- Diagnosis:
  - An ABG with co-oximetry (spectrophotometry), which uses multiple wavelengths of light to determine the amount of normal versus abnormal Hb (e.g., MetHb, COHb), is necessary.
  - Keys to diagnosis are a discrepancy between pulse oximeter saturation and measured Pao_2 (Spo_2 <90% while Pao_2 >70 mm Hg) and hypoxia that does not improve with increasing FIO_2.
  - "Chocolate brown" blood may be seen.

Usual Treatment

- Supportive (ventilation, CV support); discontinuation of the offending agent
- Pts without G6PD deficiency: Methylene blue (a transient false decrease in SpO_2 may be seen after administration)
- Pts with G6PD deficiency: Ascorbic acid (methylene blue causes hemolysis)

Assessment Points

System	Effect	Assessment by Hx	PE	Test
RESP	Tachypnea, dyspnea, hypoxia	Exposure to oxidizing drugs	RR	Co-oximetry
CV	Tachycardia, arrhythmias, death if MetHb >70%	Exposure to oxidizing drugs	HR	Co-oximetry

Key References: Cortazzo JA, Lichtman AD: Methemoglobinemia: a review and recommendations for management, *J Cardiothorac Vasc Anesth* 28(4):1043–1047, 2014; Guay J: Methemoglobinemia related to local anesthetics: a summary of 242 episodes, *Anesth Analg* 108(3):837–845, 2009.

Perioperative Implications

Preoperative Preparation

- Because medications are the most frequent cause of acquired methemoglobinemia, a complete medication Hx should be sought, including OTC medications.

Monitoring

- Traditional pulse oximeters that use two wavelengths of light will not detect MetHb. Spo_2 values are inaccurate and trend toward 85% because MetHb absorbs equally at 660 and 940 nm.
- Newer "pulse co-oximeters" can detect MetHb levels and have accurate SpO_2 values.

Airway

- Routine

Induction

- Routine

Maintenance

- Routine

Extubation

- Severe methemoglobinemia may preclude extubation until levels fall to normal.

Adjuvants

- Methylene blue or ascorbic acid to treat; avoid further administration of oxidizing agents.

Postoperative Period

- Rebound methemoglobinemia can occur for up to 24 h, so pts should have MetHb levels closely monitored and additional treatment given if necessary.

Anticipated Problems/Concerns

- Oxygen-carrying capacity is decreased proportional to the concentration of MetHb present. Pts with preexisting conditions (e.g., CAD, PVD, anemia) may have tissue hypoxia even with lower levels of MetHb, necessitating earlier treatment.

Mitochondrial Disorders

Sau Yee Chow

Risk

- Incidence 4–7:100,000; might be under-reported

Perioperative Risks

- CNS: Facial and bulbar weakness, mental retardation, seizures, learning disabilities, deafness, visual impairment, and stroke-like episodes
- CVS: Cardiomyopathy and cardiac conduction defects
- Respiratory: Weakness of muscles of respiration and respiratory failure
- Other: GI disturbances, diabetes mellitus, exocrine pancreatic insufficiency, lactic acidosis, liver failure, and renal tubular defects

Overview

- Characterized by pathologic mitochondrial dysfunction in oxidative phosphorylation.
- Variable clinical presentation due to numerous possible mutations in genes coding for the electron transport chain proteins or the ancillary machinery involved in oxidative phosphorylation.
- Cardinal features of progressive muscles weakness and exercise intolerance.
- Prognosis is variable, ranging from functional impairment to death.

Etiology

- Defects of:
  - Mitochondrial DNA (maternal inheritance)
  - Nuclear DNA (autosomal dominant or recessive mendelian pattern)

Usual Treatment

- Alleviate symptoms (e.g., anticonvulsant therapy for seizures).
- Dietary modifications: Avoid fasting, addition of midchain triglycerides.
- Avoidance of toxins (e.g., alcohol, cigarette smoke).
- Vitamins and supplements to improve efficacy of ATP generation and antioxidant to slow progression of disease: Coenzyme Q10, levocarnitine, riboflavin.
- Avoidance of physiologic stress: Cold, heat, starvation, lack of sleep.
- Current treatment and medications for mitochondrial disorder.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Aspiration risk	Abnormal speech, recurrent aspirations, aspiration pneumonias	Bulbar palsy speech pattern	Videofluoroscopic swallowing study
CV	Cardiomyopathy, cardiac conduction abnormalities	Effort tolerance, palpitations, syncope, thromboembolic stroke	Signs of heart failure, abnormal heart rate	ECG Consider transthoracic ECHO, stress testing
RESP	Poor lung function, possible aspiration pneumonia	Effort tolerance, ability to cough, symptoms to suggest pneumonia	Looking for consolidation	Baseline ABG CXR Lung function test (spirometry)
CNS	Acute neuromuscular decompensation	Triggers and manifestation, current neurologic status, preexisting deficits, prior strokes	Neuro exam	Review any previous MRI brain scans available
METAB	Acute metabolic decompensation	Triggers and manifestation, severity and frequency		Consider baseline ABG and serum lactate levels

Key References: Shipton EA, Prosser DO: Mitochondrial myopathies and anaesthesia, *Eur J Anaesthesiol* 21(3):173–178, 2004; Chow SY, Woon KL: General anesthesia for adults with mitochondrial myopathy, *A A Case Rep* 4(5):52–57, 2015.

