Assessment Points

System	Effect	Assessment by Hx	PE	Diagnostic Test
CV	Orthostatic hypotension QTc prolongation Arrhythmias	Dizziness, syncope Palpitations	Orthostatic vital signs	Autonomic function ECG
RESP	Pneumonia Bronchiectasis Restrictive lung disease	Pleuritic chest pain Productive cough SOB	Abnormal breath sounds, digital clubbing	CXR Pulm function
GI	Poor swallowing Aspiration pneumonia	Drooling, vomiting Paroxysmal crisis		Swallow study
GU	Dehydration Glomerulosclerosis	Nocturia, diaphoresis	Dry mucosa, skin turgor	BMP
CNS	Seizure Developmental delay	Seizure		EEG
MS	Scoliosis		Spinal curvature	Plain films

Key References: Ngai J, Kreynin I, Kim JT, et al.: Anesthesia management of familial dysautonomia, *Paediatr Anaesth* 16(6):611–620, 2006; Weingarten TN, Sprung J, Burgher AH: Perioperative management of familial dysautonomia: a systematic review, *Eur Jour Anaesth* 24(4):309–316, 2007.

Perioperative Implications

Preoperative Preparation

- Consider regional or neuraxial anesthesia as primary anesthetic or combined with general anesthesia to improve analgesia; poor thermal discrimination may affect assessment of blocks.
- Diminished laryngeal reflexes and dysphagia leading to abundant secretions: treat with antisialagogues.
- H_2 blockers can decrease gastric volume and acidity.
- Prevent dysautonomic crisis with anxiolytics; treat crisis with benzodiazepines or clonidine.
- Avoid medications that interact with the autonomic nervous system.
- Correct chronic dehydration secondary to dysphagia and emesis to reduce intraop hemodynamic instability. Maintenance requirements may be higher due to increased insensible losses from excessive sweating and drooling.
- Minimize narcotics as premedication because of the impaired ventilatory response to hypoxia and hypercarbia.
- Lines can often be placed without sedation given insensitivity to superficial pain.

Monitoring

- Standard monitors.
- Arterial line.
- Consider processed EEG monitor.
- Consider noninvasive cardiac output monitoring.

Induction

- Rapid sequence induction.
- Titrate induction agents carefully to minimize risk of hypotension.
- Use of nondepolarizing neuromuscular blocking drugs balanced against risk of postop hypotonia and unpredictable effect of reversal agents on the autonomic nervous system.
- Lubricate eyes to avoid corneal abrasions secondary to alacrima and corneal insensitivity.

Maintenance

- Consider mechanical ventilation with lung protective strategies, especially with restrictive lung disease.
- Consider total IV anesthesia.
- Titrate volatile anesthetic using processed EEG monitor plus minimum alveolar concentration to minimize autonomic compromise.
- Fluid management and judicious use of direct acting vasopressors and inotropes guided by noninvasive cardiac output monitoring.
- Aggressively treat blood loss.
- Vigilant temperature monitoring and correction.

Emergence

- Titrate analgesics for pain control.
- Spontaneous ventilation may be delayed. Chemoreceptor dysfunction makes $PaCO_2$ levels a poor trigger.
- Unpredictable response to reversal agents due to increased sensitivity to acetylcholine.
- Aggressive pulm toilet to decrease atelectasis and bronchiectasis.

Postoperative Care

- Multimodal analgesic regimen. Visceral and peritoneal sensations remain intact despite abolishment of peripheral pain sensation.
- Judicious use of opioids given abnormal ventilator response to hypoxia and hypercarbia.
- First-line treatment for cyclic vomiting with benzodiazepines.
- Optimization of resp function with assisted ventilation, deep suctioning, inhalational therapies, and chest physiotherapy.

Familial Periodic Paralysis

Oliver Bandschapp

Risk

- Rare; hyperPP approximately 1:200,000 and hypoPP approximately 1:100,000
- HyperPP with childhood onset; hypoPP with teenage onset

Perioperative Risks

- In hyperPP, succinylcholine may provoke severe myotonia, provide no relaxation, and cause hyperkalemia (resulting postop muscle weakness over days and rhythm disturbances).
- HypoPP associated with supraventricular or conduction defect-type cardiac arrhythmias; weakness may be enhanced by β-adrenergic blocking drugs, and postop resp muscle weakness may occur.
- Hypermetabolic crises (necessitating dantrolene use) reported in hypoPP pts.

