

FACT SHEET
Healthcare Provider

3-Methylcrotonyl-CoA Carboxylase Deficiency (3MMC or 3MCC)

Description:

3-Methylcrotonyl-CoA Carboxylase Deficiency is an autosomal recessive disorder of leucine catabolism. Deficiency of this enzyme results in an accumulation of 3-Methylcrotonyl-CoA.

Incidence in General Population:

1:75,000 live births

Symptoms:

Generally appear after 3 months of age but can be variable. Many individuals have no symptoms into adulthood. Some infants have presented with Reye-like illness with hypoketotic hypoglycemia, metabolic acidosis and liver dysfunction often precipitated by an intercurrent illness, which has led to fulminant liver failure and death in some cases. On other occasions infants present with hypotonia and failure-to-thrive in conjunction with recurrent episodes of vomiting and diarrhea. In general, the earlier symptoms present, the poorer the prognosis.

Diagnosis:

Newborn screening abnormality—(Tandem mass spectrometry): increased C5OH

A second dried blood spot filter paper card may be requested by the Newborn Screening Laboratory if the initial screening result is above the normal range. Infants with presumptive positive screening (critical) results require prompt follow up. If this occurred, the clinician would be contacted by the Metabolic Treatment Center. When notified of these results, the clinician should immediately check on the clinical status of the baby and facilitate referral to the Metabolic Treatment Center. The Metabolic Treatment Center will provide consultation and assistance with diagnostic testing.

Situations that risk metabolic decompensation:

Metabolic decompensation can be triggered by the catabolic processes that occur in the course of infections, after an immunization, increased physical activity, dehydration, or with a prolonged period of fasting.

Monitoring:

Clinical observation is the most important tool for monitoring patients with 3MCC. They should be observed and assessed for neurological status, recurrent vomiting, refusal to eat, increased lethargy, apnea or seizures. In these situations, immediate evaluation in the emergency room is necessary. In situations of metabolic decompensation, hypoglycemia can develop but normal blood glucose does not rule out metabolic instability and should not be a reason to delay therapy. It is also important for the primary care provider and the Metabolic Treatment Center to develop an ongoing collaborative relationship in caring for these patients.

Treatment:

- Reduced-protein diet with restricted leucine intake, in combination with glycine and carnitine supplements. Glycine and carnitine allow for the nontoxic removal of excess isovaleric-CoA.
- The Metabolic Treatment Center will determine the patient's diet prescription that establishes the optimum percentage of fat, carbohydrate, and protein.
- The parents should have an emergency protocol with them at all times. This protocol can be provided by the Metabolic Treatment Center, and it should contain basic information about the disorder, necessary diagnostic investigations, and guidelines for treatment.

- Infants and children with 3MCC should have regularly scheduled visits at the Metabolic Treatment Center.

Illness:

- **Any** illness can potentially lead to metabolic decompensation.
- Prevention and/or early intervention are of particular importance.
- Care should be coordinated by the Metabolic Treatment Center.

Immunization:

Immunizations must be kept current, but patients and physicians should be alerted to the need for immediate evaluation if high fever, lethargy, or vomiting occurs in the first 24 hours. Influenza vaccinations are also recommended.

Surgical/surgical procedures:

- Discuss any plans for surgical and dental procedures with the Metabolic Treatment Center.
- A surgical procedure constitutes a potentially catabolic situation and preoperative fasting should be avoided with 10% dextrose being started preoperatively and continuing postoperatively until the child is eating and drinking well. Any procedure requiring anesthesia should be done at a hospital with a metabolic service.

Growth and development:

- It is crucial to closely monitor all growth parameters on a regular basis.
- In cases with neurological deficits, the child should be referred to an early intervention program and developmental progress should be closely monitored by both the metabolic team and the primary care provider.
- Intellectual prognosis depends on early diagnosis and treatment and, subsequently, on compliance with the dietary and supplement plan.



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