Tried and True Hypertension Guidelines

By David Wood, MD; Mann Chandavimol, MD, FRCPC; and Andrew Ignaszewski, MD, FRCPC, FACC

Case

A 45-year-old male presents with a blood pressure of 150/90 mmHg on three occasions. He smokes occasionally, has a body mass index of 28, and has the following:

- Total cholesterol: 6 mmol/L
- High-density lipoprotein: 1.1 mmol/L
- Triglycerides: 2.5 mmol/L
- Serum creatinine: 110 µmol/L
- Fasting blood sugar: 6.2

What should be done for this patient?

See page 104 for a case discussion.

In this article:

Hypertension remains one of the most important health problems facing Canadians. Although the morbidity and mortality associated with hypertension are well-known (it is implicated in 35% of all atherosclerotic cardiovascular events and 24% of all premature deaths),[1] it remains highly prevalent and poorly controlled.

Almost one quarter (22%) of the adult Canadian population has high blood pressure (BP).[2] Of this staggering number, only 16% are receiving appropriate treatment (to reach a target BP of < 140/90 mmHg). The purpose of this article is to help put the general principles of the latest edition of these guidelines in the hands of the family practitioner.[3] It will highlight some of the new literature in the last two years regarding therapeutic choices for specific populations. More importantly, it will emphasise the general principles of diagnosis and management of hypertension, which remain largely unchanged and are key in fighting this national problem.

What are the diagnostic tools?

An accurate BP measurement is taken after the patient has been resting comfortably in the seated position for five minutes, with the arm supported at the level of the heart with an appropriately sized cuff

Table 1
Target organ damage in patients with hypertension

Coronary artery disease
Left ventricular hypertrophy
Left ventricular systolic dysfunction
Stroke, including transient ischemic attacks and vascular dementia
Aortic and peripheral arterial disease
Hypertensive nephropathy
Hypertensive retinopathy
Asymptomatic atherosclerosis disease

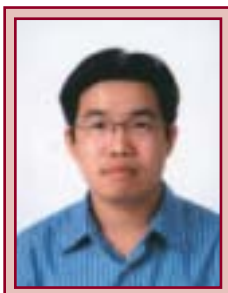
(optimal bladder width = arm circumference/2.5).[4] Patients with target organ damage (Table 1) and elevated readings (Tables 2 and 3) can be given a diagnosis of hypertension and started on therapy at or after their third visit. Without target organ damage or cardiovascular risk factors, at least four visits for up to six months may be required to make the diagnosis. However, individual judgment is required regarding the appropriate length of workup.[4]

Home BP monitoring should be considered for patients suspected to be noncompliant with medications, for diabetics, and for patients with suspected "white coat" hypertension. However, it is critical that both appropriate patient training and accurate reporting of BP values be emphasised when such monitoring is being instituted.[5] The use of standardised devices with a system in place to allow regular verifications of home measurements is extremely important.

Ambulatory 24-Hour Blood Pressure Monitoring (ABPM) is another tool now available in the diagnosis of hypertension. ABPM has been shown to be more reliable and reproducible than office readings.[5] It is particularly useful in patients with suspected "white coat" hypertension or in those not responding to therapy. It can also play a valuable role in patients exhibiting symptoms of hypotension.[6]

Table 2 illustrates the reference values for both home and ABPM, while Table 3 outlines target BP values for specific patient populations.

Dr. Wood is an internal medicine resident with a special interest in cardiology, University of British Columbia, Vancouver, British Columbia.



Dr. Chandavimol is chief cardiology fellow, University of British Columbia, Vancouver, British Columbia.

What are the basic investigations?

It is important that global cardiovascular risk is assessed during the initial screening visits. Multifactorial risk assessment models, such as the Framingham Heart Study, the Lipid Research

Dr. Ignaszewski is associate clinical professor, University of British Columbia; cardiologist Heart Transplant Program; medical director Healthy Heart Program and Heart Function Program, Vancouver, British Columbia.

Clinic Follow-up cohort, or the Dundee cohort can be used to predict more accurately an individual's cardiovascular risk.