Worry About

- Cold can trigger attack in both types of PP.
- K^+ and glucose have opposite effects in the two disorders; in hyperPP, K^+ triggers attacks and glucose is cure, whereas in hypoPP, glucose-induced hypokalemia triggers attacks and K^+ is cure.
- Cardiac complications (dysrhythmias) due to severe dyskalemia during attack.
- Respiratory insufficiency during attack.

Overview

- Channel defects in the sarcolemma lead to aberrant depolarization in the presence of dyskalemia, which inactivates sodium channels and renders muscle fibers inexcitable.
- Autosomal dominant conditions; hypoPP with reduced penetrance in females.
- HyperPP with frequent (daily) episodic attacks for minutes (to hours); episodes of weakness generalized, rarely bulbar and resp muscles involved in severe paralysis; hyperkalemia (in approximately 50%) during attacks; triggered by K^+ intake, rest after exercise, or cold; often additional EMG myotonia.
- HypoPP with less frequent but more severe episodic attacks for hours (to days); weakness may be focal or generalized, usually sparing facial and resp muscles; invariably hypokalemia during episode; triggered by carbohydrates, cold, stress, specific medications (e.g., beta-agonists, corticosteroids, insulin); no myotonia.
- Fixed proximal weakness often develops with increasing age in both types.

Etiology

- HyperPP caused by mutations in the voltage-gated sodium channel $Na_v1.4$ gene (*SCN4A*). Mutant channels (inactivation defect) lead to persistent sodium influx and depolarization, muscle membrane becomes inexcitable.
- HypoPP either caused by mutations in the *CACNAS* gene (encodes α_{1s}-subunit of dihydropyridine receptor) (type 1 hypoPP) or in approximately 10% by mutations in the *SCN4A* gene (type 2 hypoPP). Introduction of new accessory ion conduction pathways independent of normal conduction pathways, leads to paradoxical membrane depolarization in low potassium conditions causing inexcitability.

Usual Treatment

- Both types: In case of prodrome keep moving
- HyperPP: Salbutamol spray, glucose, thiazide diuretics, or carbonic anhydrase inhibitors
- HypoPP: K^+ salts, carbonic anhydrase inhibitors, or K^+-sparing diuretics

Assessment Points

System	Effect	Assessment by Hx	PE	Test
RESP	Inadequate	Noticeable SOB	Respiratory rate high	ABG
MS	Weakness	Exercise, fatigue	Limb tone Hypoactive muscle stretch reflexes	HyperPP: Ictal serum K^+ level (elevated in approximately 50%) EMG myotonia (in approximately 75%) HypoPP: Low ictal serum K^+ level Exclusion of secondary causes (TSH, fT4 fT3 levels) Glucose/insulin or ACTH infusion induces paralysis attack Plasma biochemistry after attack: elevated myoglobin, creatine kinase Muscle fiber conduction velocity may be slower than normal No EMG myotonia

Key References: Suetterlin K, Männikkö R, Hanna MG: Muscle channelopathies: recent advances in genetics, pathophysiology and therapy, *Curr Opin Neurol* 27(5):583–590, 2014; Bandschapp O, Iaizzo PA: Pathophysiologic and anesthetic considerations for patients with myotonia congenita or periodic paralyses, *Paediatr Anaesth* 23(9):824–833, 2013.

Perioperative Implications

Preoperative Preparation

- HyperPP: carbohydrate loading during fasting period; consider 24-h furosemide for K^+ depletion
- HypoPP: avoid large glucose and salt loads; 24-h acetazolamide if not already given; only glucose-free solutions IV; if Hx of frequent instability, prepare infusion with K^+; reduce pt's anxiety

Monitoring

- Both types: Temperature (esophageal) (keep warm); ECG (detection of dyskalemia); NM monitoring mandatory (minimize relaxant dose)

Airway

- Both types: no special difficulty, but may need support

Preinduction/Induction

- Both types: Regional techniques are appropriate; relaxation with short-acting nondepolarizing agents as indicated.
- HyperPP: Avoid ketamine; no succinylcholine (severe myotonia, hyperkalemia with resulting postop muscle weakness over days).

Maintenance

- Both types: Use warming blankets and keep normothermic; warm all IV fluid.
- HyperPP: Use glucose 5% as maintenance, avoid hypoglycemia; do not give K^+-containing solutions, maintain normokalemia (use glucose/insulin if needed).
- HypoPP: Use MH trigger-free anesthetic methods; glucose-free solutions as maintenance, avoid hyperglycemia; give solutions containing K^+, aim for K^+ 4–5 mEq/L; ventilation during anesthesia should be normocarbic to avoid K^+ shifts.

