

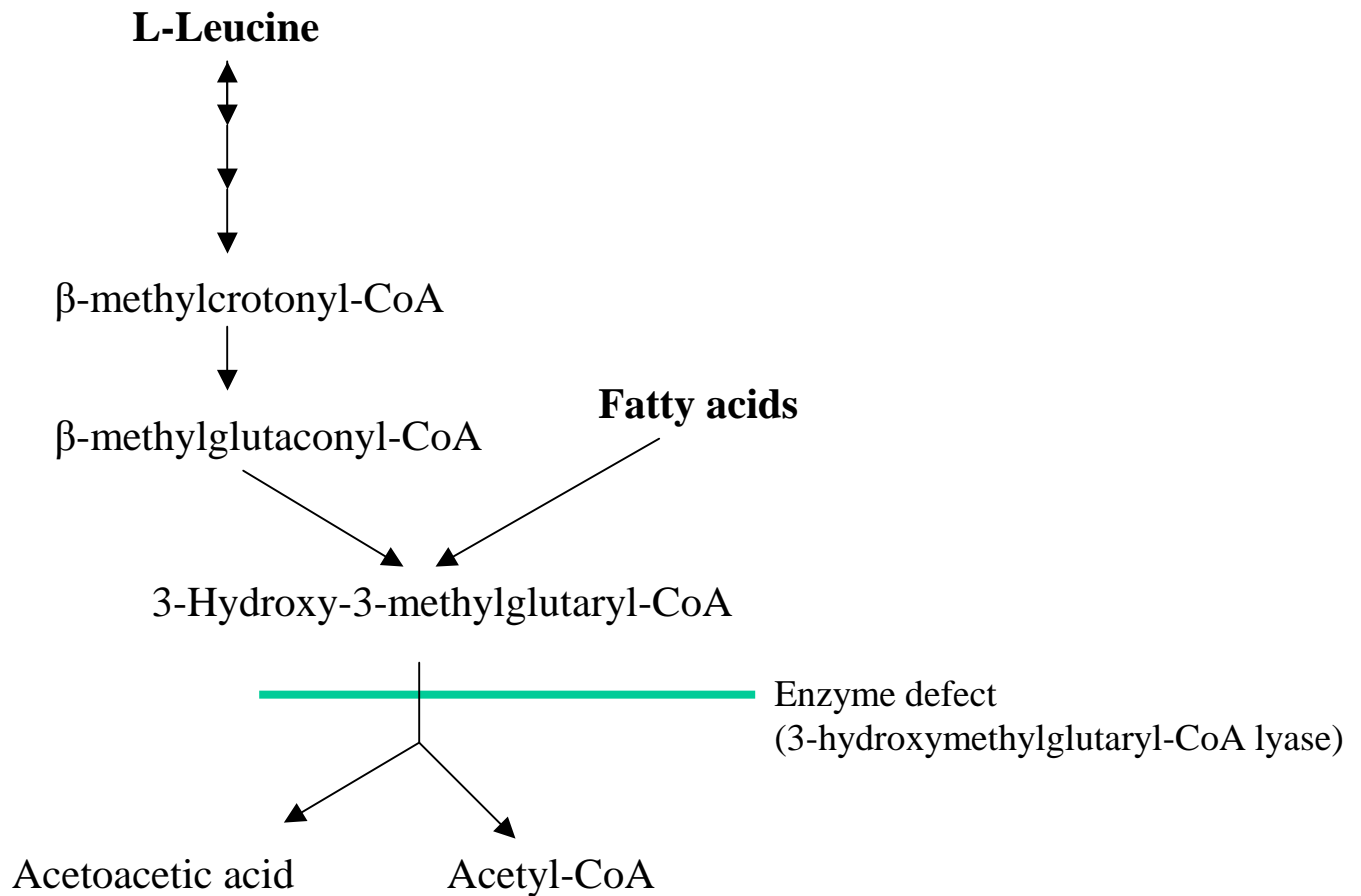
ACUTE ILLNESS PROTOCOLS

3-HYDROXYMETHYLGLUTARYL-CoA (3-HMG CoA) LYASE DEFICIENCY

INTRODUCTION

3-HMG CoA Lyase deficiency is one of several defects in the degradation pathway of leucine (a major branched-chain amino acid). Most of the defects produce metabolic ketoacidosis but ketones are absent or low despite acidosis and hypoglycemia in 3-HMG CoA Lyase deficiency. Thus, this is a cause of **hypoketotic hypoglycemia**. The pathway is as follows:

