2007 CHEP Recommendations for the Management of Hypertension

Part 1: Diagnosis & Assessment

I ACCURATE MEASUREMENT OF BLOOD PRESSURE

1) The blood pressure (BP) of all adult patients should be assessed at all appropriate visits for determination of cardiovascular risk and monitoring of antihypertensive treatment by health care professionals who have been specifically trained to measure blood pressure accurately (Grade D).

2) Use of standardized measurement techniques (Table 1) is recommended when assessing blood pressure (Grade D).

II CRITERIA FOR DIAGNOSIS OF HYPERTENSION AND RECOMMENDATIONS FOR FOLLOW-UP (Figure 1)

1) At visit 1, patients demonstrating features of a hypertensive urgency or emergency (Table 2) should be diagnosed as hypertensive and require immediate management (Grade D).

2) **If SBP is 140 mm Hg or greater and/or diastolic BP is 90 mm Hg or greater** a specific visit should be scheduled for the assessment of hypertension (Grade D). **If BP is high-normal (SBP 130 - 139 mm Hg and/or DBP 85 - 89 mm Hg) <u>in the absence of diabetes or cardiovascular disease, annual follow up is recommended</u> (Grade C).**

3) At the initial visit for the assessment of hypertension, if systolic BP (SBP) is 140 mm Hg or greater and/or diastolic (DBP) blood pressure is 90 mm Hg or greater, at least two more readings should be taken during the same visit according to the recommended procedure for accurate BP determination (Table 1). The first reading should be discarded and the latter two averaged. A history and physical examination should be performed and, if clinically indicated, diagnostic tests to search for target organ damage (Table 3) and associated CV risk factors (Table 4) should be arranged within two visits. Exogenous factors that can induce or aggravate hypertension should be assessed and removed if possible (Table 5). Schedule visit two within one month (Grade D).

*** bold typeface in the body text indicates a new or revised recommendation**

4) At visit 2 for the assessment of hypertension, patients with macrovascular target organ damage, diabetes mellitus, or chronic kidney disease (GFR < 60 ml/min) can be diagnosed as hypertensive if SBP is 140 mm Hg or greater and/or DBP is 90 mm Hg or greater (Grade D).

5) At visit 2 for the assessment of hypertension, patients without macrovascular target organ damage, diabetes mellitus, and/or chronic kidney disease can be diagnosed as hypertensive if SBP is 180 mm Hg or greater and/or DBP is 110 mm Hg or greater (Grade D). Patients without macrovascular target organ damage, diabetes mellitus, or chronic kidney disease but with lower blood pressure levels should undergo further evaluation using any of the three approaches outlined below:

   i) Office BPs:
   Using office BP measurements, patients can be diagnosed as hypertensive if the SBP is 160 mm Hg or greater or the DBP is 100 mm Hg or greater averaged across the first 3 visits, OR if the SBP averages 140 mm Hg or greater or the DBP averages 90 mm Hg or greater after 5 visits (Grade D).

   ii) Ambulatory BP monitoring (ABPM):
   Using ABPM (see Section VIII), patients can be diagnosed as hypertensive if the mean awake SBP is 135 mm Hg or greater or the DBP is 85 mm Hg or greater, OR if the mean 24 hour SBP is 130 mm Hg or greater or the DBP is 80 mm Hg or greater (Grade C).

   iii) Home BP Measurement:
   Using home BP measurements (see Section VII), patients can be diagnosed as hypertensive if the average SBP is 135 mm Hg or greater or the DBP is 85 mm Hg or greater (Grade C). If home BP measurement is less than 135/85 mm Hg, it is advisable to perform 24 h ABPM to confirm the mean 24 h ABPM is less than 130/80 mm Hg or the mean awake ABPM is less than 135/85 mm Hg before diagnosing white coat hypertension (Grade D).

6) Investigations for secondary causes of hypertension should be initiated in patients with suggestive clinical and/or laboratory features (outlined below) (Grade D).

7) If at the last diagnostic visit, the patient is not diagnosed as hypertensive, and has no evidence of macrovascular target organ damage, the patient's BP should be assessed at yearly intervals (Grade D).

8) Patients receiving lifestyle modification advice (non-pharmacological treatment) should be followed up at three-to-six month intervals. Shorter intervals (one or two monthly) are needed for patients with higher BPs (Grade D).

9) Patients on antihypertensive drug treatment should be seen monthly or every two months, depending on the level of BP, until readings on two consecutive visits are below their target (Grade D). Shorter intervals between visits will be needed for symptomatic patients and those with severe hypertension, intolerance to antihypertensive drugs or those with target organ damage (Grade D). Once the target BP has been reached, patients should be seen at three-to-six month intervals (Grade D).

III ASSESSMENT OF OVERALL CARDIOVASCULAR RISK IN HYPERTENSIVE PATIENTS

1) Global cardiovascular risk should be assessed. Multifactorial risk assessment models can be used to predict more accurately an individual's global cardiovascular risk (Grade A) and to use antihypertensive therapy more efficiently (Grade D). In the absence of Canadian data to determine the accuracy of risk calculations, avoid using absolute levels of risk to support treatment decisions (Grade C).

2) Consider informing patients of their global risk to improve the effectiveness of risk factor modification (Grade C).

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IV ROUTINE AND OPTIONAL LABORATORY TESTS FOR THE INVESTIGATION OF PATIENTS WITH HYPERTENSION

1) Routine laboratory tests should be performed for the investigation of all patients with hypertension, including:

   i) urinalysis (Grade D),

   ii) blood chemistry (potassium, sodium, and creatinine) (Grade D),

   iii) fasting glucose (Grade D),

   iv) fasting total cholesterol and high density lipoprotein cholesterol, low density lipoprotein cholesterol and triglycerides (Grade D), and

   v) standard 12-lead electrocardiography (Grade C).

2) Assess urinary albumin excretion in patients with diabetes (Grade D).

3) During the maintenance phase of hypertension management, tests (including those for electrolytes, creatinine, glucose, and fasting lipids) should be repeated with a frequency reflecting the clinical situation (Grade D).

