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***MITO 101 – Emergency Department Letter
and Illness Precautions***

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The catabolic state

Entering catabolism is a normal way of dealing with certain normal and abnormal stressors to the body. During these times our body is in a state of increased energy needs. There is a higher dependence on the body's stores of proteins, carbohydrates and fats to generate energy.

Catabolic stressors include prolonged fasting, fever, illness, surgery and anesthesia.

The catabolic state in metabolic disease

Metabolic disease, including mitochondrial disease, lead to a partial or complete disruption of the body's normal chemical processes. Certain chemicals are not turned over; these compounds build up and create cellular toxicity; certain chemicals are not made, which creates a cellular deficiency. When individuals with metabolic disease undergo a normal or abnormal catabolic stressor, they begin turning over protein, carbohydrate and fat stores as they should - but due to the inherent chemical disruption, create more than normal levels of toxic substances and less than normal levels of the required product.

In the case of mitochondrial disease, cells are less efficient at creating adequate energy from protein, fat and carbohydrate stores. In the catabolic state, the cell's request for more cellular energy is often not met. It is during these times the individual with mitochondrial disease is more vulnerable to cellular injury in various organs, including the brain. Certain organs can rapidly decompensate and enter a state of organ failure.

Illness as a common mitochondrial catabolic stressor

There are several catabolic stressors to the body, including prolonged fasting, illness, surgery and anesthesia. Of these, one that is faced commonly in the pediatric and adult population is illness. Viral illnesses are a frequent occurrence in the growing child. And there is currently no clear way to prevent a child or adult from acquiring viral infections, though hand-washing and limiting exposures to sick-contacts/contagious persons have benefits.

The patient with mitochondrial disease is not more prone to life-threatening infections. There is some anecdotal (experience-based) and small study-based evidence that mitochondrial patients have more frequent non-life-threatening viral infections such as colds, stomach-flues, bronchitis, and ear infections. This vulnerability may be due to some, yet unquantifiable, dysfunction of the immune system - though, to date, all routine measures of immune function in mitochondrial patients are normal.

There is no specific treatment for mitochondrial patients despite the potentially increased frequency of non-life-threatening infections. The precautions listed below should be followed when possible.

Precautions against catabolism

The best treatment against catabolism is preventing it from occurring. This means:

- Prevent prolonged fasting with maintaining oral fluid intake and/or IV fluids before and after a procedure/surgery
- Ensure that the fluids provided contain a source of dextrose
- Avoid medications that may be toxic to the mitochondria, such as propofol, aminoglycosides, and valproic acid, when possible
- Avoid fluids that may be toxic to the mitochondria, such as ringer's lactate
- Prevent over-sedation by volatile anesthetics
- Ensure that the patient has an illness precautions letter similar to one outlined below

Treatment of catabolism

Once a patient is already in a catabolic state, treatment should begin immediately. This treatment includes:

- Stop the oral intake of a toxic compound including any applicable medications (usually by making the patient NPO)
- Provide IV fluids with dextrose
- Give IV fluids at a higher than maintenance rate
- Insulin may be needed, not only to prevent hyperglycemia but also to provide the body with a hormonal signal to stop catabolism
- Monitor routine chemistries, glucose, ammonia, ketones and liver function for metabolic derangements
- Correct any metabolic derangements

1. Hypoglycemia - if hypoglycemic, administer 1-2 g/kg of glucose IV STAT; follow with (at least) a 10% glucose solution
2. Metabolic acidosis - administer NaHCO₃ as a bolus (1 mEq/kg) if acutely acidotic with pH < 7.22 or bicarb level < 14, followed by a continuous infusion.
3. Hyperammonemia - the elevated ammonia reflects a secondary inhibition of the urea cycle. As treatment for the metabolic decompensation proceeds, the ammonia level should diminish. A level > 200 may require treatment.

- Provide medications such as IV levo-carnitine (100 mg/kg/day, divided tid) to facilitate the removal of toxic metabolic species
- Treat any underlying infection and fever

Sample Emergency/Illness Precautions Letter

To Whom It May Concern:

X has a disorder of mitochondrial metabolism. Individuals with such a metabolic disease are more sensitive to routine illness and simple fasting than others and can have a rapid decompensation. These individuals need an urgent evaluation since they can transition quickly from well-appearing to fatally ill. Some individuals can progress to a Reye-syndrome like illness and permanent liver failure.

If X is unable to maintain oral intake with illness, he should be evaluated by a physician, with a low threshold to admit him for a short hospital stay for intravenous fluids with dextrose.

The admission should not occur exclusively for dehydration - but for any metabolic stressor that may lead to dehydration or catabolism. The goal is to admit the patient and treat them him/her prior to any dehydration or catabolism occurring.

The treatment for acute metabolic decompensation in these disorders includes:

1. Hydration with dextrose containing IV fluids. D10 should be used with insulin piggy-backed to control hyperglycemia. Insulin is a potent anabolic hormone, promoting protein and lipid synthesis. Give fluids at 1.25-1.5X times the maintenance rate. IV fluids should never contain lactated ringers.
2. Correct any biochemical abnormalities. Routine chemistries, CBC, liver function (synthetic and cellular), ammonia, glucose, ketosis and lactic acidosis should be monitored and any derangements corrected.

Hypoglycemia - if hypoglycemic, administer 1-2 g/kg of glucose IV STAT; follow with (at least) a 10% glucose solution

Metabolic acidosis - administer NaHCO₃ as a bolus (1 mEq/kg) if acutely acidotic with pH < 7.22 or bicarb level < 14, followed

by a continuous infusion.

Hyperammonemia - the elevated ammonia reflects a secondary inhibition of the urea cycle. As treatment for the metabolic decompensation proceeds, the ammonia level should diminish. A level > 200 may require treatment.

3. Eliminate toxic metabolites by making the patient NPO for 24-72 hours and by giving levo-carnitine via an IV, at a dose of at least 100 mg/kg/day divided tid. If the patient is on a higher oral dose, please use that dose for the IV treatment. Any other supplements being given should be continued by mouth if possible. Once the patient's laboratories begin to normalize, restarting the patient on their home-based diet is advised.

4. Treat any underlying infection and fever.

Medications that should generally be avoided in individuals with mitochondrial disease include valproic acid, statins, aminoglycoside antibiotics, erythromycin, and propofol. There are no absolute contraindications and these medications can be given if an alternative drug is not available or appropriate.

Some individuals with mitochondrial diseases are more sensitive to volatile anesthetics and need a much lower dose to achieve a bispectral index of <60. Sevoflurane is tolerated better than isoflurane and halothane.

Should there be any questions or concerns please contact my office at X