antihypertensive therapy with ACE inhibitor or beta-blocker.
- Treatment of Htn may be needed for several wk before any benefit to periop morbidity.
- Hypervolemia should be treated with a potassium-sparing diuretic, such as amiloride, to avoid exacerbating potassium loss.
- Potassium deficit is likely to be severe and larger than apparent from serum levels.
- Unilateral primary hyperaldosteronism (from either aldosterone producing adenoma or unilateral adrenal hyperplasia) should be treated with surgical adrenalectomy.
- Bilateral primary hyperaldosteronism should be treated medically with long-term mineralocorticoid receptor antagonist therapy.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Htn, often resistant to therapy; increased sympathetic activity, cardiac output often increased except where there is hypertensive cardiomyopathy	Exercise tolerance, dyspnea, orthopnea, Htn—headache, visual disturbance	BP (compare R to L or arms with legs with coarctation) Third heart sound Fine inspiratory crackle	BP, ECG, ABG, CXR, ECHO
HEME	Hypervolemia results in Htn, hypokalemia, metabolic alkalosis, and congestive cardiac failure	Weakness, fatigue, headache	JVP, motor power	Hematocrit, serum lytes, biocarbonate, ABG
RENAL	Hypokalemia, alkalosis	Weakness, palpitations	Motor power, arrhythmia	ECG, serum and urine lytes, ABG

Key References: Jano A, Domi R, Derdica H, et al.: Anesthetic considerations of Conn syndrome, *Clin Med Res* 3(5):123–135, 2014; Reilly CS: Adrenal disease: cortex and medulla. In Hall GM, Hunter JM, Cooper MS, editors: *Core topics in endocrinology in anaesthesia and critical care*, Cambridge, 2010, Cambridge University Press, pp 45–56.

Perioperative Implications

Preinduction/Induction/Maintenance
- Correct hypokalemia and associated electrolyte disturbance (e.g., magnesium); this may require IV supplementation preop and intraop.
- Htn may be refractory; require treatment with several classes of drugs with the potential for extreme cardiovascular instability, and there may be a disproportionate hypertensive response to laryngoscopy or surgical stimulation.
- Avoid hyperventilation and hypocapnia to prevent worsening metabolic alkalemia and subsequent intracellular potassium shift.
- Anticipate increased sensitivity to nondepolarizing neuromuscular antagonists due to hypokalemia. Consider using drugs with spontaneous organ independent metabolism (e.g., atracurium or cisatracurium, or rocuronium and sugammadex combination).

Monitoring
- Consider arterial pressure monitoring.
- Consider central venous cath insertion for access and administration of concentrated potassium and magnesium in the face of hypervolemia, or for monitoring filling pressure where there is cardiomyopathy and heart failure.
- Urinary cath.
- Peripheral nerve stimulation for neuromuscular function.

General Anesthesia
- Hypokalemia may potentiate muscle relaxants and arrhythmia.
- Surgical manipulation of the aldosterone producing structure may cause severe Htn.
- High pH decreases availability of intracellular calcium.

Regional Anesthesia
- Local anesthetic mixtures with sympathomimetic may exacerbate preexisting Htn.
- Altered pharmacokinetics resulting from hypervolemia and end organ damage such as renal dysfunction may need dose adjustments.

Postoperative Period
- Appropriate care predicated on surgical procedure, co-morbidities, and hemodynamic stability.
- Monitor and correct ongoing electrolyte abnormalities.
- Consider glucocorticoid supplementation, though it should not be required if there is at least one intact adrenal gland.

Anticipated Problems/Concerns
- Labile blood pressure.
- Increased sympathetic activity leads to activation of the renin-angiotensin system.
- Arrhythmia from severe hypokalemia.
- Generalized muscle weakness from hypokalemia.

Hyperaldosteronism, Secondary

Marc Chikhani | Jonathan G. Hardman

Risk
- High renin states, and greater risks may be associated with the primary problem, leading to hyperreninemia.
- End organ damage from long-standing Htn (e.g., chronic kidney disease, cardiomyopathy).
- Abnormal glucose tolerance in up to 50% of pts with hyperaldosteronism.

Perioperative Risks
- Risks include hypernatremia and hypervolemia with high total body sodium.
- Htn may be refractory to treatment, with increased risk of cardiovascular complications, including malignant hypertensive crisis.
- Hypokalemia and hypomagnesaemia with low intracellular potassium and magnesium may cause cardiac arrhythmia and general muscle weakness.