V ASSESSMENT FOR RENOVASCULAR HYPERTENSION

1) Patients presenting with two or more of the following clinical clues listed below suggesting renovascular hypertension should be investigated (Grade D).

   i) sudden onset or worsening of hypertension and age older than 55 years or younger than 30 years

   ii) the presence of an abdominal bruit

   iii) hypertension resistant to three or more drugs

   iv) a rise in creatinine of > 30% associated with use of an angiotensin-converting enzyme inhibitor or angiotensin II receptor antagonist

v) other atherosclerotic vascular disease, particularly in patients who smoke or have dyslipidemia; and

vi) recurrent pulmonary edema associated with hypertensive surges

2) The following tests are recommended when available to aid in the usual screening for renal vascular disease: captopril-enhanced radioisotope renal scan, Doppler sonography, magnetic resonance angiography, CT-angiography **(for those with normal renal function)** (Grade B). **Captorpril-enhanced radioisotope renal scan is not recommended for those with chronic kidney disease (GFR < 60 mL/min) (Grade D).**

VI ENDOCRINE HYPERTENSION

A Hyperaldosteronism: Screening and Diagnosis

1) Screening for hyperaldosteronism should be considered for at least the following patients (Grade D):

i) hypertensive patients with spontaneous hypokalemia (K^+ less than 3.5 mmol/L)

ii) hypertensive patients with marked diuretic-induced hypokalemia (K^+ less than 3.0 mmol/L)

iii) patients with hypertension refractory to treatment with three or more drugs; and

iv) hypertensive patients found to have an incidental adrenal adenoma

2) Screening for hyperaldosteronism should include assessment of plasma aldosterone and plasma renin activity (Table 6A).

3) For patients with suspected hyperaldosteronism (on the basis of the screening test, Table 6 [section iii]), a diagnosis of primary aldosteronism should be established by demonstrating inappropriate autonomous hypersecretion of aldosterone using at least one of the maneuvers listed in Table 6A (iv). When the diagnosis is established, the abnormality should be localized using any of the tests described in Table 6A (v).

B Pheochromocytoma Screening and Diagnosis

1) If pheochromocytoma is strongly suspected, the patient should be referred to a specialized hypertension center, particularly if biochemistry screening tests (Table 6B) have already been found to be positive (Grade D).

2) The following patients should be considered for screening for pheochromocytoma (Grade D):

   i) patients with paroxysmal and/or severe (BP ≥180/110 mm Hg) sustained hypertension refractory to usual antihypertensive therapy

   ii) patients with hypertension and multiple symptoms suggestive of catecholamine excess (e.g., headaches, palpitations, sweating, panic attacks and pallor)

   iii) patients with hypertension triggered by beta-blockers, monoamine oxidase inhibitors, micturition, or changes in abdominal pressure; and

   iv) patients with incidentally discovered adrenal mass, hypertension and multiple endocrine neoplasia 2A or 2B, von Recklinghausen's neurofibromatosis, or von Hippel-Lindau disease

3) For patients with positive biochemical screening tests, localization of pheochromocytomas should employ magnetic resonance imaging (preferable), computed tomography (if magnetic resonance imaging is unavailable), and/or iodine I-131 meta-iodobenzylguanidine scintigraphy (Grade C for each modality).

VII HOME MEASUREMENT OF BLOOD PRESSURE

1) Home BP readings can be used in the diagnosis of hypertension (Grade C).

2) The use of home BP monitoring on a regular basis should be considered for patients with hypertension, particularly those with:

   i) diabetes mellitus (Grade D),

   ii) chronic kidney disease (Grade C),

   iii) suspected nonadherence (Grade D),

iv) demonstrated white coat effect (Grade C); and

v) BP controlled in the office but not at home (masked hypertension) (Grade C).

3) **When white coat hypertension is suggested by home monitoring, its presence should be confirmed with ABPM before making treatment decisions (Grade D).**

4) **Patients should be advised to purchase and use only home BP monitoring devices that are appropriate for the individual and have met standards of the Association for the Advancement of Medical Instrumentation or the most recent requirements of the British Hypertension Society protocol or the International Protocol for validation of automated BP measuring devices. Patients should be encouraged to use devices with data recording capabilities or automatic data transmission to increase the reliability of reported home BP values (Grade D).**

5) **Home values of 135 mm Hg or greater SBP or 85 mm Hg or greater DBP should be considered elevated and associated with an increased overall mortality risk analogous to office readings of 140 mm Hg or greater SBP or 90 mm Hg or greater DBP (Grade C).**

6) Health care professionals should ensure that patients who measure their BP at home have adequate training, and if necessary, repeat training in measuring their BP. Patients should be observed to determine that they measure BP correctly and they should be given adequate information about interpreting these readings (Grade D).

7) The accuracy of all individual patients' validated devices (including electronic devices) must be regularly checked against a device of known calibration (Grade D).

8) Home BP values for assessing white coat hypertension or sustained hypertension should be based on duplicate measures, morning and evening, for an initial seven-day period. First day home BP values should not be considered (Grade D).

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VIII AMBULATORY BLOOD PRESSURE MEASUREMENT

1) Ambulatory BP readings can be used in the diagnosis of hypertension (Grade C).

2) ABPM should be considered when an office-induced increase in BP is suspected in treated patients with:

   i) BP that is not below target despite receiving appropriate chronic anti-hypertensive therapy (Grade C), or

   ii) symptoms suggestive of hypotension (Grade C), or

   iii) fluctuating office BP readings (Grade D).

3) Physicians should use only ABPM devices that have been validated independently using established protocols (Grade D).

4) Therapy adjustment should be considered in patients with 24 h ambulatory SBP of 130 mm Hg or greater and/or DBP of 80 mm Hg or greater and/or awake SBP of 135 mm Hg or greater and/or DBP of 85 mm Hg or greater (Grade D).

5) The magnitude of changes in nocturnal BP should be taken into account in any decision to prescribe or withhold drug therapy based upon ambulatory BP (Grade C) because a decrease in nocturnal BP of less than 10% is associated with increased risk of CV events.

IX ROLE OF ECHOCARDIOGRAPHY

1) Routine echocardiographic evaluation of all hypertensive patients is not recommended (Grade D).

2) An echocardiogram for assessment of left ventricular hypertrophy is useful in selected cases to help define the future risk of cardiovascular events (Grade C).

3) Echocardiographic assessment of left ventricular mass as well as systolic and diastolic left ventricular function is recommended for hypertensive patients suspected to have left ventricular dysfunction or coronary artery disease (Grade D).

