FATTY ACID OXIDATION DISORDERS (FAOD)

FAOD includes:

- Medium chain acyl co-A dehydrogenase deficiency (MCADD)
- Very long chain acyl Co-A dehydrogenase deficiency (VLCAD)
- Long chain hydroxyacyl co-A dehydrogenase deficiency (LCHAD)
- Trifunctional protein deficiency (TFP)
- Carnitine Palmitoyl Transferase Deficiency Type 1 (CPT1)
- Carnitine Palmitoyl Transferase Deficiency Type 2 (CPT2)
- Carnitine Uptake Defect (CUD)
- Glutaric Aciduria Type 2 (GA2)

What are FAOD?

FAOD are a group of autosomal recessive disorders caused by the deficiency or absence of any of the enzymes needed for beta-oxidation. Children born with this condition appear normal at birth but untreated patients may present with low blood sugar which can lead to seizures, coma and death. One type of FAOD, VLCAD (or very long chain acyl-CoA dehydrogenase deficiency) may present with cardiomyopathy and increased creatine kinase (CK) levels.

Confirmatory Testing

Please refer to the table below:

FAOD	Confirmatory Testing
Medium chain acyl co-A dehydrogenase deficiency (MCADD)	Gene Testing and Plasma Acylcarnitine
Very long chain acyl Co-A dehydrogenase deficiency (VLCAD)	Gene Testing and Plasma Acylcarnitine
Long chain hydroxyacyl co-A dehydrogenase deficiency (LCHAD)	Gene Testing
Trifunctional protein deficiency (TFP)	Gene Testing
Carnitine Palmitoyl Transferase Deficiency Type 1 (CPT1)	Gene Testing
Carnitine Palmitoyl Transferase Deficiency Type 2 (CPT2)	Gene Testing and Plasma Acylcarnitine
Carnitine Uptake Defect (CUD)	Gene Testing and Plasma Acylcarnitine
Glutaric Aciduria Type 2 (GA2)	Gene Testing

Further confirmatory testing may be required after referral to a metabolic specialist.

FATTY ACID OXIDATION DISORDERS (FAOD)

Treatment of FAOD

Treatment is through the dietary restriction of fat. VLCAD patients are treated with a special milk formula containing medium chain triglycerides. Initiation of management should be done in consultation with an attending physician/metabolic specialist.

Preliminary / Initial Management During Metabolic Crisis

Metabolic crises may be caused by illness, prolonged fasting or stressful situations such as surgery and severe infection. The goal of treatment is to reverse the catabolic state and prevent hypoglycemia.

WHAT TO DO

If unwell and cannot tolerate oral intake:

- Nothing per orem
- Ensure patient's airway is secure
- Insert IV access. Monitor glucose levels. For patients with VLCAD, collect samples for serum CK. May request for other investigations (i.e. CBC, Blood gas) as needed. May give fluid boluses if the patient requires it.
- Start D10% 0.3 NaCl at full maintenance. Assess the patient and clinically, if there is need to increase fluid, may do so up to 1.2 or 1.5X the maintenance.
- Monitor input and output strictly (q6 hours). Check for the color of urine.

If unwell and can tolerate oral intake:

- Insert oro- or nasogastric tube and start continuous feeding with a high glucose formula
- Insert IV access. Monitor glucose levels. For patients with VLCAD, collect samples for serum CK. May request for other investigations (i.e. CBC, Blood gas) as needed. May give fluid boluses if the patient requires it.
- Start D10% 0.3 NaCl at 5-10 cc/hr.
- Monitor input and output strictly (q6 hours). Check for the color of urine.

**Patients with VLCAD may have rhabdomyolysis. Monitor CK levels and hydrate adequately. If CK levels continually rise, hemodialysis may be indicated.*
**Inform the metabolic doctor on call for further guidance regarding on-going management*
**If the patient is well, coordinate with a metabolic specialist regarding further management.*

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FATTY ACID OXIDATION DISORDERS

Carnitine Uptake Defect (CUD)

What is Carnitine Uptake Defect (CUD)?

Carnitine uptake defect is also known as carnitine transporter deficiency. It is due to an abnormality in the transport that facilitates carnitine's entry into certain cells. In some instances, it has been found that neonates who test positive for this condition do not actually have the condition but instead reflect the decreased levels of their mothers.

CLINICAL MANIFESTATIONS

Patients may present with hypoketotic hypoglycemia, modest hepatomegaly and Reye-like syndrome, progressive heart failure and muscle weakness. Most patients present with a progressive cardiomyopathy associated with skeletal myopathy.

