

# THE 2001 CANADIAN HYPERTENSION RECOMMENDATIONS



**This article highlights those recommendations that are new, revised or important to improve blood pressure control in Canada. New recommendations of specific interest include an updated section on management of hypertension in individuals with diabetes.**

Prepared by the Canadian Hypertension Recommendations Working Group

**H**ypertension is one of the most common reasons for an adult patient to visit a physician and is estimated to be the third leading risk associated with death worldwide.<sup>1</sup> The last reliable data on hypertension prevalence and control in Canada is 10 to 15 years old.<sup>2</sup> At that time, 22% of adult Canadians had high blood pressure (BP) and only 16% of those had their hypertension treated and controlled.

Preliminary data (Campbell-unpublished) suggest a significant increase in prescriptions of major classes of antihypertensive agents. This coincides with the introduction of the annual recommendations and implementation process. Whether this reflects an improvement in treatment and control of hypertension, however, is uncertain. Unfortunately, our national health surveillance is inadequate to determine whether hypertension prevalence, awareness, treatment or control has changed.

What data are available encourages all health-care professionals to prioritize hypertension as a public health issue and aggressively identify, treat and control hypertensive patients according to the best available evidence and recommendations.

This is the third year Canada has comprehensively updated its hypertension recommendations.<sup>3-5</sup> The recommendations are linked to an expanding implementation effort.<sup>6</sup> This is a brief summary of the 2001 recommendations, highlighting those recommendations that are new, revised or important in improving BP control in Canada. New recommendations of specific interest are an updated section on management of hypertension in individuals with diabetes, including new recommendations for initial therapy, and a new recommendation to lower BP following the acute phase of strokes or transient ischemic attacks (TIAs).



Table 1

### Screening for Renovascular Hypertension

Patients with the characteristics listed below, who are candidates for angioplasty or revascularization, should be screened for renovascular hypertension with a post captopril renogram:

- Uncontrolled hypertension despite therapy with  $\geq 3$  drugs;
- Deteriorating renal function; and
- Recurrent episodes of flash pulmonary edema.

The arbitrary classification of old and young persons at age 60 has been removed. Evidence for an age effect is required, as opposed to the previous requirement for evidence in the specific age categories. This has resulted in a more aggressive threshold for initiating therapy in those aged  $> 60$ . The recommendation to switch first-line therapies when there is inadequate response has been changed to a recommendation to combine first-line therapies. This recognizes the need for multiple drugs (to control hypertension) and the sequential method of adding medications used in major therapeutic trials. There are also new comprehensive sections on management of patients with pheochromocytoma and hyperaldosteronism.

The purpose of this summary is to provide a rapid update to the 2000 Canadian Hypertension Recommendations.<sup>4,5</sup> A full publication of the comprehensive recommendations will be published separately. The latter publication is intended to be a scientific reference and not a clinical practice guideline. A slide kit and clinical practice algorithms, supporting the full 2001 recommendations, will soon be available to download at [www.chs.md](http://www.chs.md).

The methods for producing the recommendations have been published previously, but there have been some revisions.<sup>7</sup> In 2001, a separate meeting of those involved in the production of recommendations was held to discuss new, changed or controversial recommendations and evidence. In 2000, a voting process was adopted which excludes

recommendations with which  $\geq 30\%$  of those involved in the subgroups, central review committee and steering committee disagree. This process was continued in 2001, but individuals with a direct conflict of interest on specific recommendations were excluded from voting on those recommendations. Those with conflict of interest participated in the discussions following disclosure. The recommendations were based on the results of literature searches (to at least March 2001), personal knowledge of published literature, contact with authors and major clinical trials published prior to November 2001.

