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:	If unwell and can 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.	• 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.

FATTY ACID OXIDATION DISORDERS

Very long-chain acyl-CoA dehydrogenase deficiency

What is Very long-chain acyl-CoA dehydrogenase (VLCAD) Deficiency?

Very long-chain acyl-CoA dehydrogenase catalyzes the dehydrogenation of C22-C12 straight chain fatty acids, and because the long chain fatty acids constitute a major proportion of the fatty acids, VLCAD deficiency is generally a more severe condition than MCAD or SCAD deficiency and multiple tissues are affected.

CLINICAL MANIFESTATIONS

The clinical presentation of symptomatic VLCAD deficiency is heterogenous with phenotypes of different severities., There are three forms described: (1) severe childhood form with neonatal onset and cardiomyopathy; (2) milder childhood form with delayed onset of symptoms often triggered by metabolic stress and presents as hypoketotic hypoglycemia and; (3) adult form which presents with isolated skeletal muscle involvement with recurrent episode of muscle pain, rhabdomyolysis and myoglobinuria.[1,2]

PATHOPHYSIOLOGY

VLCAD catalyzes the dehydrogenation of acyl CoA esters of 14-20 carbon length in the first step of mitochondrial fatty acid oxidation.[2,3] VLCAD deficiency results in lack of production of energy from ß-oxidation of long-chain fatty acids, because heart and muscle tissue depend heavily on energy from long chain fatty acid oxidation, a VLCAD deficiency severely affect these tissues.[1]

Inheritance: autosomal recessive[1]

CONFIRMATORY TESTING

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

Overview of Disease Management

Treatment of this disorder include avoidance of fasting by frequent feeding, overnight continuous feeding, reduction of amount of long chain fat in diet while supplying essential fatty acids in the form of canola, walnut oil or safflower oil and supplementation with medium chain triglycerides.[1,3] Initiation of management should be done in consultation with an attending physician/ metabolic specialist.

Prognosis

Fifty percent of patients die within 2 months of initial symptomatology.[3] However, timely and correct diagnosis leads to dramatic recovery so that early detection could prevent the onset of arrhythmias, heart failure, metabolic insufficiency and death.

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.

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. Collect samples for urine ketones and serum creatine kinase (CK). May request for investigations (i.e. CBC, liver transaminases, blood gas, 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). Check color of urine and may request for urinalysis to check for urine myoglobin.
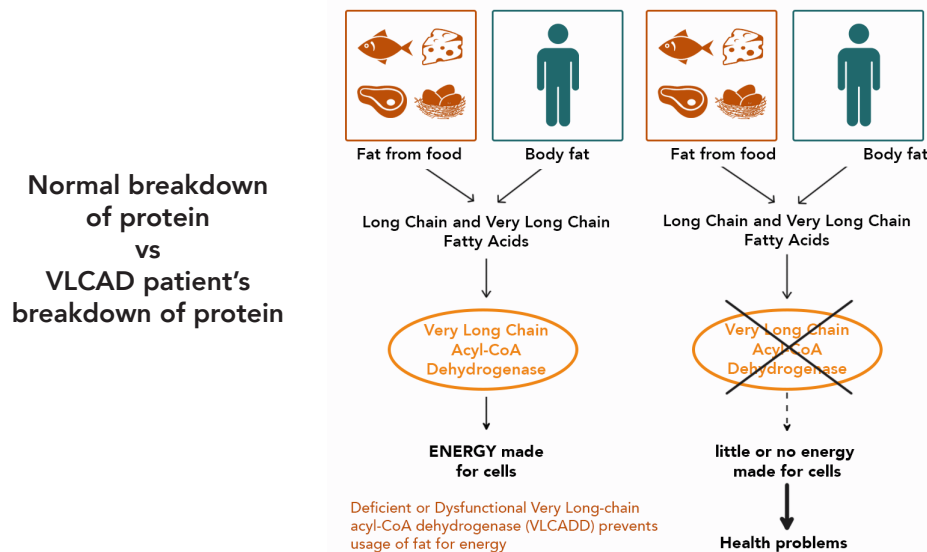
If unwell and can tolerate oral intake:

- Encourage regular feeding
- Insert IV access. Monitor glucose levels. Collect samples for urine ketones and serum creatine kinase (CK). May request for investigations (i.e. CBC, liver transaminases, blood gas, etc.) as needed.
- Start D10% 0.3NaCl at 5-10 cc/hr
- Monitor input and output strictly (q6 hours). Check color of urine and may request for urinalysis to check for urine myoglobin.

i
*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

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

Fat from food   Body fat   Fat from food   Body fat

Long Chain and Very Long Chain Fatty Acids

Long Chain and Very Long Chain Fatty Acids

Very Long Chain Acyl-CoA Dehydrogenase

Very Long Chain Acyl-CoA Dehydrogenase

ENERGY made for cells

little or no energy made for cells

Deficient or Dysfunctional Very Long-chain acyl-CoA dehydrogenase (VLCADD) prevents usage of fat for energy

Health problems

[1] 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.
[2] Nyhan WL, Barshop BA and Ozand P. Chapter 41: Very long chain acyl-CoA dehydrogenase deficiency. Atlas of Metabolic Diseases 2nd ed. Great Britain:Oxford University Press, 2005 pp 267-270.
[3] Wood JC, Mager MJ, Rinaldo P et al. Diagnosis of very long chain acyl-dehydrogenase deficiency from an infant's newborn screening card. Pediatrics 2001l108:e19-e21.
[4] Moczulski D, Majak I, Mamczur D. An overview of ß-oxidation disorders. Postepy Hig Med Dosw 2009;63:266-277.