

**\*Elevated C4-OH Acylcarnitine**  
**3-Hydroxyacyl-Coenzyme A Dehydrogenase Deficiency (HADH)**  
**Previously Named Medium/Short Chain Acyl-CoA Dehydrogenase**  
**(M/SCHAD)**

**\*Elevated C3-DC Acylcarnitine**  
**Malonic Aciduria (MAL)**

**Differential Diagnosis:** 3-hydroxyacyl-CoA dehydrogenase deficiency (**HADH**), previously named MEDIUM/Short-chain hydroxyacyl-CoA dehydrogenase deficiency (M/SCHAD); Malonyl-CoA decarboxylase deficiency (Malonic Aciduria (MAL))

**Condition Description:** **HADH** deficiency is a fatty acid oxidation (FAO) disorder. Fatty acid oxidation occurs during prolonged fasting and/or periods of increased energy demands (fever, stress) when energy production relies increasingly on fat metabolism. In an FAO disorder, fatty acids and potentially toxic derivatives accumulate because of a deficiency in one of the mitochondrial FAO enzymes.

**Condition Description:** **Malonic aciduria** is caused by deficiency of malonyl-CoA decarboxylase which converts intra-mitochondrial malonyl-CoA to acetyl-CoA. This results in an increase in malonic acid and its derivatives.

**MEDICAL EMERGENCY - Take the Following IMMEDIATE Actions:**

- Contact family **IMMEDIATELY** to inform them of the newborn screening result and ascertain clinical status (poor feeding, vomiting, and lethargy).
- Consult/referral with pediatric metabolic specialist (See attached list).
- Immediately evaluate the newborn for hypoglycemia, lethargy, metabolic acidosis.
- Immediately evaluate the infant; check blood glucose and urine ketones, or if infant is ill, initiate treatment as recommended by metabolic specialist and transport **IMMEDIATELY** to tertiary center with metabolic specialist.
- Emergency treatment if symptomatic.
- Initiate timely confirmatory/diagnostic testing as recommended by specialist.
- Initial testing: plasma acylcarnitine profile, plasma insulin, plasma methylmalonic acid, and urine organic acids.
- Repeat newborn screen if the second screen has not been done.
- Educate family about need for infant to avoid fasting. If infant becomes even mildly ill (poor feeding, vomiting, or lethargy), immediate treatment with IV glucose is needed.
- Educate family about signs, symptoms and need for urgent treatment of metabolic acidosis and hypoglycemia.
- Report findings to newborn screening program.

**Diagnostic Evaluation:**

**HADH** the plasma acylcarnitine analysis will show increased C4-OH acylcarnitine. Urine organic acids will show increased hydroxyl-dicarboxylic acids. Plasma insulin may be elevated. HADH gene sequencing can confirm the diagnosis.

**Malonic Aciduria** the plasma acylcarnitine analysis will confirm increased C3-DC and urine organic acid analysis will show increased malonic acid.

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**Clinical Considerations:**

**HADH** the neonate is usually asymptomatic, although hypoglycemia and hyperinsulinism may be present. Severe hypoglycemia and severe hyperinsulinism may appear later. Sudden death in infancy has been reported.

**Malonic aciduria** may present acutely in the neonate. The presentation can include hypoglycemia, lactic acidosis, and marked lethargy. More commonly, malonic aciduria presents during infancy or later childhood with developmental delay, seizures, vomiting, failure to thrive, hypotonia, hypoglycemia, metabolic acidosis, and cardiomyopathy.

**Additional Information:**

**American College of Medical Genetics and Genomics**

<https://www.acmg.net/StaticContent/ACT/C4-OH.pdf>

<https://www.acmg.net/StaticContent/ACT/C3-DC.pdf>

**\*Because C3DC and C4OH are isomers our MSMS protocols cannot distinguish between the two compounds.**