PATHOPHYSIOLOGY



In the presence of catabolism or substantially reduced food intake (e.g. infection, severe exertion), the combination of an increased cellular requirement for energy

and reduced glucose intake results in proteolysis with release of amino acids and fatty acids. Enhanced leucine and fatty acid degradation is an attempt by the body to produce the needed energy in the form of ketones. When 3-HMG-CoA lyase is deficient, the increased fluxes in both leucine degradation and fatty acid oxidation result in an accumulation of 3-hydroxymethylglutaryl-CoA. The accumulated substrate produces **metabolic acidosis**, inhibits gluconeogenesis resulting in **hypoglycemia**, and inhibits the urea cycle resulting in **hyperammonemia**.

PRESENTATION

- Vomiting
- Lethargy
- Encephalopathy
- Hypotonia
- Failure to thrive
- Hepatomegaly
- Reye syndrome picture
- Developmental delay
- Seizures
- Sudden death

Parents of children with metabolic disorders know the early signs of decompensation in THEIR children. Listen to them !!!

ASSESSMENT

Assess for dehydration, fever, infection or other stressors that may precipitate an acute metabolic episode. Clinical decompensation can occur rapidly in an infant and may be more gradual in older children.

INVESTIGATIONS

- Blood glucose (? hypoglycemia)
- pH, blood gases, (? metabolic acidosis)
- electrolytes (? low bicarbonate)

- ammonia (? hyperammonemia)
- urine ketones (? absent or trace)
- urinalysis
- AST, ALT, AP, PT, PTT
- urine organic acids
- culture of blood, throat, urine as indicated

ASSESS BIOCHEMICAL PARAMETERS REGULARLY AND FREQUENTLY WHILE SICK

TREATMENT

1. INDICATION FOR IV (NEVER less than 10% dextrose infusion)
(One or more indication is sufficient for IV)

- Vomiting
- Hypoglycemia
- Poor PO intake
- Dehydration Do not rely on ketones as indicating dehydration!
- Decreased alertness
- Metabolic acidosis

Start 10% glucose continuous infusion at 1.5x maintenance to provide 7-8mg/kg/min

2. DO NOT ADMINISTER LIPIDS IN ANY FORM

3. HYPOGLYCEMIA

Push 25% dextrose 2ml/kg and follow with a continuous 10% dextrose infusion at 1.5x maintenance to provide 7-8mg/kg/min glucose

4. METABOLIC ACIDOSIS (Bicarbonate level<16)

Must be treated aggressively with IV Sodium bicarbonate (1 mEq/kg). Treating conservatively in the expectation of a re-equilibration of acid/base balance as other biochemical/clinical parameters are normalized can lead to tragic consequences.

5. CARNITINE

Should be provided PO (100-200 mg/kg/day divided TID) or IV (30-50 mg/kg/day).

6. PRECIPITATING FACTORS

Should be treated aggressively to help minimize further catabolism

7. APPARENTLY WELL

If drinking oral fluids well and none of the above factors present, there is no need for emergent IVI. But history of earlier vomiting, pyrexia, or other stressor should be taken seriously and a period of observation undertaken to ensure that PO fluids are taken frequently and well tolerated, with glucose status monitored periodically.

In conjunction with this protocol, please call or have paged the genetics metabolism fellow on call, or failing this, the metabolic attending on call at your hospital or nearest pediatric tertiary care center