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DIAGNOSIS & ASSESSMENT TABLES

TABLE 1: Recommended Technique for Measuring Blood Pressure*

i) Measurements should be taken with a sphygmomanometer known to be accurate. A recently calibrated aneroid or a validated and recently calibrated electronic device can be used (see text for further discussion). Aneroid devices or mercury columns need to be clearly visible at eye level.

ii) Choose a cuff with an appropriate bladder size matched to the size of the arm. For measurements taken by auscultation, bladder width should be close to 40% of arm circumference and bladder length should cover 80 – 100% of arm circumference. When using an automated device, select the cuff size as recommended by its manufacturer.

iii) Place the cuff so that the lower edge is 3 cm above the elbow crease and the bladder is centered over the brachial artery. The patient should be resting comfortably for 5 minutes in the seated position with back support. The arm should be bare and supported with the antecubital fossa at heart level, as a lower position will result in an erroneously higher SBP and DBP. There should be no talking, and patients' legs should not be crossed. At least three measurements should be taken in the same arm with the patient in the same position. The first reading should be discarded and the latter two averaged. Blood pressure also should be assessed after 2 minutes standing (with arm supported) and at times when patients report symptoms suggestive of postural hypotension. Supine BP measurements may also be helpful in the assessment of elderly and diabetic patients.

iv) Increase the pressure rapidly to 30 mm Hg above the level at which the radial pulse is extinguished (to exclude the possibility of a systolic auscultatory gap).

v) Place the bell or diaphragm of the stethoscope gently and steadily over the brachial artery.

vi) Open the control valve so that the rate of deflation of the cuff is approximately 2 mm Hg per heart beat. A cuff deflation rate of 2 mm Hg per beat is necessary for accurate systolic and diastolic estimation.

vii Read the systolic level -- the first appearance of a clear tapping sound (phase I Korotkoff)-- and the diastolic level (the point at which the sounds disappear (phase V Korotkoff). Continue to auscultate at least 10 mm Hg below phase V to exclude a diastolic auscultatory gap. Record the blood pressure to the closest 2 mm Hg on the manometer (or 1 mm Hg on electronic devices) as well as the arm used and whether the patient was supine, sitting or standing. Avoid digit preference by not rounding up or down. Record the heart rate. The seated blood pressure is used to determine and monitor treatment decisions. The standing blood pressure is used to examine for postural hypotension, if present, which may modify the treatment.

viii) If Korotkoff sounds persist as the level approaches 0 mm Hg, then the point of muffling of the sound is used (phase IV) to indicate the diastolic pressure.

ix) In the case of arrhythmia, additional readings may be required to estimate the average systolic and diastolic pressure. Isolated extra beats should be ignored. Note the rhythm and pulse rate.

x) Leaving the cuff partially inflated for too long will fill the venous system and make the sounds difficult to hear. To avoid venous congestion, it is recommended that at least one minute should elapse between readings.

xi) Blood pressure should be taken in both arms on at least one visit and if one arm has a consistently higher pressure, that arm should be subsequently used for blood pressure measurement and interpretation.

*** These are instructions for blood pressure measurement when using a sphygmomanometer and stethoscope; many steps may not apply when using automated devices. Re-printed with permission of CHEP**

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Table 2: Examples of hypertensive urgencies and emergencies *

Asymptomatic diastolic BP ≥ 130 mm Hg

Hypertensive encephalopathy

Acute aortic dissection

Acute left ventricular failure

Acute myocardial ischemia

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Table 3: Examples of target organ damage *

Cerebrovascular Disease

- Stroke
  - Ischemic stroke and transient ischemic attack
  - Intracerebral hemorrhage
  - Aneurysmal sub-arachnoid hemorrhage
- Dementia
  - Vascular dementia
  - Mixed vascular dementia and dementia of the Alzheimer's type

Hypertensive Retinopathy

Left Ventricular Dysfunction

Coronary Artery Disease

- Myocardial infarction
- Angina pectoris
- Congestive heart failure

Chronic Kidney Disease

- Hypertensive nephropathy (GFR < 60 ml/min/1.73 m^2)
- Albuminuria

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Peripheral Artery disease

Intermittent claudication

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Table 4: Examples of key cardiovascular risk factors for atherosclerosis *

Prior history of clinically overt atherosclerotic disease *indicates a very high risk for a recurrent atherosclerotic event (e.g., Peripheral arterial disease, previous stroke or TIA)*

Non-Modifiable

Age ≥ 55

Male

Family history of premature cardiovascular disease (age < 55 in men and < 65 in women)

Modifiable

Sedentary lifestyle

Poor dietary habits

Abdominal obesity

Impaired glucose tolerance or diabetes mellitus

Smoking

Dyslipidemia

Stress

Target organ damage

Left ventricular hypertrophy

Microalbuminuria or proteinuria

Chronic kidney disease (glomerular filtration rate < 60 ml/min/1.73 m^2)

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Table 5: Examples of exogenous factors that can induce/aggravate hypertension*

Prescription Drugs:

- NSAIDs, including coxibs
- Corticosteroids and anabolic steroids
- Oral contraceptive and sex hormones
- Vasoconstricting/sympathomimetic decongestants
- Calcineurin inhibitors (cyclosporin, tacrolimus)
- Erythropoietin and analogues
- Monoamine oxidase inhibitors (MAOIs)
- Midodrine

Other substances and conditions:

- Licorice root
- Stimulants including cocaine
- Salt
- Excessive alcohol use
- Sleep apnea

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Table 6A: Hyperaldosteronism: Screening and diagnosis *

i. Plasma aldosterone and plasma renin activity (see ii below for conversion factors) should be measured under standardized conditions, including the collection of morning samples taken from patients in a sitting position after resting at least 15 minutes. Antihypertensive drugs may be continued, with the exception of aldosterone antagonists, angiotensin receptor blockers, beta-adrenergic antagonists and clonidine.

ii. Renin, Aldosterone and Ratio Conversion Factors:

A. To estimate:	B. From:	Multiply (B) by:
Plasma renin concentration (ng/mL)	Plasma renin activity (ng/mL/hr)	0.206
Plasma renin activity (g/L/sec)	Plasma renin activity (ng/mL/hr)	0.278
Plasma aldosterone concentration (pmol/L)	Plasma aldosterone concentration (ng/dL)	28

iii. Definition of a positive screening test: plasma aldosterone/renin activity ratio greater than 550 pmol/L/ng/ml/hr (or 140 pmol/L/ng/L when renin is measured as renin mass or concentration).

iv. Maneuvers to demonstrate autonomous hypersecretion of aldosterone:

a) saline loading tests (2L of normal saline over 4 h with primary aldosteronism defined as failure to suppress plasma aldosterone to less than 280 pmol/L; or oral sodium 300 mmol/day

for three days with primary aldosteronism defined as failure to suppress plasma aldosterone to less than 240 pmol/L);

b) fludrocortisone suppression test (oral sodium loading plus oral fludrocortisone 0.25 mg per day for 2 days) positive for primary aldosteronism: plasma aldosterone of 140 pmol/L or greater in upright and/or supine positions;

c) a plasma aldosterone/PRA ratio greater than 1400 pmol/L/ng/ml/hr with a plasma aldosterone greater than 440 pmol/L; and

d) captopril suppression test (primary aldosteronism defined as failure to suppress plasma aldosterone to less than 240 pmol/L two hours after 25 mg of oral captopril).

v. Differentiating potential causes of primary aldosteronism:

a) For patients with established primary aldosteronism attempts to differentiate potential causes should be made and may include localization with adrenal CT-scan (standard: 3 mm contiguous cuts) or magnetic resonance imaging (where available), or assessment of plasma aldosterone before (supine) and after 2 h to 4 h of upright posture.

b) For patients with established primary aldosteronism and negative imaging studies, selective adrenal venous sampling should be considered because it may be the only way to reliably differentiate unilateral from bilateral overproduction of aldosterone. Adrenal venous

sampling should be conducted in centres with experience in performing this diagnostic technique.

