beta-ketothiolase

2M3HBA = 2-methyl-3-hydroxybutyric acidemia

MHBD = 2-methyl-3-hydroxybutyryl-CoA dehydrogenase

MGA = 3-methylglutaconic aciduria

IEM = inborn error of metabolism

* = Maternal MCC and holocarboxylase deficiency have been reported as having been identified in newborn screening.

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

Disclaimer: These standards and guidelines are designed primarily as an educational resource for physicians to help them provide quality clinical 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 record the rationale for any significant deviation from these standards and guidelines.

