



## Newly diagnosed with Pearson Syndrome

*The following are recommendations for families of those newly diagnosed with Pearson Syndrome. They are based on recommendations from The Champ Foundation's first Pearson Syndrome Conference, held on February 5, 2018 and were updated following the Pearson Syndrome conference held May 30, 2020. Clinicians in attendance included Dr. Suneet Agarwal (Boston Children's Hospital), Dr. Peter Aziz (Cleveland Clinic), Dr. Rebecca Ganetzky (CHOP), Dr. Amy Goldstein (CHOP), Dr. Elad Jacoby (Sheba Medical Center), and Dr. Sumit Parikh (Cleveland Clinic). These recommendations were reviewed and updated in February 2023 by members of The Champ Foundation's Science Advisory Board.*

*These guidelines do not substitute for medical advice and all interventions should be approved and decided by your child's doctors.*

### **1. Understanding Pearson Syndrome**

Pearson Syndrome is a very rare primary mitochondrial disorder due to a mitochondrial DNA deletion. While each case is different, individuals are often at risk of anemia, impaired vision, hearing loss, cardiac rhythm disturbances, endocrine dysfunction, pancreatic insufficiency, challenges with feeding and growth and kidney problems.

### **2. Consider registering in the Champ Foundation Registry (CFR)**

The CFR is a research study to investigate single large-scale mitochondrial DNA deletion (SLSMD) disorders, such as Pearson syndrome, Kearns-Sayre Syndrome, and CPEO. Any individual or caregiver of an individual with a SLSMD disorder may register. The CFR aims to: (1) Identify individuals with single large-scale mitochondrial deletion disorders, such as Pearson syndrome, Kearns-Sayre Syndrome, and CPEO; (2) Gather past and future information on individuals with SLSMD through voluntary registration, self-reported survey questionnaires, patient-mediated medical record collection, and optional biospecimen sharing; (3) Make data collected through the CFR available to researchers and clinicians who are studying SLSMD disorders to answer questions regarding the disease, including its causes, potential treatments, and other topics; (4) Be the primary hub of clinical trial recruitment for individuals with SLSMD disorders. The co-principal investigators of the CFR are Elizabeth Reynolds and Dr. Sumit Parikh (Cleveland Clinic Scientific Advisor to The Champ Foundation).

### **3. Consider participating in the Pearson Syndrome Natural History Study**

The purpose of this study is to better understand the natural history of the disease. This will help support future research studies, and could help find treatments and cures for Pearson syndrome and other single large-scale mitochondrial DNA deletion disorders. To participate in the Natural History Study, participants must first register on the CFR and complete an eligibility screening process. Contact [contact@thechampfoundation.org](mailto:contact@thechampfoundation.org) if you are interested in participating or in more information.

### **4. Set up a team of doctors**

Pearson Syndrome can affect multiple organ systems in the body. Your child's medical team may include a hematologist, endocrinologist, cardiologist, ophthalmologist, neurologist, gastroenterologist, geneticist, and nephrologist. It may be of value to find a specialist for each, even if your child does not currently present symptoms. This enables you to be comfortable with the doctor, establish baseline values, and monitor changes.

### **5. Review mitochondrial disease guidelines.**

You or your doctors may be interested in general care guidelines for patients with mitochondrial diseases. The Mitochondrial Care Network developed a guide for those newly diagnosed with mitochondrial disease, and can be found here: [bit.ly/mitoguide22](https://bit.ly/mitoguide22). The Mitochondrial Medicine Society developed patient care standards for primary mitochondrial diseases, and can be found here [bit.ly/mitocare](https://bit.ly/mitocare).

### **6. Gather emergency letters from appropriate doctors**

People with Pearson Syndrome may be more sensitive to physiological stressors. This means minor illnesses, dehydration, fever, temperature extremes, surgery, anesthesia, and fasting can be particularly dangerous. Avoiding these situations is very important, but when your child is having a sick day, it is of critical importance that emergency room doctors have the most up-to-date recommendations for patient care. These recommendations should include guidelines for: (1) labs to be drawn and monitored, (2) fluids to be provided in case of dehydration, (3) response to lactic acidosis, (4) specific drugs to be avoided, (5) precautions during anesthesia and surgery, and (6) provision of supplements and antioxidants. An example emergency letter is attached.



### **7. Medications and the “mito cocktail”**

There is currently no approved treatment or cure for Pearson Syndrome. Many doctors, however, suggest a therapeutic trial of coenzyme Q10, along with a combination of additional nutrients such as creatine, arginine, L-Carnitine, thiamine, vitamins C and E, alpha-lipoic acid, and folic acid. Be sure to work directly with your doctor to determine what medications and vitamins, and what dosages, are best for your child.

### **8. Connect with other families**

Connecting with other families living with a Pearson Syndrome diagnosis can provide emotional support and a wealth of useful information. If interested, request to join the Facebook group “Pearson Syndrome Family.”

