Appendix C: Examples of Secondary Causes of Hypertension

Indications for a secondary cause of hypertension are: 1) severe or refractory hypertension; 2) an acute rise over previously stable values; 3) age < 30 years without family history; and/or 4) no nocturnal fall in blood pressure (BP) on during a 24-hour ambulatory BP monitoring period.

Table 1. Examples of identifiable secondary causes of hypertension and initial investigations

Aldosteronism (Primary)	
Signs/symptoms: • Spontaneous hypokalemia (though more than one-half of patients are normokalemic) • Profound diuretic-induced hypokalemia (< 3.0 mmol/L) • Hypertension refractory to treatment with 3 or more drugs • Hypertension and adrenal incidentaloma	*Initial Investigations:* • Plasma renin activity and plasma aldosterone concentration Note: ideally measured before 10 am after 1 hour of ambulation, if possible. Patient should be on an unrestricted salt diet. Certain medications affect aldosterone and renin. If safe, suggested drug-free periods prior to testing are: o Beta-blockers = 1 week o ACE-I, ARB, diuretics, NSAIDs = 2 weeks o Spironolactone, eplerenone, amiloride, triamterene, potassium-wasting diuretics = 4 weeks.
Sleep Apnea	
Signs/symptoms: • Loud snoring • Daytime somnolence and fatigue	*Initial Investigations:* • Sleep diary • Overnight oximetry
Renovascular Disease	
Signs/symptoms: • ↑ > 30% creatinine after introducing angiotensin converting enzyme inhibitor (ACE-I) or angiotensin II receptor blocker (ARB) • Hypertension with diffuse atherosclerosis or an unilateral small kidney • Episodes of flash pulmonary edema • Abdominal bruit (not very sensitive)	*Initial Investigations may include:* • Magnetic resonance angiography (MRA) • Computed tomography angiography (CTA)
Kidney Disease (Primary)	
Signs/symptoms: • ↓ estimated glomerular filtration rate (eGFR) and/or abnormal urinalysis Refer to BCGuidelines.ca – *Chronic Kidney Disease – Identification, Evaluation and Management of Adult Patients.*	*Initial Investigations:* • eGFR • Urinalysis - albumin to creatinine ratio (ACR), hematuria • Physical exam & medical history • Renal ultrasound
Cushing's Syndrome	
Signs/symptoms: • Cushingoid facies • Central obesity • Proximal muscle weakness • Ecchymoses	*Initial Investigations may include any of:* • late-night salivary cortisol levels • 24-hour urine free cortisol (UFC) • low-dose (1-mg overnight or 48-hour [2-mg/24-hour]) dexamethasone suppression test (LDDST)

Pheochromocytoma	
Signs/symptoms: • Paroxysmal elevations in BP • Headache • Palpitations • Sweating	*Initial Investigations:* • 24-hour urine for catecholamines and metanephrinesn Note: False positives can be caused by tricyclic antidepressants, antipsychotics, levodopa, decongestants, labetalol, sotalol, buspirone, ethanol, acetaminophen, phenoxybenzamine, withdrawal from clonidine (and other drug withdrawal) and major physical stress (e.g., surgery, stroke, sleep apnea).
Oral Contraceptives	
Signs/symptoms: • ↑ BP temporally related to oral contraceptive use	*Initial Investigations:* –
Coarctation of the Aorta	
Signs/symptoms: • ↑ BP in right arm with diminished or delayed femoral pulses, and low BP in the legs	*Initial Investigations:* • Echocardiogram Note: most occur just distal to the left subclavian origin.
Hypo/Hyperthyroidism	
Signs/symptoms: Refer to BCGuidelines.ca – *Thyroid Function Tests in the Diagnosis and Monitoring of Adults.*	*Initial Investigations:* • Thyroid-stimulating hormone (TSH)
Hyperparathyroidism	
Signs/symptoms: • Bone pain • Non-specific symptoms • Patients often asymptomatic	*Initial Investigations:* • Parathyroid hormone (PTH) • Ionized calcium • Phosphate