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Table 6B: Pheochromocytoma: Screening and diagnosis *

i. Biochemical screening tests for pheochromocytomas:

a) To screen for pheochromocytomas, 24 h urinary total metanephrines (sensitivity 95%) and urinary metanephrine-to-creatinine ratio (sensitivity 100%) should be assessed. Plasma catecholamines and, where available, plasma metanephrines may also be considered if clinical suspicion is high, particularly during a hypertensive episode or for those with familial forms. Urinary or plasma VMA measurements should not be used as screening tests. In a low risk setting, plasma fractionated free metanephrine measurements can be used to rule out pheochromocytoma.

b) In the presence of borderline biochemical test results (e.g., plasma noradrenaline and adrenaline levels of approximately 500ng/L to 2000 ng/L) or potentially false positive results, repeated testing and/or the clonidine suppression test may be used.

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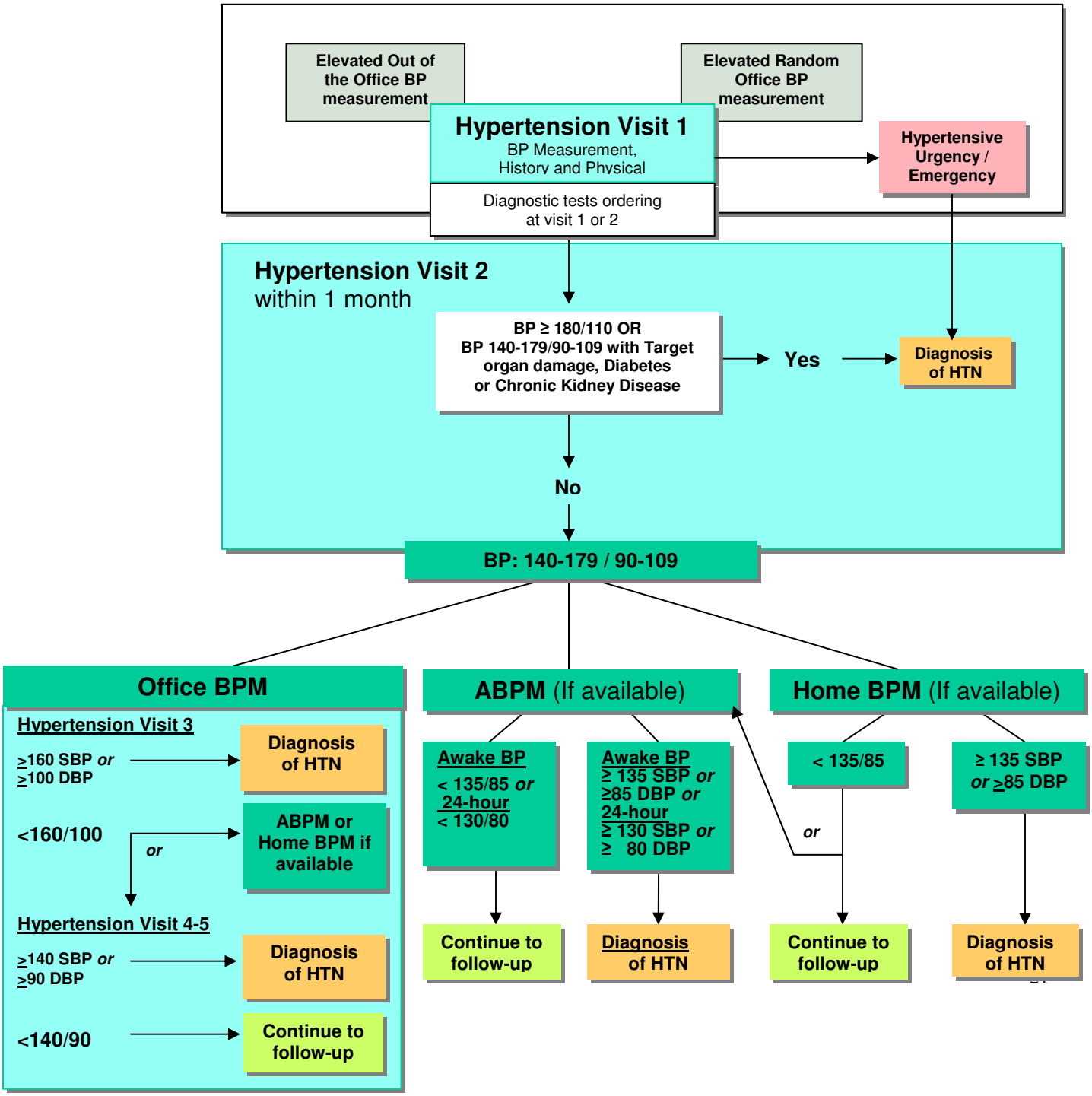
Programme Éducatif Canadien sur l'Hypertension

Canadian Hypertension Education Program

Figure 1. The expedited assessment and diagnosis of patients with hypertension: Focus on validated technologies for blood pressure assessment *



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I LIFESTYLE MANAGEMENT

A Physical Exercise

1) For non-hypertensive individuals (to reduce the possibility of becoming hypertensive) or for hypertensive patients (to reduce their blood pressure) prescribe the accumulation of 30 to 60 minutes of moderate intensity dynamic exercise (such as walking, jogging, cycling or swimming) 4 -7 days per week (Grade D). Higher intensities of exercise are no more effective (Grade D).

B Weight Reduction

1) Height, weight, and waist circumference (WC) should be measured and body mass index (BMI) calculated for all adults (Grade D).

2) Maintenance of a healthy body weight (BMI 18.5 to 24.9 kg/m²; WC <102 cm for men and < 88 cm for women) is recommended for non-hypertensive individuals to prevent hypertension (Grade C) and for hypertensive patients to reduce blood pressure (Grade B). All overweight hypertensive individuals should be advised to lose weight (Grade B).

3) Weight loss strategies should employ a multidisciplinary approach that includes dietary education, increased physical activity, and behavioral intervention (Grade B).

C Alcohol Consumption

1) To reduce blood pressure, alcohol consumption should be in accordance with Canadian low-risk drinking guidelines in both normotensive and hypertensive individuals**.** Healthy adults should limit alcohol consumption to 2 drinks or less per day, and consumption should not exceed 14 standard drinks per week for men and 9 standard drinks per week for women (Grade B).

