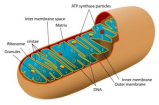
SOCIETY FOR AMBULATORY ANESTHESIA
Outpatient • Office Based • Non-Operating Room

2022 SAMBA ANNUAL MEETING
MAY 11 – 14, 2022

Anesthetic Considerations for Patients With Mitochondrial Disease



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SAMBA real world cases, May 2022

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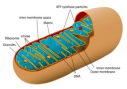

Mitochondrial defects

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- Mitochondrial function is dependent on hundreds of different proteins.
- Mitochondrial myopathies represent a wide variety of molecular defects and thus a wide range of different diseases with similar phenotypes. The specific defect in the underlying the mitochondrial disease might not be known.
- Increases in lactate or pyruvate, increases in systemic acylcarnitines, or altered amounts of amino acids can occur.
- Metabolic abnormality in a patient with a myopathy or encephalopathy, should raise the possibility of a mitochondrial defect.
- Abnormal metabolites may be partially causative for the disease symptoms such as acidosis

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Systemic Clinical Effects

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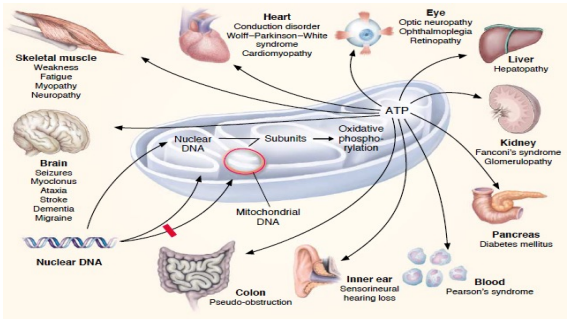

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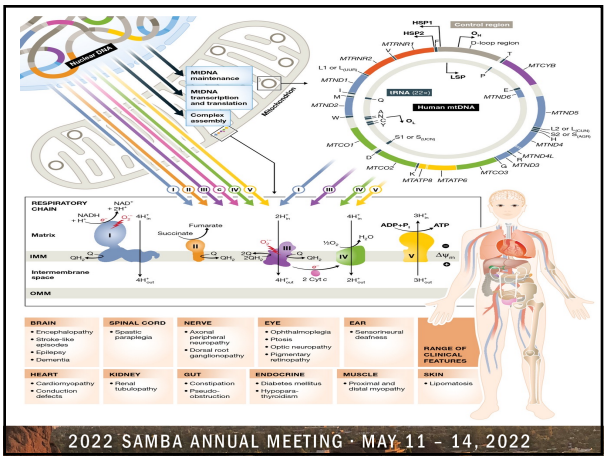

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Father with disease	Mother with disease (all mitochondria mutant)	Mother with disease (some mitochondria normal, others mutant)
Children do not have the disease	Children have the disease (assuming complete penetrance)	Children may or may not have the disease (and severity may vary)

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Anesthesia for patients with mitochondrial disease - the good news

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- Most exposures to anesthetics for mitochondrial patients are without apparent complications
- Patients can tolerate a wide variety of anesthetics including the volatile anesthetics, propofol and local anesthetics.

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Anesthetic Decisions

- These patients are at increased risk from the stress of surgery and anesthesia.
- Primary complications of mitochondrial myopathies include respiratory failure, cardiac depression, conduction defects and dysphagia.
- Mitochondrial patients often require **smaller doses** of general anesthetics, local anesthetics, sedatives, analgesics, and paralytics
- **Avoid increasing the metabolic burden** of patients by not requiring prolonged fasting, and preventing hypoglycemia, PONV, hypothermia (with resulting shivering), prolonged orthopedic tourniquet application, acidosis, and hypovolemia.

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IV fluids

- Avoid glucose in those patients on ketogenic diet
- Supply glucose at maintenance rates with perioperative serum glucose monitoring in patients not on ketogenic diet
- Avoid lactate to their fluids
- **Use D5 NS or 1/2 NS**