Worry About
- The underlying primary medical disorder that leads to increased renin and, hence, increased aldosterone secretion.
- Hypertensive response to intubation or surgical incision.
- Hypokalemia and associated muscle weakness or potential for arrhythmia.
- Metabolic alkalosis.

Overview
- Secondary hyperaldosteronism is a renin-dependent oversecretion of the mineralocorticoid aldosterone secreted from the zona glomerulosa of the adrenal cortex.
- Renin is released from the JGA as a response to decreased renal perfusion pressure. Osmoreceptors in the macula densa will also stimulate renin release in the presence of decreased sodium concentration in the distal tubule.
- Renin enzymatically alters angiotensinogen to angiotensin I. ACE (found in the pulmonary and renal vascular endothelium) then converts angiotensin I to angiotensin II. Angiotensin II, a potent vasoconstrictor, then stimulates release of aldosterone from the zona glomerulosa of the adrenal medulla.
- Aldosterone promotes restoration of circulating volume by correcting water and sodium depletion.
- Diagnosis is suggested by increases in both plasma renin (>2 ng/mL) and aldosterone, but the ratio of plasma aldosterone concentration to renin activity is <10 ng/dL per ng/mL/h (ratio >35 strongly suggests primary hyperaldosteronism).
- In some situations, such as pregnancy and chronic renal disease, increased aldosterone is an adaptive response and is not necessarily deleterious.

Etiology
- Any pathophysiologic process that causes a chronic and relative decrease of perfusion pressure in the juxtaglomerular apparatus has the potential to cause secondary hyperaldosteronism. Examples include:
  - Increased central venous pressure and therefore increased capillary hydrostatic pressure.
  - Decreased cardiac output.
  - Vasodilation.
  - Impaired plasma protein synthesis and excess loss.
- Common causes:
  - Heart failure (increased venous pressure and reduced cardiac output).
  - Liver disease with cirrhosis (peripheral and splanchnic vasodilation and reduced albumin synthesis).
  - Nephrotic disease (protein loss).
- Renovascular (hyper-reninemic) Htn: Related to atherosclerosis (renal artery stenosis) or fibromuscular dysplasia.
- Renovascular disease causing decreased renal perfusion pressure independent of systemic pressure: Renal artery stenosis, aortic coarctation.
- Renin-secreting tumors (e.g., tumor of the juxtaglomerular apparatus or renal cell carcinoma).
- Pregnancy.

Usual Treatment

- Aldosterone antagonists, such as spironolactone (up to 300 mg/d) or the newer drug eplerenone (up to 100 mg/d).
- Both spironolactone and eplerenone are mineralocorticoid receptor antagonists and therefore have a potassium-sparing diuretic effect. Eplerenone is more selective for the mineralocorticoid receptor than spironolactone and has fewer glucocorticoid or androgen receptor antagonist side effects.
- Htn may be refractory to treatment with aldosterone antagonist alone and may require formal antihypertensive therapy with ACE inhibitor or beta-blocker.
- Treatment of Htn may be needed for several wk before any benefit to periop morbidity.
- Assess volume status thoroughly; there may be occult hypovolemia if diuretic treatment has been started.
- Hypervolemia should be treated with a potassium-sparing diuretic such as amiloride to avoid exacerbating potassium loss.
- Potassium deficit is likely to be severe and larger than apparent from serum levels.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Htn, often resistant to therapy; increased sympathetic activity, cardiac output often decreased even in absence of Htn. May have unexplained congestive failure	Exercise tolerance, dyspnea, orthopnea, Htn-headache, visual disturbance	BP (compare R to L or arms with legs with coarctation) Third heart sound Fine inspiratory crackle Oedema	BP, ECG, ABG, CXR, ECHO
HEME	Hypervolemia or hypovolemia (or decreased plasma volume in edematous states) may result in Htn or hypotension, hypokalemia, metabolic acidosis	Syncope, weakness, fatigue	JVP, postural BP, motor power	Serum electrolytes, bicarbonate, ABG
RENAL	Increased renal tubular sodium absorption Azotemia may be caused by decreased renal perfusion or ineffective plasma volume. In setting of renal artery stenosis, ACE inhibitors may exacerbate renal failure; hypokalemia, alkalosis	Htn, decreased urine output, chronic renal disease, weakness	Abdominal bruit suggests renal artery stenosis Edema	ECG, serum and urine lytes, ABG, abdominal ultrasound with renal artery Doppler or contrast CT imaging, renal biopsy.
HEPAT	Cirrhosis is an edematous state and may be associated with occult hypovolemia, altered pharmacokinetics, hypoalbuminemia, coagulopathy, encephalopathy, variceal bleeding risk	Alcohol excess, hepatitis, other liver disease, bruising after minor injury.	Pallor, jaundice, ascites, asterixis ephalopathy, porto-systemic anastomoses, bruising, hepatomegaly	Full blood count including coagulation studies and platelets, serum lytes, hepatic enzymes, bilirubin, ammonia, abdominal ultrasound, liver biopsy