All patients diagnosed with hypertension should receive the following basic investigations: urinalysis, complete blood count, electrolytes, serum creatinine, fasting cholesterol profiles, and a standard 12-lead electrocardiogram. For patients with diabetes or known renal disease, 24-hour urinary protein excretion should be measured.[4] The presence or absence of macroalbuminuria influences both the choice of therapeutic agent and BP target (Table 3).[3] It should be noted that routine echocardiographic evaluation of all hypertensive patients is not currently recommended. It is useful, however, in the assessment of left ventricular hypertrophy in selected cases to help define the risk of future cardiovascular events.[4]

In general, patients undergoing antihypertensive treatment should be followed monthly until two BP readings are below their target level (Table 3).[3,4] Once the goal BP has been achieved, and the evaluation for target organ damage is completed, it is recommended that the patient be followed at three- to six-month intervals.[4]

Table 2
Reference blood pressure values

Office blood pressure	< 140/90 mmHg
Home blood pressure	< 135/85 mmHg
Ambulatory blood pressure monitoring	< 135/85 mmHg

Table 3
Target values for blood pressure control

Conditions	Target
18 to 80 years old, systolic and diastolic hypertension 60 to 80 years old, isolated systolic hypertension Chronic hypertension following a stroke	< 140/90 mmHg
Diabetic Non-diabetic nephropathy	< 130/80 mmHg
Diabetic nephropathy with proteinuria > 1 g/24 hrs	< 125/75 mmHg

What are

Table 4
Most often used combinations of two medications

Diuretic + ACE inhibitor or ARB
Diuretic + beta-blocker
Calcium channel blocker (DHP) + beta blocker
Calcium channel blocker (DHP) + ACE inhibitor or ARB
Alpha-blocker + beta-blocker

ACE inhibitors: Angiotensin converting enzyme inhibitors
ARBs: Angiotensin receptor blockades
DHP: Dihydropyridine

the current treatment options?

Approach to Combining Medications

Firstly, most patients do not achieve sufficient BP control with only a single agent. Almost two-thirds of patients in some recent trials have required multiple agents to achieve BP targets.[7]

Secondly, anti-hypertensive drugs can be divided into two main groups: those interfering with renin-dependent mechanisms [beta blockers,

Table 5
2001 Canadian Guidelines for Hypertension

Conditions	Initial Therapy	Second-line Therapy	Notes
Uncomplicated HTN	Thiazides, beta blockers, ACE inhibitors, long-acting CCBs	Combination of first-line drugs	1. Alpha blockers not as first-line therapy 2. Beta blockers not recommended as first-line if patient is > 60
Isolated systolic HTN in the elderly	Thiazides, long-acting CCBs		
Angina or prior MI	Beta blockers, ACE inhibitors	Long-acting CCBs	Short-acting CCBs not recommended
Systolic dysfunction	ACE inhibitors (beta blockers thiazide or loop diuretics and/or spironolactone as additive therapy)	ARBs, hydralazine/ isosorbide dinitrate, long-acting CCBs	Non-DHP CCBs not recommended
Diabetes mellitus **without** nephropathy	ACE inhibitors	Cardio-selective beta blockers, thiazides, long-acting CCBs, ARBs	
Diabetes mellitus **with** nephropathy	ACE inhibitors, ARBs	Cardio-selective beta blockers, thiazides, long-acting CCBs	If serum creatinine is > 150 µmol/L, consider replacing thiazide with loop diuretic for volume control

ACE inhibitors: Angiotensin converting enzyme inhibitors
ARBs: Angiotensin receptor blockades
CCBs: Calcium channel blockers
DHP: Dihydropyridine
HTN: hypertension
MI: myocardial infarction

angiotensin conversion enzyme inhibitors (ACEI), and angiotensin II receptor antagonists (ARB)] and those interfering with sodium-dependent mechanisms [diuretics (thiazides) and long-acting dihydropyridine calcium channel blockers (CCB)].