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IV Solution Cheat Sheet

Type	Description	Osmolality	Use	Miscellaneous
Normal Saline (NS)	0.9% NaCl in Water Crystalloid Solution	Isotonic (308 mOsm)	Increases circulating plasma volume when red cells are adequate	• Replaces losses without altering fluid concentrations. • Helpful for Na+ replacement
1/2 Normal Saline (1/2 NS)	0.45% NaCl in Water Crystalloid Solution	Hypotonic (154 mOsm)	Raises total fluid volume	• Useful for daily maintenance of body fluid, but is of less value for replacement of NaCl deficit. • Helpful for establishing renal function. • Fluid replacement for clients who don't need extra glucose (diabetics)
Lactated Ringer's (LR)	Normal saline with electrolytes and buffer	Isotonic (275 mOsm)	Replaces fluid and buffers pH	• Normal saline with K+, Ca++, and lactate (buffer) • Often seen with surgery
D5W	Dextrose 5% in water Crystalloid solution	Isotonic (in the bag) *Physiologically hypotonic (260 mOsm)	Raises total fluid volume. Helpful in rehydrating and excretory purposes.	• Provides 170-200 calories/1,000cc for energy. • **Physiologically hypotonic** -the dextrose is metabolized quickly so that only water remains - a hypotonic fluid
D5NS	Dextrose 5% in 0.9% saline	Hypertonic (560 mOsm)	Replaces fluid sodium, chloride, and calories.	• Watch for fluid volume overload
D5 1/2 NS	Dextrose 5% in 0.45% saline	Hypertonic (406 mOsm)	Useful for daily maintenance of body fluids and nutrition, and for rehydration.	• Most common postoperative fluid
D5LR	Dextrose 5% in Lactated Ringer's	Hypertonic (575 mOsm)	Same as LR plus provides about 180 calories per 1000cc's.	• Watch for fluid volume overload
Normosol-R	Normosol	Isotonic (295 mOsm)	Replaces fluid and buffers pH	• pH 7.4 • Contains sodium, chloride, calcium, potassium and magnesium • Common fluid for OR and PACU

nurseslabs

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Adverse Outcomes

- Respiratory depression can occur from the combination of anesthetics and existing muscle weakness.
- Reports of late, profound respiratory depression and/or CNS white matter degeneration in patients seemingly only mildly affected preoperatively, and who have had relatively uneventful anesthetic courses during surgery

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Considerations

- All general anesthetic agents studied has been shown to depress mitochondrial function, most notable are the volatile anesthetics and propofol
- Consider direct inhibition of the respiratory chain separately from the indirect effects of anesthetics on physiologic functions also affected by mitochondrial function such as respiratory drive, cardiac contractility, muscle strength.
- Anesthetics may depress certain systems by mitochondrial-independent mechanisms, such as GABA enhancement, but still lead to **additive inhibition** of organ systems affected by mitochondrial defects.

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Volatile Agents

- Does not require metabolism for excretion, thus advantageous over IV anesthetics, which are dependent on energy requiring metabolism.
- Each of the volatile anesthetics depresses respiration, through different mechanisms.
- Isoflurane and desflurane depress the ventilatory response to CO2 response more than does sevoflurane.
- Sevoflurane and desflurane cause more direct muscle relaxation.
- **Sevoflurane** would seem to be mildly advantageous in patients with mitochondrial defects.

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Propofol

- Propofol has been shown to affect mitochondrial function by at least four different mechanisms.
- Decreases ventilatory drive, cardiac output, and contractility.
- Excretion of propofol is metabolism dependent.
- **Both propofol and thiopental have been used as induction agents successfully when used in a limited regimen such as for an induction bolus.**
- Some patients with mitochondrial defects may be susceptible to adverse reactions from propofol.

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Opioids and Muscle Relaxants

- Generally, has not been shown to alter mitochondrial function, with possible exception of morphine.
- Must be considered carefully in patients who may already have respiratory compromise.

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Local analgesics

- Patients with defects in fatty acid metabolism may have an increased sensitivity to toxicity from bupivacaine.

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Medication	Mitochondrial Effects
Barbiturates	Complex I inhibition
Etomidate	Complex I inhibition, mild inhibition complex III
Propofol	Acylcarnitine transferase, complexes I/II/IV inhibition
Benzodiazepines	Complex I/II/III inhibition
Ketamine	Increase energy consumption +/– reports of complex I
Dexmedetomidine	None reported
Fentanyl/remifentanil	Minimal
Morphine	Mild complex I inhibition
Volatile Anesthetics	Complex I inhibition
Bupivacaine (Etidocaine)	Acylcarnitine translocase Mild complex I

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Recommendations

- Minimizing preoperative fasting to avoid hypovolemia, hypoglycemia and increased metabolism of fatty acids
- Use muscle relaxants cautiously in patients with a preexisting myopathy or decreased respiratory drive
- Avoid lactate as some patients have difficulty metabolizing lactate and may become acidotic
- Tourniquets and pressure points to minimize regions of poor perfusion and oxygen delivery
- Avoid swings in body temperature as mitochondrial patients are unable to adapt well to either hypothermia or hyperthermia
- Slow titration of volatile and parenteral anesthetics to minimize hemodynamic changes, consider EEG monitoring
- Minimize PONV and use multimodal analgesic techniques

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Safe for Ambulatory Surgery?

- Equipment, medical, and clinical resources
- Pathway for inpatient admission
- Consultation with geneticist, cardiologists, endocrinologist and other subspecialties
- Educate patient and family (or vice versa)
- Collaborative perioperative preparation, communications, and discussions
- Consider hospital setting and/or admission
  - Previous significant adverse reactions to anesthesia and/or surgery
  - Patient has moderate to severe clinical manifestations of the mitochondria and/or other medical co-morbidities
  - Limited resources at home during recovery

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