Key References: Davies M, Hardman JG: Anaesthesia and adrenocortical disease, *Contin Educ Anaesth Crit Care Pain* 5(4):122–126, 2005; Reilly CS: Adrenal disease: cortex and medulla. In Hall GM, Hunter JM, Cooper MS, editors: *Core topics in endocrinology in anaesthesia and critical care*, Cambridge, 2010, Cambridge University Press, pp 45–56.

Perioperative Implications

Preinduction/Induction/Maintenance

- Dependent on primary underlying medical problem causing increased renin secretion.
- Assess cardiac function and circulating volume status to guide choice of induction agent; beware of altered pharmacokinetics; anticipate severe cardiovascular instability.
- Correct hypokalemia and associated electrolyte disturbance (e.g., magnesium); this may require IV supplementation preop and intraop.
- Htn may be refractory; require treatment with several classes of drugs with the potential for extreme cardiovascular instability. There may be a disproportionate hypertensive response to laryngoscopy or surgical stimulation.
- Avoid hyperventilation and hypocapnia to prevent worsening metabolic alkalemia and subsequent intracellular potassium shift.
- Anticipate increased sensitivity to nondepolarizing neuromuscular antagonists due to hypokalemia. Consider using drugs with spontaneous organ independent metabolism (e.g., atracurium or cisatracurium, or rocuronium and sugammadex combination).

Monitoring

- Consider arterial pressure monitoring.
- Consider central venous cath insertion for access and administration of concentrated potassium and magnesium in the face of hypervolemia, or for monitoring filling pressure where there is cardiomyopathy and heart failure.
- Urinary cath.
- Peripheral nerve stimulation for neuromuscular function.

General Anesthesia

- Consider underlying and associated underlying medical comorbidities.
- Hypokalemia may potentiate muscle relaxants and arrhythmia.
- High pH decreases availability of intracellular calcium.

Regional Anesthesia

- Pt with severe edema may be unable to tolerate supine operating positions while awake.
- Local anesthetic mixtures with sympathomimetic may exacerbate preexisting Htn.
- Altered pharmacokinetics resulting from hypervolemia, edema, and end organ damage such as hepatic and renal dysfunction may need dose adjustments.

Postoperative Period

- Appropriate care predicated on surgical procedure, comorbidities, and hemodynamic stability.
- Monitor and correct ongoing electrolyte abnormalities.
- Altered pharmacokinetics may be associated with prolonged recovery times from anesthetic agents and exaggerated response to opioid analgesia.

Anticipated Problems/Concerns

- Labile BP
- Pts with preexisting Htn, left ventricular hypertrophy, and cardiac failure are at increased risk of morbidity and mortality from stroke and MI.
- Increased sympathetic activity leads to further activation of the renin-angiotensin system.
- Arrhythmia from severe hypokalemia.
- Generalized muscle weakness from hypokalemia.

Hypercalcemia

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Perioperative Risks

- Pts with normal renal and CV function who have moderate hypercalcemia (11.5–13 mg/dL) have no special preop problems but may exhibit lethargy, anorexia, nausea, and polyuria.
- Lithium and thiazide diuretics should be held.
- Severe hypercalcemia (>13 mg/dL) carries risk for hypovolemia and acid-base abnormalities; therefore, normal intravascular volume and electrolyte status should be restored prior to surgery.
  - Neuromuscular symptoms may occur with associated muscle weakness.
  - Neurologic disturbances ranging from poor concentration to coma can develop.
  - CV effects include Htn, dysrhythmias, heart block, ST segment elevation mimicking MI, cardiac arrest, and digitalis sensitivity.
- Total serum Ca^{2+} >14 mg/dL is a medical emergency and requires immediate treatment and delay of elective surgical procedures.

Worry About

- Volume status (hypovolemia secondary to polyuria, fluid overload secondary to treatment).
- Electrolyte disturbances.
- Dysrhythmias and/or ECG changes.
- Organ system manifestations of hypercalcemia and underlying disease.
- Longstanding hypercalcemia can lead to calcification in the myocardium, blood vessels, brain, and kidneys. Beware of seizures from cerebral calcifications. Polyuria that is unresponsive to vasopressin may result from renal calcifications.