Perioperative Implications

- No clinical trials studying the effects of anesthetic agents and techniques and incidence of intraop and postop complications in pts with mitochondrial disorders. The current available data consist of level 4 evidence.

Preoperative Preparation

- Communication with the pt's neurologist is crucial; a targeted preop assessment should be done because the organ systems affected in mitochondrial disorders are highly variable among individuals.
- Optimize nutritional state and pulmonary function.
- Consider premedication with prokinetic agents and nonparticulate antacid.
- Continue all medications and supplements for mitochondrial disorder up to day of surgery.
- Minimize duration of fasting, ensure normoglycemia, and avoid dehydration; list as first case of the day.
- Risk counseling.

Induction

- RSI in pts at high risk of aspiration.
- Consider avoidance of depolarizing neuromuscular blockers in view of risk of hyperkalemia.
- Reasonable to consider use of rocuronium with sugammadex available on standby.
- Propofol has been associated with decoupling of oxidative phosphorylation; experience is scarce on whether it should be avoided, but has been used successfully.

Monitoring

- Standard mandatory monitoring.
- Consider intra-arterial line: Continuous BP monitoring for pts with cardiomyopathy, early detection of arrhythmias, and frequent blood sampling for electrolytes, lactate, and glucose.
- Consider temp monitoring, especially for prolonged procedures greater than 2-h duration.
- Urinary cath to monitor urine output for adequacy of organ perfusion and fluid balance.
- Neuromuscular monitoring (unpredictable response to nondepolarizing neuromuscular blockers, aids timing of reversal and extubation).

Maintenance

- The association between mitochondrial myopathy and malignant hyperthermia remains unproven in current literature. Malignant Hyperthermia Association of the United States recommends volatile agents not be routinely avoided and succinylcholine to be used with care
- Consider increasing depth of inhalational and concurrent use of remifentanil to avoid depolarizing neuromuscular blockers
- Concerns: Acute decompensation with lactic acidosis, electrolyte abnormalities, acute encephalopathy, neuromuscular weakness, and cardiac dysfunction or arrhythmias.
- Avoid IV fluids containing lactate.

Extubation/Postoperative Period

- Ensure adequate reversal of neuromuscular blockers and extubate awake.
- Comanagement with neurologist.
- Avoid postop respiratory compromise; early and aggressive chest physiotherapy and early mobilization.
- Avoid decompensation: ensure adequate hydration, maintain normoglycemia and normothermia, and monitor for and correct electrolyte abnormalities.
- Adequate analgesia; use of multimodal approach.
- Appropriate postop placement; high dependency ward or ICU as indicated.
- Thromboembolic prophylaxis as appropriate.

Mitochondrial Myopathy

Jerry H. Kim | Jeremy M. Geiduschek

Risk

- More common than previously thought. Prevalence ranges from 1:7000–15,000.
- Occurrence is usually sporadic or maternally inherited.

Perioperative Risks

- Metabolic acidosis
- Respiratory and cardiac insufficiency/failure
- Delayed emergence

Worry About

- Respiratory failure following sedation.
- Consider aspiration risk.
- Metabolic acidosis.
- Hypotension during induction.

Overview

- Clinically heterogeneous collection of diseases with myopathy of mitochondrial origin as common trait. Defects can be in electron transport, fatty acid, and amino acid metabolism.
- Commonly associated with encephalopathy.
- Nomenclature rapidly changing to reflect discovery of specific genetic mutations. The following all are mitochondria-based disorders that may include a myopathic component: Kearns-Sayre syndrome (KSS); Pearson syndrome (PS); maternally inherited Leigh syndrome (MILS); late-onset Leigh syndrome; mitochondrial encephalomyopathy, lactic acidosis, and stroke-like symptoms (MELAS); myoclonic epilepsy with ragged red fibers (MERRF); Leber hereditary optic neuropathy (LHON); chronic progressive external ophthalmoplegia (CPEO); and neuropathy, ataxia, and retinitis pigmentosa (NARP).
- Onset is variable. Most severe phenotypes present in infancy.
- Most common symptom is muscle weakness, and most common sign is lactic acidosis, resulting from the inefficient metabolism of pyruvate and shift to anaerobic respiration.
- Muscle biopsy often used for suspected cases. Hallmark is appearance of ragged red fibers.
- Biochemical analysis of mitochondria often needed to make exact diagnosis.
- Anesthetic sensitivity may manifest as decreased MAC of inhaled anesthetics (e.g., complex I disorders), increased respiratory insufficiency from sedatives and narcotics, and decreased hepatic clearance or renal excretion of IV agents.

Etiology

- Genetic variation in either mtDNA or nDNA.
- Large-scale mtDNA deletions (e.g., KSS, PS, PEO) are most often acquired sporadically.
- Single-base mtDNA changes (e.g., MELAS, MERRF, MILS, LHON) are often inherited maternally and usually affect mitochondrial protein synthesis (via mRNA, tRNA, or rRNA) or components of the electron-transport chain (i.e., complex I, III, IV, V).
- Single-base nDNA changes (e.g., late-onset Leigh syndrome) are often inherited in mendelian patterns (autosomal dominant or recessive).

Usual Treatment

- Supportive measures
- Dietary vitamins and supplements, coenzyme Q