Therefore, it is logical to combine drugs from different categories first. In cases where a third drug is needed, the most effective course, if this has not already been done, is to add a diuretic. A thiazide is added when the renal function is normal, and furosemide is added when the creatinine clearance is below 30 mL/minute.

The combination approach is not only more effective in lowering BP, but it also decreases dose-dependent, undesirable adverse effects. The addition of the second drug allows the clinician to avoid increasing the dose of the first prescribed drug, thus decreasing dose-dependent side effects (Table 4).

Recent Randomised Controlled Trials

The current 2001 Canadian Guidelines for Hypertension outline initial and second-line therapy for a number of specific patient populations (Table 5).[3] The 2002 guidelines will be published this spring and will need to incorporate a number of recent randomised studies that have generated much debate in both the academic press and general media (Table 6).[8-11]

Case discussion

He should be started on a thiazide diuretic. He should also receive appropriate diet and exercise counselling.

The recently published ALLHAT (Antihypertensive and Lipid Lowering treatment to prevent Heart Attack Trial) data seems to suggest that thiazide diuretics should be the initial treatment in nearly all hypertensive patients and should be the basis for all hypertensive combinations.[10] Both the LIFE (Losartan Intervention for Endpoint Reduction in Hypertension) and SCOPE (Study on Cognition and Prognosis in the Elderly) studies seem to indicate that ARB based strategies seem to have an additional benefit of decreasing the risk of nonfatal stroke in the elderly.[8,9] The

Table 6

Recent, randomised hypertension trials

ALLHAT 33,357 patients age > 55 with hypertension (HTN) and one additional risk factor (50% women, 35% black)

Intervention
- Thiazide-type diuretic (chlorthalidone) vs ACE inhibitor (lisinopril) vs CCB (amlodipine).
- Arm with alpha blocker (doxazosin) stopped early due to increase risk of CHF, as compared to chlorthalidone.

Outcomes
- Mean followup 4.9 years.
- No difference in primary end point of fatal congestive heart disease or nonfatal myocardial infarction (MI).
- No difference in all-cause mortality.
- For amlodipine vs chlorthalidone, outcomes were similar except for a higher 6-year rate of CHF with amlodipine.
- For lisinopril vs chlorthalidone, lisinopril had higher 6-year rate of combined CVD, stroke, and CHF.

Conclusion
- Thiazide-type diuretics are superior in preventing CVD and are less expensive and should be initial therapy.

Comments
- 35% of patients were African-American with known poor response to ACE inhibitors.
- Five-year systolic BP was significantly higher in amlodipine and lisinopril compared to chlorthalidone.

LIFE 9,193 patients aged 55-80 with essential HTN and left ventricular hypertrophy on ECG

Intervention
- ARB (Losartan) vs beta blocker (Atenolol) with hydrochlorothiazide as second agent if necessary on both arms.

Outcomes
- Mean followup 4.7 years.
- Significant decrease in primary composite end point (CVD mortality, Stroke, and MI) with losartan.
- Differences were mainly due to 25% reduction in stroke with losartan.

Conclusion
- ARBs provide equal cardioprotection to beta blockers and more protection from strokes.

Comments
- Most patients in both groups were also receiving a thiazide.

SCOPE 4,937 patients age > 70 with essential HTN and normal cognitive function

Intervention
- Initially placebo vs ARB (candesartan); Placebo group later offered thiazide, CCB, or beta blocker.

Outcomes
- Minimal followup of 3 years.
- No significant difference in primary composite end point of death, MI, stroke.
- 28% relative reduction in nonfatal stroke with candesartan.
- No significant effect on risk of dementia.

Conclusion
- ARB based treatment strategy appears to decrease the risk of nonfatal stroke.

PROGRESS 6,105 patients with history of TIA or CVA (hemorrhagic or ischemic) within the last 5 years (half normotensive, half hypertensive)

Intervention
- Placebo vs ACE inhibitor (perindopril) thiazide-type diuretic (Indapamide) could be added if appropriated.
- 60% in treatment arm received both drugs, 40% received perindopril alone.