### **9. Join our efforts to find a cure**

Research is necessary to better understand how to treat Pearson Syndrome, and is the only hope for children suffering from this debilitating disease. If you are interested in working with The Champ Foundation to help find new therapeutic approaches for treating this condition, please contact us at [contact@thechampfoundation.org](mailto:contact@thechampfoundation.org).



## Pearson Syndrome Emergency Letter Example

*The following is an adapted emergency letter from Dr. Sumit Parikh for Pearson Syndrome patients*

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 (typically through IV dextrose), correcting secondary metabolic derangements, avoiding pharmacological mitochondrial toxins, and providing cofactor and/or salvage therapies

General guidelines on this topic as well as other aspects of care for these patients is available online at [bit.ly/mitocare](http://bit.ly/mitocare).

### Laboratory Parameters

- Basic chemistries, glucose, CBC, liver function (synthetic and cellular), ammonia, glucose, ketosis and lactic acidosis should be monitored and any derangements corrected
- 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
- Hypothyroidism and/or cortisol deficiency can develop during critical illness. These should be assessed for and treated when needed.

### IV fluids and Nutrition

- 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
- Clinical and laboratory assessment of the patient's cardiac and renal status should 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 not 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 or parenteral feeding should be provided as soon as medically feasible (typically within 24-48 hours). 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

### Medication contraindications

- Medications that should generally be avoided during times of illness in individuals with mitochondrial disease include valproic acid, statins, metformin, high-dose acetaminophen, aminoglycoside antibiotics, linezolid and erythromycin
- 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 select anti-HIV therapy, traditional neuroleptics, and select chemotherapeutic agents may worsen mitochondrial function in some individuals

#### 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. 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

#### Anesthesia

- Questions on anesthetic sensitivity in mitochondrial patients remain though patients are at an increased risk of anesthesia-related complications
- Some individuals with mitochondrial metabolic diseases might be 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
- One should consider slow titration and adjustment of volatile and parenteral anesthetics to minimize hemodynamic changes
- Caution must be used with muscle relaxants in those mitochondrial patients with underlying myopathy, neuropathy or decreased respiratory drive
- Debate remains as to the potential risk of propofol administration in mitochondrial disease patients. However, propofol has been routinely used in 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
- Local anesthetics are generally well-tolerated in patients with mitochondrial defect
- There is no clear established link between malignant hyperthermia and mitochondrial disease

#### Fasting and surgery

- During pre- and post-operative fasting, catabolism should 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
- A pre-operative admission to begin IV dextrose during a period of fasting is recommended
- IV fluids should not contain Lactated Ringers solution. Normal saline alone should not be used unless the patient cannot tolerate dextrose containing IV fluids
- Routine chemistries, a complete blood count, liver function (synthetic and cellular), ammonia, glucose, ketosis and lactic acidosis should be monitored and any derangements corrected

#### Stroke Management

- Stroke-like episodes in primary mitochondrial disease typically have correlating visible magnetic resonance imaging abnormalities.
- IV arginine hydrochloride a dose of 0.5 grams/kg should be administered urgently in the acute setting of a stroke-like episode associated with the MELAS m.3243 A>G mutation in the *MTTL1* gene and considered in a stroke-like episode associated with other primary mitochondrial cytopathies as other etiologies are being excluded.
- Patients should be reassessed after 3 days of continuous IV therapy.
- The use of daily oral arginine supplementation to prevent strokes should be considered in MELAS syndrome



**Table: Medication Cautions**

Medication	Common Uses	Concern in Mitochondrial Disease
Acetaminophen	Analgesic, fever prevention, headaches	Chronic or frequent use may deplete glutathione and cause hepatopathy
Aminoglycosides	Antibiotic	Hearing loss
Antiretrovirals	HIV therapy	Impaired mtDNA replication and worsening peripheral neuropathy, liver dysfunction or myopathy
Botulinum toxin	Dystonia, Spasticity	Worsening of weakness
Butterbur	Headache	May contain pyrrolizidine alkaloids (oxidants) and cause hepatopathy
Metformin	Diabetes	Lactic acidosis
Topiramate	Epilepsy, Headache, Intracranial Hypertension	Lactic acidosis
Statins	Hypercholesterolemia	Worsening myopathy and elevated creatine kinase (CK)
Valproic Acid	Epilepsy, Headache, Mood disorders, Movement disorders, Tone abnormalities	Irreversible liver failure and onset of hepato-encephalopathy, especially in <i>POLG</i> -related disorders; worsening of seizures
Vigabatrin	Epilepsy	Inhibition of the mitochondrial nucleoside salvage pathway and worsening of mtDNA depletion disorders

*With the exception of valproic acid in *POLG*-related disorders, these medications are **not contraindicated** and **may be used** with caution*