(Note: one standard drink is considered 13.6 g or 17.2 ml of ethanol, or approximately 1.5 oz of 80 proof (40%) spirits, 5 oz of 12% wine or 12 oz of 5% beer.)

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D Dietary Recommendations

1) It is recommended that hypertensive patients **and normotensive individuals at increased risk of developing hypertension** consume a diet that emphasizes fruits, vegetables and low-fat dairy products, **dietary and soluble fiber, whole grains and protein from plant sources** and that is reduced in saturated fat and cholesterol (Dietary Approaches to Stop Hypertension [DASH] diet) see **Table 1** (Grade B).

E Salt Intake

1) **For prevention of hypertension, in addition to a well balanced diet, a dietary sodium intake of <100 mmol/day is recommended (Grade B).**

2) In hypertensive patients, dietary sodium intake should be limited to 65 -100 mmol/day (Grade B).

F Potassium, Calcium and Magnesium Intake

1) Supplementation of potassium, calcium and magnesium is not recommended for the prevention or treatment of hypertension (Grade B).

G Stress management

1) In hypertensive patients in whom stress may be contributing to blood pressure elevation, stress management should be considered as an intervention (Grade D). Individualized cognitive behavioral interventions are more likely to be effective when relaxation techniques are employed (Grade B).

II INDICATIONS FOR DRUG THERAPY FOR ADULTS WITH HYPERTENSION WITHOUT COMPELLING INDICATIONS FOR SPECIFIC AGENTS

1) Antihypertensive therapy should be prescribed for average diastolic blood pressures of 100 mm Hg or higher (Grade A) or average systolic blood pressures of 160 mm Hg or higher (Grade A) in patients without macrovascular target organ damage or other cardiovascular risk factors (**see Tables 3 and 4 from accompanying CHEP Diagnosis paper**).

2) Antihypertensive therapy should be strongly considered if diastolic blood pressure readings average 90 mm Hg or higher in the presence of macrovascular target organ damage or other independent cardiovascular risk factors (Grade A).

3) Antihypertensive therapy should be strongly considered if systolic blood pressure readings average 140 mm Hg or higher in the presence of macrovascular target organ damage (Grade C for 140 mm Hg to 160 mm Hg; Grade A for higher than 160 mm Hg).

III CHOICE OF THERAPY FOR ADULTS WITH HYPERTENSION WITHOUT COMPELLING INDICATIONS FOR SPECIFIC AGENTS

A Recommendations for individuals with diastolic ± systolic hypertension

1) Initial therapy should be monotherapy with a thiazide diuretic (Grade A); a beta-blocker (in patients younger than 60 years, Grade B); an ACE inhibitor (in non-blacks, Grade B); a long-acting CCB (Grade B); or an ARB (Grade B). If there are adverse effects, another drug from this group should be substituted. Hypokalemia should be avoided in patients treated with thiazide diuretic monotherapy (Grade C).

2) Additional antihypertensive drugs should be used if target blood pressure levels are not achieved with standard dose monotherapy (Grade B). **Add-on drugs should be chosen from first line choices.** Useful choices include a thiazide diuretic or CCB with either an ACE inhibitor, ARB or beta- blocker (Grade C for the combination of dihydropyridine CCB and ACE inhibitor; Grade B for the combination of **thiazide diuretic with a dihydropyridine CCB and Grade D for all other combinations).** Caution should be exercised in combining a nondihydropyridine CCB and a beta-blocker (Grade D).

3) If blood pressure is still not controlled with a combination of 2 or more first line agents, or there are adverse effects, other antihypertensive drugs may be added (Grade D).

4) Possible reasons for poor response to therapy (**see Table 2**) should be considered (Grade D).

5) Alpha-blockers are not recommended as first-line agents for uncomplicated hypertension (Grade A); beta blockers are not recommended as first-line therapy for uncomplicated hypertension in patients aged 60 years or greater (Grade A); ACE inhibitors are not recommended as first-line therapy for uncomplicated hypertension in black patients (Grade A). However, these agents may be used in patients with certain comorbid conditions or in combination therapy (**Table 3**).

B Recommendations for individuals with isolated systolic hypertension

1) Initial therapy should be monotherapy with a thiazide diuretic (Grade A); a long-acting dihydropyridine CCB (Grade B) or an ARB (Grade B). If there are adverse effects, another drug from this group should be substituted. Hypokalemia should be avoided in patients treated with thiazide diuretic monotherapy (Grade C).

2) **Additional antihypertensive drugs should be used if target blood pressure levels are not achieved with standard dose monotherapy (Grade B). Add-on drugs should be chosen from first-line choices (Grade D).**

3) If blood pressure is still not controlled with a combination of two or more first-line agents, or there are adverse effects, other classes of drugs (such as alpha-blockers, ACE inhibitors, centrally acting agents or nondihydropyridine CCBs) may be added/substituted (Grade D).

4) Possible reasons for poor response to therapy (**see Table 2**) should be considered (Grade D).

5) Alpha-blockers are not recommended as first-line agents for uncomplicated isolated systolic hypertension (Grade A); beta-blockers are not recommended as first-line therapy for isolated systolic hypertension in patients aged 60 years or greater (Grade A). However, both agents may be used in patients with certain comorbid conditions or in combination therapy.

IV GLOBAL VASCULAR PROTECTION THERAPY FOR ADULTS WITH HYPERTENSION WITHOUT COMPELLING INDICATIONS FOR SPECIFIC AGENTS

1) Statin therapy is recommended in hypertensive patients with 3 or more cardiovascular risk factors as defined in **Table 4** (Grade A in patients older than 40 years) or with established atherosclerotic disease (Grade A regardless of age).

2) Strong consideration should be given to the addition of low dose ASA therapy in hypertensive patients (Grade A in patients older than 50 years). Caution should be exercised if blood pressure is not controlled (Grade C).

V GOAL OF THERAPY FOR ADULTS WITH HYPERTENSION WITHOUT COMPELLING INDICATIONS FOR SPECIFIC AGENTS

1) The systolic blood pressure treatment goal is a pressure level of less than 140 mm Hg (Grade C). The diastolic blood pressure treatment goal is a pressure level of less than 90 mm Hg (Grade A).

VI TREATMENT OF HYPERTENSION IN ASSOCIATION WITH ISCHEMIC HEART DISEASE

A Recommendations for hypertensive patients with coronary artery disease

1) An ACE inhibitor is recommended for patients with hypertension and documented coronary artery disease (Grade A).

2) For patients with stable angina, beta-blockers are preferred as initial therapy (Grade B). Long-acting CCBs may also be used (Grade B).

3) Short acting nifedipine should not be used (Grade D).

