Appendix G - Examples of Secondary Causes of Hypertension

DISORDER	SUGGESTIVE HISTORY / FINDINGS / INVESTIGATION
General	• Severe or refractory hypertension • An acute rise over previously stable values • Age < 30 years without family history • No nocturnal fall in BP on 24-hour monitor
Renovascular Disease (1-2%)*	• ↑ creatinine after introducing ACEI or ARB • Hypertension with diffuse atherosclerosis or a unilateral small kidney • Episodes of flash pulmonary edema • Abdominal bruit (not very sensitive) • **Initial investigation**: captopril renogram (if safe, stop diuretics for 2 days, and ACEI/ARBs for 5 days, before exam); alternatively duplex Doppler ultrasonography or spiral CT angiography or MR angiography
Primary Kidney Disease (2-3%)	• ↓eGFR and /or abnormal urinalysis • **Initial investigation**: renal ultrasound, complete blood count, calcium, phosphates, electrolytes, urine analysis
Primary Aldosteronism (0.3%)	• 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 • Incidental adrenal adenoma • **Initial investigation**: plasma renin activity and plasma aldosterone concentration • **Note**: Ideally measured before 10 am after 1 hr of ambulation if possible. Patient should be on an unrestricted-salt diet. Certain medications affect aldosterone and renin. Where safe, suggested drug-free periods prior to testing are, beta-blockers: 1 wk; ACE, ARB, diuretics, NSAIDs: 2 wks; spironolactone*, estrogen*, high-dose amiloride*: 6 wks. * drug free period is mandatory
Cushing's Syndrome (<0.1%)	• Cushingoid facies, central obesity, proximal muscle weakness, and ecchymoses • **Initial investigation**: overnight 1 mg dexamethasone suppression test, or 24-hour urine cortisol
Pheochromocytoma (<0.1%)	• Paroxysmal elevations in BP • Headache, palpitations, and sweating • **Initial investigation**: 24-hour urine for catecholamines and metanephrines • **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)

DISORDER	SUGGESTIVE HISTORY / FINDINGS / INVESTIGATION
Oral Contraceptives (0.5-1%)	• New elevation temporally related to oral contraceptive use
Sleep Apnea	• Primarily obese men who snore loudly • Daytime somnolence and fatigue • **Initial investigation**: overnight oximetry
Coarctation of the Aorta	• ↑ BP in right arm with diminished or delayed femoral pulses, and low BP in the legs • **Initial investigation**: echocardiogram (most occur just distal to the left subclavian origin)
Hypo/Hyperthyroidism	• ↑/↓ TSH
Primary Hyperparathyroidism	• Elevated serum calcium • **Initial investigation**: PTH / ionized calcium/ phosphate

Abbreviations: *BP, Blood Pressure; ACEI, Angiotensin Converting Enzyme Inhibitor; ARB, Angiotensin Receptor Blocker; CT, Computer Tomography; MR, Magnetic Resonance; eGFR, Estimated Glomerular Filtration Rate; TSH, Thyroid Stimulating Hormone; PTH, Parathyroid Hormone*

* Frequency estimates were obtained from Harrison's Internal Medicine Online on May 28th, 2007. Web site: www.accessmedicine.com

The investigation and management of secondary causes of hypertension is beyond the scope of this guideline. Please consult current medical texts for investigation and management advice, or consider referral to an appropriate specialist.