

MEDIUM CHAIN ACYL-CoA DEHYDROGENASE (MCAD) DEFICIENCY

Marc E. Tischler, PhD;
University of Arizona

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- fatty acids are considered long chain (having more than 12 carbons), medium chain (6-12 carbons) and short chain (less than 6 carbons)
- fatty acid oxidation:
 - ✓ long and medium chain fatty acids enter the cell from the blood and undergo oxidation in the mitochondria, the energy-producing compartment found in cells
 - ✓ to enter the mitochondrial compartment, fatty acids must be converted to their fatty acyl-carnitine form
 - ✓ in the mitochondria the fatty acyl-carnitine is converted to the fatty acyl-CoA form and carnitine is recycled
 - ✓ fatty acyl-CoA is oxidized by the β -oxidation pathway to produce usable energy that can drive cell processes such as glucose biosynthesis
 - ✓ during their processing long chain fatty acyl-CoA becomes medium chain fatty acyl-CoA
- **medium chain acyl-CoA dehydrogenase deficiency**
 - ✓ only affects the processing of medium chain fatty acids
 - ✓ though some usable energy can be produced from the oxidation of long chain fatty acids to medium chain fatty acids this is very limited (~25% of normal)

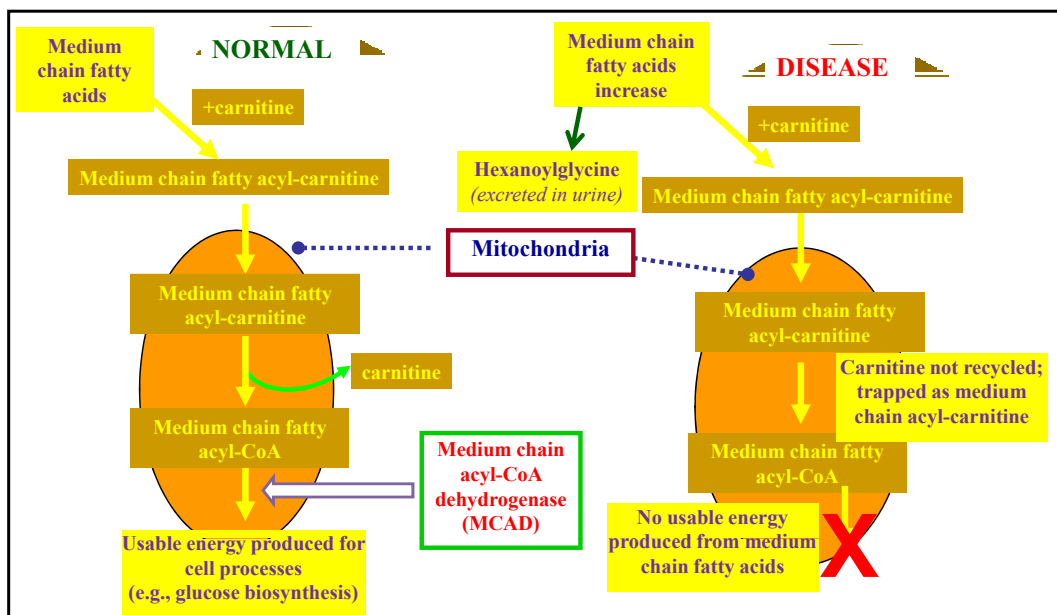


Figure 1. Long chain (not shown) and medium chain fatty acids enter the cell, are converted to the fatty acyl-carnitine and enter mitochondria (left). In mitochondria, fatty acyl-carnitine is converted to fatty acyl-CoA and carnitine is recycled. Fatty acyl-CoA is oxidized to produce usable energy to drive cell processes such as glucose biosynthesis. In **medium chain fatty acyl-CoA dehydrogenase (MCAD)** deficiency (X), carnitine is trapped as **medium chain fatty acyl carnitine**. This in turn decreases available carnitine for the small amount of long chain fatty acids oxidized for limited energy production. Medium chain fatty acids also increase in the blood. One of these, hexanoic acid, combines with glycine to form **hexanoylglycine** that is excreted in the urine.

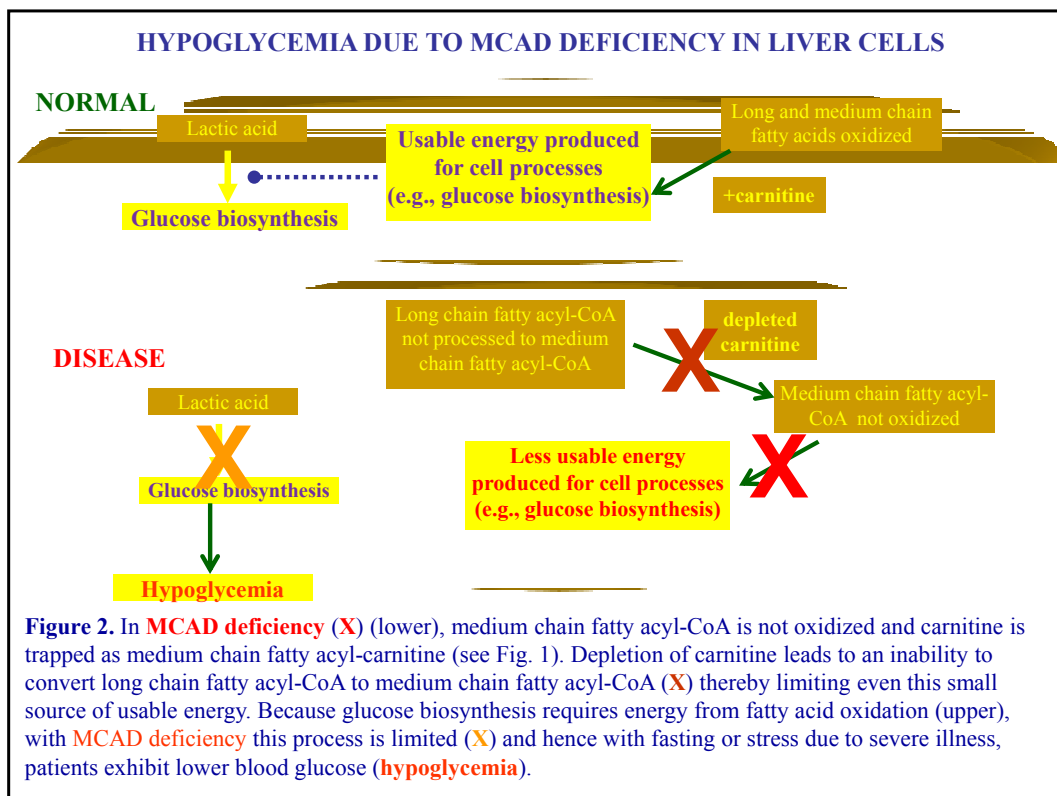


Figure 2. In **MCAD deficiency** (X) (lower), medium chain fatty acyl-CoA is not oxidized and carnitine is trapped as medium chain fatty acyl-carnitine (see Fig. 1). Depletion of carnitine leads to an inability to convert long chain fatty acyl-CoA to medium chain fatty acyl-CoA (X) thereby limiting even this small source of usable energy. Because glucose biosynthesis requires energy from fatty acid oxidation (upper), with **MCAD deficiency** this process is limited (X) and hence with fasting or stress due to severe illness, patients exhibit lower blood glucose (**hypoglycemia**).