B Recommendations for patients with hypertension who have had a recent ST-elevation myocardial infarction or non-ST segment elevation myocardial infarction

1) Initial therapy should include both a beta-blocker and an ACE inhibitor (Grade A). An ARB can be used if the patient is intolerant to an ACE inhibitor (Grade A in patients with left ventricular systolic dysfunction).
2) Long-acting CCBs may be used in post myocardial infarction patients when beta-blockers are contraindicated or not effective. Nondihydropyridine CCBs should not be used when there is heart failure as evidenced by pulmonary congestion on examination or radiograph (Grade D).

VII TREATMENT OF HYPERTENSION IN ASSOCIATION WITH HEART FAILURE

1) Patients with hypertension and evidence of heart failure should have an objective assessment of left ventricular ejection fraction, either by echocardiogram or nuclear imaging (Grade D).

2) In patients with systolic dysfunction, ACE inhibitors (Grade A) and beta-blockers (Grade A) are recommended for initial therapy. Aldosterone antagonists (Grade B) are also recommended for patients with NYHA Class III or IV symptoms of heart failure. Other diuretics are

recommended as additional therapy if needed (Grade B for thiazide diuretics for blood pressure control, Grade D for loop diuretics for volume control).

3) An ARB (Grade A) is recommended if ACE inhibitors are not tolerated (Grade A).

4) A combination of hydralazine and isosorbide dinitrate is recommended if ACE inhibitors and ARBs are contraindicated or not tolerated (Grade B).

5) For hypertensive patients with heart failure whose blood pressure is not controlled, an ARB may be added to an ACE inhibitor and other antihypertensive drug treatment (Grade A). Careful monitoring should be used if combining an ACE inhibitor and an ARB due to potential adverse effects such as hypotension, hyperkalemia and worsening renal function (Grade C). Additional therapies may also include long-acting dihydropyridine CCBs (Grade C).

VIII TREATMENT OF HYPERTENSION IN ASSOCIATION WITH CEREBROVASCULAR DISEASE

1) Strong consideration should be given to the initiation of antihypertensive therapy after the acute phase of a non-disabling stroke or transient ischemic attack (Grade A).

2) Caution is indicated in deciding whether to lower blood pressure in the acute stroke situation; pharmacological agents and routes of administration should be chosen to avoid precipitous falls in blood pressure (Grade D).

3) Following the acute phase of a stroke, patients should have their blood pressure chronically controlled to a target of less than 140/90 mm Hg (Grade C).

4) Treatment with an ACE inhibitor/diuretic combination is preferred (Grade B).

IX TREATMENT OF HYPERTENSION IN ASSOCIATION WITH LEFT VENTRICULAR HYPERTROPHY

1) Hypertensive patients with left ventricular hypertrophy should be treated with antihypertensive therapy to lower the rate of subsequent cardiovascular events (Grade C).

2) **The choice of initial therapy can be influenced by the presence of left ventricular hypertrophy (Grade D). Initial therapy can be drug treatment using ACE inhibitors, ARBs, long-acting CCBs, or thiazide diuretics. Direct arterial vasodilators such as hydralazine or minoxidil should not be used.**

X TREATMENT OF HYPERTENSION IN ASSOCIATION WITH NON-DIABETIC CHRONIC KIDNEY DISEASE

1) For patients with non-diabetic chronic kidney disease, target blood pressure is < 130/80 mm Hg (Grade C).

2) **For patients with hypertension and proteinuric chronic kidney disease (urinary protein > 500 mg/24hr or albumin:creatinine ratio [ACR] > 30 mg/mmol), initial therapy should be an ACE inhibitor (Grade A) or an ARB if there is intolerance to ACE inhibitors (Grade D).**

3) Thiazide diuretics are recommended as additive antihypertensive therapy (Grade D). For patients with chronic kidney disease and volume overload, loop diuretics are an alternative (Grade D).

4) In most cases, combination therapy with other antihypertensive agents may be needed to reach target blood pressures (Grade D).

XI TREATMENT OF HYPERTENSION IN ASSOCIATION WITH RENOVASCULAR DISEASE

1) Renovascular hypertension should be treated in the same manner as hypertension without compelling indications, except for caution in the use of ACE inhibitors or ARBs due to the risk of acute renal failure in bilateral disease or unilateral disease with a solitary kidney (Grade D).

2) Close follow-up and early intervention (angioplasty and stenting or surgery) should be considered for patients with: uncontrolled hypertension despite therapy with three or more drugs, deteriorating kidney function, bilateral atherosclerotic renal artery lesions (or tight atherosclerotic stenosis in a single kidney), or recurrent episodes of flash pulmonary edema (Grade D).

XII TREATMENT OF HYPERTENSION IN ASSOCIATION WITH DIABETES MELLITUS

1) Persons with diabetes mellitus should be treated to attain systolic blood pressures of less than 130 mm Hg (Grade C) and diastolic blood pressures of less than 80 mm Hg (Grade A). (These target blood pressure levels are the same as the blood pressure treatment thresholds.)

2) **For persons with diabetes and normal urinary albumin excretion (albumin to creatinine ratio [ACR] < 2.0 mg/mmol in men and < 2.8 mg/mmol in women) and without chronic**

kidney disease, with blood pressures greater than or equal to 130/80 mm Hg despite lifestyle interventions, any of: an ACE inhibitor (Grade A for persons aged greater than or equal to 55 years, Grade B for persons aged less than 55 years), ARB (Grade A for persons with left ventricular hypertrophy and age greater than or equal to 55 years, Grade B for persons without left ventricular hypertrophy irrespective of age), dihydropyridine CCB (Grade A for persons 55 years of age or older, Grade B for persons younger than 55 years), or thiazide diuretic (Grade A for persons 55 years of age or older, Grade B for persons younger than 55 years) is recommended, with special consideration to the ACE inhibitor and ARB given their additional renal benefits.

If these drugs are contraindicated or cannot be tolerated, a cardioselective beta-blocker (Grade B) or nondihydropyridine CCB (Grade B) can be substituted. Additional antihypertensive drugs should be used if target blood pressure levels are not achieved with standard dose monotherapy (Grade B). Add-on drugs should be chosen from first-line choices.

3) For persons with diabetes and albuminuria **(persistent albumin to creatinine ratio [ACR] > 2.0 mg/mmol in men and > 2.8 mg/mmol in women),** an ACE inhibitor or an ARB is recommended as initial therapy (Grade A). If blood pressure remains greater than or equal to 130/80 mm Hg despite lifestyle interventions and the use of an ACE inhibitor or ARB, **additional antihypertensive drugs should be used to obtain target blood pressure.**

4) For persons with diabetes and a normal urinary albumin excretion rate **(ACR < 2.0 mg/mmol in men and < 2.8 mg/mmol in women) with no chronic kidney disease and** with isolated systolic hypertension, a long-acting dihydropyridine CCB (Grade C) is an alternative initial choice to an ACE inhibitor (Grade B), ARB (Grade B), or a thiazide diuretic (Grade C).
5) Alpha-blockers are not recommended as first-line agents for the treatment of hypertension in persons with diabetes (Grade A).