Outcomes
- Mean followup 4 years.
- 28% reduction in stroke recurrence in treatment arm (in both the hypertensive and non-hypertensive patients).
- A 34% relative reduction in dementia preceded by recurrent stroke but not in an overall population.

Conclusion
- Lowering BP in stroke patients with ACE inhibitor/diuretic decreases the incidence of stroke recurrence and severity.

Comments
- In patients receiving perindopril alone, there was no reduction in stroke recurrence (despite a 5/3 mmHg reduction in BP), suggesting benefit comes from adding the thiazide, which further reduced BP of 12/5 mmHg.

Legend for Table 6

ACE: angiotensin-converting enzyme
CCB: calcium channel blocker
CHF: congestive heart failure
CVD: cardiovascular disease
BP: blood pressure
ARB: angiotensin receptor blocker
TIA: transient ischemic attack
CVA: cardiovascular accident

PROGRESS (Perindopril Protection Against Recurrent Stroke Study) study found that the combination of an ACE inhibitor and a thiazide diuretic decreased the risk of recurrent stroke in patients with a previous transient ischemic attack or cardiovascular accident, regardless of their initial BP.[11] Ongoing analysis of the Syst-Eur data shows that lowering BP in the elderly also impacts the development and progression of dementia.[12,13]

It remains to be seen how these new studies will be incorporated into the latest iteration of the Canadian recommendations for the management of hypertension. In the end, it may prove that lowering BP with any combination of agents will have the same impact on the significant morbidity and mortality associated with hypertension.

When is a referral to a specialist needed?

Refractory hypertension

This is usually defined as BP that is not adequately controlled with three antihypertensives.

Suspected secondary hypertension

This includes potentially curable disorders, such as: pheochromocytoma, Cushing's syndrome, primary aldosteronism, hyperthyroidism, myxedema, coarctation of the aorta, renal vascular disease, and renal parenchymal diseases.

Other

Selected patients with multiple cardiovascular risk factors and/ or target organ damage. CME

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Take-home message

1. Hypertension remains highly prevalent and poorly controlled.
2. In selected patients (those suspected of "white coat" hypertension or poor compliance, patients with refractory hypertension, and patients not responding to therapy or exhibiting symptoms of hypotension), the use of home BP monitoring and/or ABP monitoring should be considered in their diagnosis and management.
3. Although all patients are initially started on monotherapy, the majority of patients will require multiple medications to achieve their BP targets. In particular, patients with diabetes mellitus and/ or nephropathy often require several medications to achieve lower target BP levels.
4. There is still a great deal of debate in regard to whether the benefits seen in recent randomised trials were attributable to specific agents used or to the degree of BP lowering achieved.
5. The Canadian Consensus Guidelines on Hypertension are updated annually and are published each spring. These guidelines provide the latest evidence-based information on diagnosis and management. These guidelines recommend appropriate treatment of hypertension and have become the standard of practice.

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FAQs

Hypertension Guidelines

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By David Wood, MD; Mann Chandavimol, MD, FRCPC; and Andrew Ignaszewski, MD, FRCPC

1. What agent should be used as initial therapy in a newly diagnosed hypertensive patient?

In almost all cases, a thiazide diuretic—see Table 5 in the article for the 2001 Canadian Guidelines for Hypertension.

2. What should I add if the BP remains above target on a thiazide?

Angiotensin-converting enzyme (ACE) inhibitor/angiotensin receptor blocker (ARB) or beta blocker.

3. What should I add if the BP is still elevated on a thiazide and ACE inhibitor?

It is safe to add a beta blocker or a long-acting calcium channel blocker.

4. Are there differences in treatment for non-Caucasians?

Yes. Both beta blockers and ACE inhibitors appear to be less effective in African-Americans. Asian patients appear to have an increased incidence of cough with ACE inhibitors.

5. What should I do if the patient remains hypertensive on a thiazide, ACE inhibitor, and beta blocker?

At this point, you should refer the patient to a specialist.

For an in-depth article on hypertension, please go to page 99.