### Diagnosis

Although there are no substantive changes to this section, diagnosis is critical to the management of hypertension. The recommendations highlight the importance of assessing the BP of all adults using the proper measurement technique at all appropriate visits. Hypertension can be diagnosed immediately if there is a hypertensive urgency or crisis and can be diagnosed in three visits in the presence of target organ damage among patients who are clinically stable. Diagnosis requires up to five visits, however, if there is no target organ damage and the initial BP is  $< 180/105$  mmHg. Although the recommendation for five visits represents a substantive workload, those whose BP falls to  $< 140/90$  mmHg with observation have a normal prognosis and can

Table 2

### Screening for Pheochromocytoma

Patients with the following characteristics should be considered for screening for pheochromocytoma with a 24-hour urine for metanephrines and creatine\*:

- Paroxysmal and/or severe sustained hypertension refractory to usual antihypertensive therapy;
- Hypertension and symptoms suggestive of catecholamine excess (two or more of headaches, palpitations, sweating, etc.);
- Hypertension triggered by beta blockers, monoamine oxidase inhibitors, micturation, or changes in abdominal pressure;
- Incidentally discovered adrenal adenoma; or
- Multiple endocrine neoplasia (MEN) 2A or 2B; von Recklinghausen's neurofibromatosis, or von Hippel-Lindau disease.

\*Assessment of urinary vanillylmandelic acid is inadequate.

avoid labeling and interventions that may harm them.<sup>8</sup> Self-measurement and 24-hour ambulatory measurement continue to be recommended for consideration in assessing office-induced BP elevation and the former to improve patient compliance. Only devices meeting international standards should be used.<sup>9</sup> Daytime BP < 135/85 mmHg, with ambulatory and self-measurement, is associated with a normal prognosis.

Routine laboratory assessment should be performed at diagnosis and should include the following:

- Blood for electrolytes;
- Creatinine;
- Fasting glucose;
- Complete blood count;
- Lipid profile (total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol and triglycerides);
- A urinalysis; and
- An electrocardiogram.

Criteria for screening patients for renovascular hypertension, using a post captopril renogram (Table 1) and pheochromocytoma (Table 2), with a 24-hour urine for metanephrines and creatinine, is provided. Screening patients for pheochromocytoma by assessment of urinary

vanillylmandelic acid (VMA) is inadequate.

More recent studies have confirmed hyperaldosteronism is relatively common. Screening for hyperaldosteronism should include assessment of a plasma aldosterone and plasma renin activity, measured in morning samples taken from patients in a sitting position after resting at least 15 minutes. Antihypertensive drugs, with the exception of aldosterone antagonists, may be continued prior to testing. The criteria for selecting patients to be screened for hyperaldosteronism is shown in Table 3. Comprehensive recommendations for the diagnosis and management of pheochromocytoma and hyperaldosteronism will be published with the detailed 2001 hypertension recommendations.

The recommendations say to quantitatively assess a patient's cardiovascular risk and adopt a multifactorial approach for treating hypertension. A variety of methods can be used (Table 4).<sup>10-14</sup>

Individualized lifestyle modification is recommended for all patients with hypertension and those at risk of developing hypertension. A diet consistent with Canada's Guide to Healthy Eating (*i.e.*, high in fresh fruit, vegetables and low-fat dairy products, and

Table 3

### Screening for Hyperaldosteronism

Screening for hyperaldosteronism should be considered for at least hypertensive patients with the following characteristics\*:

- Spontaneous hypokalemia;
- Profound diuretic-induced hypokalemia (< 3.0 mmol/L);
- Hypertension refractory to treatment with  $\geq$  drugs; and
- Incidental adrenal adenomas.

\* Screening for hyperaldosteronism should include assessment of a plasma aldosterone and plasma renin activity measured in morning samples taken from patients in a sitting position after resting at least 15 minutes. Antihypertensive drugs, with the exception of aldosterone antagonists, may be continued prior to testing.

low in saturated fat), and limitation of salt additives and foods with excessive added salt, will lower BP. Other lifestyle changes effective in reducing BP include the following:

- Weight loss (4.5 kg [10 pounds] minimum) in those who are overweight;
- Regular physical activity (optimum 45 to 60 minutes of moderate activity [brisk walk] four to five times per week); and
- Low-risk alcohol consumption (zero to two drinks per day — < 14 drinks per week in men and < 9 drinks per week in women).

Cognitive behavior modification for stress management is effective in some individuals. Because smoking is a major cardiovascular risk factor, has greater than additive risk in hypertensive persons and reduces or abolishes the beneficial outcomes associated with antihypertensive therapy, smoking cessation should be strongly encouraged in all hypertensive patients.

