SAMPLE EMERGENCY LETTER

PLEASE NOTE

This sample letter is intended to serve only as a guide. Give this letter to your family physician to individualize for you or your child. UMDF's intent on providing this sample is to provide guidance and should not be used without your physician's input.

To whom it may concern:

PATIENT:
DATE OF BIRTH:
DIAGNOSIS:

(Insert patient's name) has a disorder of ***. Some individuals with metabolic and mitochondrial diseases are more sensitive to physiologic stressors such as minor illness, dehydration, fever, temperature extremes, surgery, anesthesia, and prolonged fasting/starvation. During such stress, rapid systemic decompensation may occur. Preventative measures are aimed at avoiding, or at very least not exacerbating such decompensation.

Mainstays of treatment during or prior to acute metabolic decompensation in mitochondrial and metabolic disease includes keeping patients well-hydrated, providing sufficient anabolic substrate, correcting secondary metabolic derangements, avoiding pharmacological mitochondrial toxins, and providing cofactor and/or salvage therapies.

IV fluids and substrate therapy

- Dextrose/electrolyte therapy should be considered if a patient is unable to maintain oral fluid intake in the face of a catabolic stressor, including fever, illness or vomiting.
- A hospital admission should be considered, not exclusively for dehydration, but to prevent catabolism by providing an anabolic food in the form of dextrose.
- Routine chemistries, CBC, liver function (synthetic and cellular), ammonia, glucose, ketosis and lactic acidosis should be monitored and any derangements corrected.
- Assessment of the patient's cardiac and renal status must be performed prior to aggressive fluid therapy

- Hydration and substrate therapy involves providing 5 or 10% dextrose containing IV fluids given at 1.25-1.5X times the maintenance rate. A high dextrose delivery with D10 or D20 might be needed, especially if acidosis or metabolic derangements are not correcting with 5% dextrose containing fluids. When a higher dextrose delivery is given, insulin may also be needed. Insulin not only controls hyperglycemia but also serves as a potent anabolic hormone, promoting protein and lipid synthesis. Insulin is typically given in the intensive-care-unit setting with the initial dose in the 0.05-0.1 U/kg/hour range, and titrated accordingly
- IV fluids should never contain Lactated Ringers solution
- Fluids should be weaned based on laboratory parameters, oral intake and resolution of the underlying metabolic stressor
- Once the initial crisis passes, enteral feeding should be considered. Protein can be added if hyperammonemia has resolved and there is no concomitant disorder of protein catabolism. If there is no primary or secondary fatty acid oxidation dysfunction, lipids may also be added
- Once the patient's laboratories begin to normalize, restarting the patient on their home-based diet is advised.

Laboratory Parameters

- If acutely acidotic with a pH < 7.22 or bicarbonate level < 14 mM, metabolic acidosis can be controlled by administering sodium bicarbonate as a bolus (1 mEq/kg) followed by a continuous infusion
- Hyperammonemia can occur due to secondary inhibition of the urea cycle. As treatment for the metabolic decompensation proceeds, the ammonia level should diminish. A level > 200 uM may require salvage therapy or dialysis
- Any underlying infection and fever should be aggressively treated

Antioxidant therapy

- Levo-carnitine therapy during an acute illness may be beneficial. It should be given intravenously at a dose of at least 100 mg/kg/day. Doses of up to 300 mg/kg/day have been used. If the patient is on a higher oral dose, that dose should be used intravenously for treatment
- Any other home-based supplements and antioxidants being given should be continued by mouth if possible.

Medication contraindications

- Medications that should generally be avoided during times of illness in individuals with mitochondrial disease include valproic acid, statins, aminoglycoside antibiotics, and erythromycin. These medications should be used with extreme caution if given long-term.
- There are no absolute contraindications and these medications can be given if an alternative medication is not available or appropriate as long as a prior adverse reaction to the medication has not occurred
- Should a medication such as valproate be used for the first time during an acute illness, liver enzymes, ammonia and synthetic liver function should be closely monitored
- In addition to the medications noted above, long-term use of anti-HIV therapy, traditional neuroleptics, and select chemotherapeutic agents may worsen mitochondrial function.

Anesthesia

- Questions on anesthetic sensitivity in mitochondrial patients remain
- Some individuals with mitochondrial metabolic diseases are more sensitive to volatile anesthetics and need a much lower dose to achieve a bispectral (BIS) index of <60. This effect has been seen more in patients with reduced complex 1 capacity. Sevoflurane might be better tolerated than isoflurane and halothane
- Debate remains as to the potential risk of propofol administration in mitochondrial disease patients. However, propofol has been routinely used in many mitochondrial patients for brief periods of sedation (less than 30-60 minutes) without apparent clinical problems. Limiting propofol use to short procedures and brief periods of sedation is advisable for now

Fasting with surgery

- During pre- and post-operative fasting, catabolism can be prevented by using dextrose-containing IV fluids. IV fluids are continued until the time of discharge, since they are intended to deter catabolism and not simply treat dehydration
- IV fluids should never contain Lactated Ringers solution
- Routine chemistries, a complete blood count, liver function (synthetic and cellular), ammonia, glucose, ketosis and lactic acidosis should be monitored and any derangements corrected

Please contact my office if you have any questions regarding this letter.

Sincerely,

(Your doctor's signature)

UMDF RESOURCES

For additional information on the topics covered in this booklet, as well as other topics, please explore the United Mitochondrial Disease Foundation website at: **www.umdf.org.**

A few links that may be of particular interest include:

www.umdf.org/askthemitodoc: Questions and answers provided by a team of mitochondrial disease experts.

www.umdf.org/diseasetype: For more in depth information on specific disorders and articles to share with your health care professionals.

www.umdf.org/partofthecure: Want a free membership? See what the UMDF offers in your state. You will find information on UMDF groups, activities, events, and local resources.

www.umdf.org/mito101: A primer for physicians and patients. Mito 101 is a compilation of information intended to familiarize general practitioners and families alike with the most common problems raised by mitochondrial diseases.

www.umdf.org/symposium: Looking for an opportunity to learn more about mitochondrial disorders and to network with others facing similar challenges? The annual Mitochondrial Medicine Symposium is designed for you! On this link you will find all of the up-to-date details.

www.umdf.org/researchgrants: Learn how the UMDF spends its research dollars. This peer-review process selects best-of -the-best applications for funding.

www.umdf.org/AACT: UMDF's Adult Advisory Committee Team. ACTT represents and serves the unique needs of the affected adult community ensures that those needs are adequately represented to UMDF resulting in enhanced services to the affected adult population.