Extubation

- HyperPP: Evidence of muscle weakness should be treated with IV calcium gluconate or chloride 10% 10 mL slowly over 5 min; anticholinesterase drugs may worsen/trigger myotonic symptoms.
- HypoPP: Evidence of muscle weakness should be treated with IV potassium chloride; normal reversal as indicated clinically; maintenance by IPPV if evidence of weakness in postop phase; severe postop weakness may be aggravated by Ca^{2+}.

Adjuvants

- Both types: Anticipate usual analgesic requirements for age and surgery; regional techniques are appropriate.
- HyperPP: Some experimental evidence suggests that condition (e.g., postop weakness) may be helped by phenytoin or by salbutamol.
- HypoPP: Ca^{2+}-channel blockers do not appear to be contraindicated in pts with concomitant CV disease.

Anticipated Problems/Concerns

- Both types: Cold triggers attack.
- HyperPP: Succinylcholine may not give relaxation, and therefore intubation may be difficult; severe myotonia may create resp difficulty; hypoglycemia and K^+ can trigger hyperkalemic attack; hyperkalemia can cause cardiac arrhythmia.
- HypoPP: May have associated supraventricular or conduction defect arrhythmias; resp muscle weakness may occur postop; must maintain serum K^+ above 4.0 mEq/L.

Fanconi Syndrome

Rayhan A. Tariq | Henry Liu

Risk

- FS can be inherited, acquired, or caused by exogenous factors.
- Incidence is sporadic. Exact incidence in USA is not clear.
- Most diseases associated with FS are inherited in an autosomal recessive pattern.
- Cystinosis is the most common cause in pediatric pts.

Perioperative Risks

- Potential for hypotension secondary to hypovolemia
- Renal failure, proximal renal tubular dysfunction
- Lyte imbalance (especially hypokalemia causing tachyarrhythmias)

Worry About

- Polyuria, polydipsia, and the resulting dehydration
- Type 2 renal tubular acidosis (defect in the reabsorption of bicarbonate in the proximal tubule)
- Hypokalemia-induced ventricular arrhythmogenicity
- Hypophosphatemia and associated osteomalacia and loss of bone density
- Hypokalemia may cause muscular weakness
- May be part of a genetic syndrome, such as Lowe syndrome (oculocerebrorenal syndrome)

Overview

- Disease of the proximal convoluted tubules in which glucose, amino acids, uric acid, phosphate, and bicarbonate are passed into urine, not being reabsorbed.
- Signs and symptoms reflect the tubular abnormality, including polyuria, polydipsia, and acidosis due to bicarbonate loss.
- Pts are very likely to have renal failure at the time of surgery.
- Muscle weakness due to hypokalemia.
- Renal phosphate wasting presents as osteomalacia or rickets.
- Most pts have proteinuria, although it is often minimal.
- Severe photophobia might be present with cystinosis (cystinosis is the most common cause of inherited form of FS).
- FS is different from Fanconi anemia characterized by progressive pancytopenia.

Etiology

- May be hereditary or acquired.
- Common hereditary causes are cystinosis (most common cause in children), Wilson disease, Lowe syndrome, galactosemia, glycogen storage diseases, and hereditary fructose intolerance mitochondrial cytopathies.
- Can be acquired via exposure to heavy metals (lead) and medications such as tetracycline (particularly when outdated), cisplatin, tenofovir, adefovir, rifampin, deferasirox, and aminoglycoside antibiotics.
- Dysproteinemias, such as multiple myeloma, amyloidosis, light-chain nephropathy, and benign monoclonal gammopathy may cause FS in adults.

Usual Treatment

- Mainstay of treatment is replenishment of lytes and fluids lost in urine.
- Metabolic acidosis due to bicarbonate loss is corrected by the administration of HCO_3^-, (usually 3–10 mg/kg/d of sodium bicarbonate in divided doses).
- Addition of a thiazide diuretic (1–3 mg/kg per d) of hydrochlorothiazide may be necessary to avoid volume expansion, which amplifies the excretion of bicarbonate by lowering the renal threshold (also need K^+ supplementation to account for extra K^+ lost in the urine with the use of TZD diuretic).
- For preventing bone disease, phosphate and vitamin D supplementation are necessary in addition to correction of metabolic acidosis.
- Losses of glucose and amino acids are not usually symptomatic and do not require treatment.
- Kidney transplantation in pts with renal failure due to cystinosis.
- Liver transplantation in case of Wilson disease.