XIII CONCORDANCE STRATEGIES FOR PATIENTS

1) Adherence to an antihypertensive prescription can be improved by a multi-pronged approach as outlined in **Table 5**.

XIV TREATMENT OF SECONDARY HYPERTENSION DUE TO ENDOCRINE CAUSES

1) Treatment of hyperaldosteronism and pheochromocytoma are outlined in **Tables 6A and 6B**.

THERAPY TABLES

Table 1: Dietary Approaches to Stop Hypertension (DASH) diet

Food Group	Daily Serving	Examples and Notes
Grains	7-8	Whole wheat bread, oatmeal, popcorn
Vegetables	4-5	Tomatoes, potatoes, carrots, beans, peas, squash, spinach
Fruits	4-5	Apricots, bananas, grapes, oranges, grapefruit, melons
Low-fat or fat-free dairy foods	2-3	Fat-free (skim)/low-fat (1%) milk, fat-free/low-fat yogurt, fat-free/low-fat cheese
Meats, poultry, fish	≤2	Select only lean meats. Trim away fats. Broil, roast or boil. No frying. Remove skin from poultry.
Nuts, seeds, dry beans	4-5/week	Almonds, peanuts, walnuts, sunflower seeds, soybeans, lentils
Fats and oils	2-3	Soft margarines, low-fat mayonnaise, vegetable oil (olive, corn, canola, or safflower)
Sweets	5/week	Maple syrup, sugar, jelly, jam, hard candy, sorbet

(DASH eating plan available at:
http://www.nhlbi.nih.gov/health/public/heart/hbp/dash/new_dash.pdf)

Table 2: Possible reasons for poor response to antihypertensive therapy*

Non-compliance	
	Dietary
	Medication
Associated Conditions	
	Obesity
	Cigarette smoking
	Excessive alcohol consumption
	Sleep apnea
	Chronic pain and/or mental illness
Drug Interactions	
	Nonsteroidal anti-inflammatory drugs (including cyclo-oxy-genase-2 (COX-2) inhibitors)
	Oral contraceptives
	Corticosteroids and anabolic steroids
	Sympathomimetics and decongestants
	Cocaine
	Amphetamines
	Erythropoietin
	Cyclosporine, Tacrolimus
	Licorice
	Over the counter dietary supplements (e.g., ephedra, ma haung, bitter orange)
Suboptimal Treatment Regimens	
	Dosage too low
	Inappropriate combinations of antihypertensive agents
Volume Overload	
	Excessive salt intake
	Renal sodium retention (pseudotolerance)
Secondary hypertension	
	Renal insufficiency
	Renovascular disease
	Primary hyperaldosteronism
	Thyroid disease
	Pheochromocytoma and other rare endocrine causes

Note that causes of “pseudo-resistance” (such as white coat hypertension or pseudo-hypertension in the elderly) should be ruled out first.

(Adapted from: McAlister FA, Zarnke KB, Campbell NR, Feldman RD, Levine M, Mahon J, Grover SA, Lewanczuk R, Leenen F, Tobe S, Lebel M, Stone J, Schiffrin EL, Rabkin SW, Ogilvie RI, Larochelle P, Jones C, Honos G, Fodor G, Burgess E, Hamet P, Herman R, Irvine J, Culleton B, Wright JM; Canadian

Hypertension Recommendations Working Group. The 2001 Canadian recommendations for the management of hypertension: Part two--Therapy. *Can J Cardiol.* 2002;18(6):625-41)

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Table 3: Considerations in the Individualization of Antihypertensive Therapy*

ACE angiotensin-converting enzyme; TIA transient ischemic attack; ARB angiotensin receptor blocker

	Initial therapy	*Second-line therapy*	*Notes and/or Cautions*
HYPERTENSION WITHOUT OTHER COMPELLING INDICATIONS			
Diastolic+/- systolic hypertension	Thiazide diuretics, beta- blockers, ACE inhibitors, ARBs, or long-acting calcium channel blockers (consider ASA and statins in selected patients)	Combinations of first-line drugs	Beta-blockers are not recommended as initial therapy in those over 60 years of age. Hypokalemia should be avoided by using potassium-sparing agents in those who are prescribed diuretics as monotherapy. ACE inhibitors are not recommended in blacks. ACE inhibitors and ARBs are teratogenic and marked caution is required if prescribing to women of child bearing potential.
Isolated systolic hypertension without other compelling indications	Thiazide diuretics, ARBs or long-acting dihydropyridine calcium channel blockers.	Combinations of first-line drugs	Same as diastolic+/- systolic hypertension
DIABETES MELLITUS			
Diabetes mellitus with nephropathy	ACE inhibitors or ARBs	Addition of thiazide diuretics, cardioselective beta-blockers, long-acting calcium channel blockers or use an ARB/ACEI combination	If the serum creatinine level is >150 µmol/L, a loop diuretic should be used as a replacement for low-dose thiazide diuretics if volume control is required
Diabetes mellitus without nephropathy	ACE inhibitors, ARBs, dihydropyridine CCBs or thiazide diuretics	Combination of first-line drugs or if first line agents are not tolerated addition of cardioselective beta-blockers and/or long-acting non dihydropyridine calcium channel blockers	Albumin to creatinine ratio [ACR] < 2.0 mg/mmol in men and < 2.8 mg/mmol in women
CARDIOVASCULAR AND CEREBROVASCULR DISEASE			
Angina	Beta-blockers and ACE inhibitors except in low risk revascularized patients	Long-acting calcium channel blockers	Avoid short-acting nifedipine
Prior myocardial infarction	Beta-blockers and ACE inhibitors (ARBs if ACEI- intolerant)	Long-acting calcium channel blockers	
Heart failure	ACE inhibitors (ARBs if ACEI-intolerant), beta blockers and spironolactone	ARBs or hydralazine/isosorbide dinitrate (thiazide or loop diuretics, as additive therapy)	Avoid nondihydropyridine calcium channel blockers (diltiazem, verapamil). Monitor potassium and renal function if combining and ACE inhibitor and ARB.
Left ventricular hypertrophy	ACE inhibitors, ARBs, dihydropyridine calcium channel blockers, diuretics, (beta-blockers for patients under 55 years)		Avoid hydralazine and minoxidil
Past cerebrovascular accident or TIA	ACE inhibitor/diuretic combinations		This does not apply to acute stroke. Blood pressure reduction reduces recurrent cerebrovascular events in patients with stable past cerebrovascular disease.