PATHOPHYSIOLOGY

Carnitine is necessary for transport of long-chain fatty acids into mitochondria to enter the ß-oxidation cycle.[2] Genetic defects of the carnitine transporter results in failure of tissues of the cardiac and skeletal muscle and in the renal tubules to concentrate intracellular levels of carnitine, thus reducing available cofactor for the carnitine cycle.[3]

Inheritance: autosomal recessive[2]

CONFIRMATORY TESTING

Plasma acylcarnitine and gene testing. Further confirmatory testing may be required after referral to a metabolic specialist.

Overview of Disease Management

Oral carnitine therapy at 100mg/kg/day into four divided doses is recommended.[2,3] Initiation of management should be done in consultation with an attending physician/metabolic specialist.

Prognosis

Patients on long term therapy report normal skeletal muscles tone, no episodes of metabolic decompensation, and essentially normal intellect.[3]

Preliminary / Initial Management During Metabolic Crisis

Metabolic crises may be caused by illness, prolonged fasting or stressful situations such as surgery and severe infection. The goal of treatment is to reverse the catabolic state, correct the acidosis and prevent essential amino acid deficiency.

FATTY ACID OXIDATION DISORDERS

Carnitine Uptake Defect (CUD)

WHAT TO DO

If unwell and cannot tolerate oral intake:

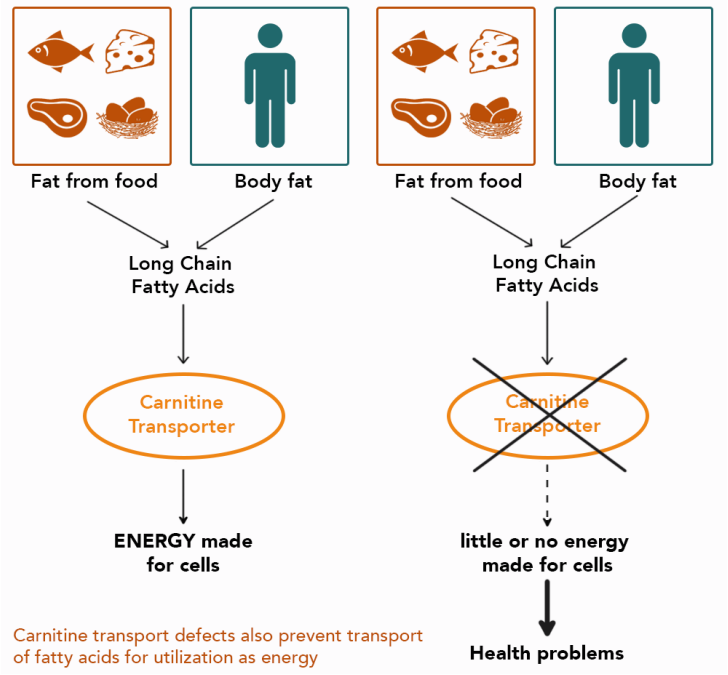
- Nothing per orem
- Ensure patient's airway is secure
- Insert IV access. Monitor glucose levels. May request for investigations (i.e. CBC, etc.) as needed.
- May give fluid boluses if the patient requires it.
- Start D10% 0.3NaCl at full maintenance. Assess the patient and clinically, if there is need to increase fluid, may do so up to 1.2 or 1.5x the maintenance.
- Monitor input and output strictly (q6 hours).

If unwell and can tolerate oral intake:

- Encourage regular feeding
- Insert IV access. Monitor glucose levels. May request for investigations (i.e. CBC, etc.) as needed.
- Start D10% 0.3NaCl at 5-10 cc/hr
- Monitor input and output strictly (q6 hours)

**Inform the metabolic doctor on call for further guidance regarding on-going management*
**If the baby's confirmatory test is negative, consider doing plasma acylcarnitine analysis of the patient's mother to rule out maternal CUD.*
**If the patient is well, coordinate with a metabolic specialist regarding further management.*

Normal breakdown of protein vs CUD patient's breakdown of protein



[1] *Chapter 37: Carnitine transporter deficiency. Nyhan WL, Barshop BA and Ozand P. Atlas of Metabolic Diseases 2nd ed. Great Britain:Oxford University Press, 2005 pp 246-250.*
[2] *Wilcken B. Disorders of Carnitine Cycle and Detection by Newborn Screening. Ann Acad Med 2008;37 (12):71-73.*
[3] *Hsu HW, Zytkovicz TH, Comeau AM et al. Spectrum of Medium chain acyl-coA dehydrogenase deficiency detected by newborn screening. Pediatrics 2008;121:e1108-e1114.*