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NON-DIABETIC CHRONIC KIDNEY DISEASE			
Non-diabetic chronic kidney disease with proteinuria	ACE inhibitors (ARBs if ACEI-intolerant), diuretics as additive therapy	Combinations of additional agents	Avoid ACE inhibitors or ARBs if bilateral renal artery stenosis or unilateral disease with solitary kidney. Patients placed on an ACE inhibitor or an ARB should have their serum creatinine and potassium carefully monitored.
Renovascular disease	Similar to diastolic +/- systolic hypertension without compelling indications for other medications		Avoid ACE inhibitors or ARBs if bilateral renal artery stenosis or unilateral disease with solitary kidney.
OTHER CONDITIONS			
Peripheral arterial disease	Does not affect initial treatment recommendations	Does not affect initial treatment recommendations	Avoid beta-blockers with severe disease
Dyslipidemia	Does not affect initial treatment recommendations	Does not affect initial treatment recommendations	
Global vascular protection	Statin therapy for patients with 3 or more cardiovascular risk factors or with atherosclerotic disease Low dose ASA in patients with controlled blood pressure		Caution should be exercised if blood pressure is not controlled.

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Table 4: Cardiovascular risk factors for consideration of statin therapy in non-dyslipidemic patients with hypertension*

Risk Factor
Male sex
Age 55 years or older
Left ventricular hypertrophy
Other ECG abnormalities:
Left bundle branch block, left ventricular strain pattern, abnormal Q-waves, or ST-T changes compatible with ischemic heart disease
Peripheral arterial disease
Previous stroke or transient ischemic attack
Microalbuminuria or proteinuria
Diabetes Mellitus
Smoking
Family history of premature cardiovascular disease
Total cholesterol to HDL ratio $\geq$ 6

*If hypertensive patients have 3 or more of these risk factors, statins should be considered.

(Derived from: Sever PS, Dahlof B, Poulter NR, Wedel H, Beevers G, Caulfield M, Collins R, Kjeldsen SE, Kristinsson A, McInnes GT, Mehlsen J, Nieminen M, O'Brien E, Ostergren J; ASCOT investigators. Prevention of coronary and stroke events with atorvastatin in hypertensive patients who have average or lower-than-average cholesterol concentrations, in the Anglo-Scandinavian Cardiac Outcomes Trial--Lipid Lowering Arm (ASCOT-LLA): a multicentre randomised controlled trial. *Lancet*. 2003;361(9364):1149-58.)

Table 5: Strategies to improve patient adherence*

1) Assist your patient to adhere

- **i)** Tailoring pill-taking to fit patients' daily habits
- **ii)** Simplifying medication regimens to once-daily dosing
- **iii)** Replacing 2 antihypertensive agents with a fixed dose combination (where available and appropriate), provided it is the same combination the patient is already taking
- **iv)** Utilizing unit-of-use packaging (of several medications to be taken together)

2) Assist your patient in getting more involved in their treatment

- **v)** Encouraging greater patient responsibility/autonomy in monitoring their blood pressure and adjusting their prescriptions
- **vi)** Educating patients and patients' families about their disease/treatment regimens

3) Improve your management in the office and beyond

- **vii)** Assessing adherence to pharmacological and non-pharmacological therapy at every visit
- **viii)** Encouraging adherence with therapy by out of office contact (either by phone or mail), particularly over the first three months of therapy
- **ix)** Coordinating with work-site healthcare givers to improve monitoring of adherence with pharmacological and lifestyle modification prescriptions
- **x)** Utilizing electronic medication compliance aids

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Table 6A. Treatment recommendations for patients with hyperaldosteronism*

1) Treatment of confirmed unilateral aldosterone-producing adenoma (APA) is surgical removal by laparoscopic adrenalectomy.

2) Patients should be treated for 8 - 10 weeks prior to surgery, to correct metabolic abnormalities and to control blood pressure.

3) For primary aldosteronism patients with adrenal hyperplasia, bilateral adenoma, or increased risk of peri-operative complications, treatment is medical.

4) Medical treatment should be initiated with spironolactone 25-400 mg per day (usual doses are 100-200 mg). For those intolerant to spironolactone, amiloride 10-20 mg per day is an alternative. Addition of thiazide diuretics, beta-blockers and/or CCBs may be useful to control blood pressure.

5) Because many APA patients will remain hypertensive following the surgical removal of an APA, these patients should be followed and if necessary treated according to the usual guidelines for non-endocrine hypertension.

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Table 6B. Treatment recommendations for patients with pheochromocytoma*

1) Alpha-blockers (prazosin, doxazosin, and phenoxybenzamine) should be used as first-line agents in suspected pheochromocytoma. Alpha methyldopa or clonidine may also be used.

2) Treatment of benign pheochromocytoma should be surgical resection. The following issues should be considered:
   i) Until surgery is performed, the use of beta-blockers should be avoided, unless there are arrhythmias present and adequate alpha- blockade has been achieved
   ii) Surgical resection should be carefully planned in advance with involvement of a team of surgical, medical, intensivist and anesthesia consultants who have experience in the management of patients with pheochromocytoma
   iii) Laparoscopic surgery should be considered before open surgery for resection of pheochromocytoma except for very large tumours
   iv) Administration for 10 to 14 days of phenoxybenzamine (10-20 mg bid-tid), prazosin (1-3 mg bid-tid) or doxazosin (2-4 mg bid-tid) is indicated for patients with severe paroxysmal or sustained hypertension
   v) The tyrosine hydroxylase inhibitor metyrosine (0.25-1g four times daily) should also be considered
   vi) Immediately prior to surgery, administration of intravenous fluids should be considered to ensure adequate volume expansion in order to avoid shock after tumour removal
   vii) For hypertensive crises before/during surgery, phentolamine hydrochloride should be readily available and if necessary, administered intravenously
   viii) Intravenous propranolol should be employed for treatment of arrhythmias.

3) For patients with pheochromocytoma diagnosed during early pregnancy, if a decision is made to terminate the pregnancy, this should be carried out under alpha and beta-blockade (as above), followed immediately by tumor resection. In late pregnancy, alpha and beta-blockade, followed by elective cesarean section and immediate tumor resection are recommended.

4) For patients with inoperable or metastatic malignant pheochromocytoma, blood pressure control and adrenergic symptoms may be controlled with alpha-adrenergic blockade (phenoxybenzamine, prazosin, doxazosin) plus beta-blockade and/or tyrosine hydroxylase inhibition with metyrosine. A combination of cyclophosphamide, vincristine, and dacarbazine may be used for chemotherapy or metastatic pheochromocytoma. Treatment with high dose I131 –MIBG induces only a moderate response, but may help control of blood pressure.

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