Drug treatment is recommended if the diastolic BP (DBP) is > 90 mmHg and there is cardiovascular disease, other target organ damage or cardiovascular risk factors. Most hypertensive patients have additional risk factors or target organ damage. If these are not present, however, the lower cardiovascular risk has resulted in a recommendation to treat DBP > 100 mmHg or systolic BP > 160 mmHg. Initial drugs for diastolic and combined sys-

tolic and diastolic hypertension include diuretics, long-acting dihydropyridine calcium channel blockers (CCBs) and angiotensin converting enzyme (ACE) inhibitors. Beta blockers are recommended as first-line therapy in those < age 60. Alpha blockers are not recommended as first-line therapy and short-acting CCBs should not be used as antihypertensive agents. For isolated systolic hypertension, initial therapy should be with a low-dose thiazide-like diuretic or a long-acting dihydropyridine CCB.

In individuals with diabetes mellitus, ACE inhibitors are recommended as first-line therapy in all situations. Low dose thiazide-like diuretics and long-acting dihydropyridine CCBs are recommended as alternative first-line agents in isolated systolic hypertension. Angiotensin II receptor blockers (ARBs) are recommended as alternative first-line agents to ACE inhibitors in the presence of diabetic renal disease (*i.e.*, microalbuminuria > 30 mg/24 hours).

As in the previous year, one of the most important aspects of the recommendations is the need to control BP in treated patients. The reduction of BP to < 140/90 mmHg is recommended in most patients, including the elderly. The reduction of BP to < 130/80 mmHg also is recommended in patients with diabetes mellitus or renal dysfunction. Lowering BP to < 125/75 mmHg is recommended in patients with renal dysfunction and > 1 g/day proteinuria.

Table 4

**Cardiovascular Risk Assessment**

Cardiovascular risk assessment methods, based on Framingham data, can be performed in many ways:

- For desktop computers at [www.hyp.ac.uk/bhs/management.html](http://www.hyp.ac.uk/bhs/management.html);
- For palm-type devices at [www.statcoder.com/cardiac.htm](http://www.statcoder.com/cardiac.htm);
- Through the use of risk charts at [www.hyp.ac.uk/bhs/management.html](http://www.hyp.ac.uk/bhs/management.html) or J Hypertens 1999; 17:151.83;<sup>10</sup>
- By calculators with the formula incorporated;
- Can be found in JAMA 2001; 285:2486-97<sup>11</sup>, Circulation 1999; 100:1481-92<sup>12</sup>, J Human Hypertens 1999; 13:569-92<sup>13</sup> or BMJ 2000; 320:709-10.<sup>14</sup>

A new change is the recommendation to use combinations of medications if the initial choice is ineffective and to switch to alternative first-line agents only if there is intolerance or adverse effects. The average BP lowering of a single drug is about 10/5 mmHg. In the large outcome trials, sequential addition of antihypertensive medications were prescribed to achieve BP targets and the use of multiple agents was necessary in a large proportion of patients. Table 5 indicates combinations of first-line agents that have an additive hypotensive effect when used in combination for the treatment of uncomplicated hypertension. Other first-line, dual agent therapies have less than additive hypotensive effects and are recommended only for specific indications (*i.e.*, beta blockers and ACE inhibitors in patients following a myocardial infarction).

When using triple or quadruple therapy in uncomplicated hypertension, all potential antihypertensive combinations of first-line agents are effective. Individual physicians need to assess their personal skill and experience in determining the need for speciality consultation for resistant hypertension. In patients who have little response to appropriate single or combination medications, consider non-adherence, secondary hypertension, interfering

drugs or lifestyle and/or office-induced increases in BP (whitecoat effect).

In specific patient subgroups there are further treatment recommendations (Table 6). A notable change is the recommendation to strongly consider antihypertensive therapy in those who have had a non-disabling stroke or TIA after the acute phase. The Perindopril Protection Against Recurrent Stroke Study (PROGRESS) demonstrated a reduction in recurrent cerebrovascular events when BP was lowered in both hypertensive and normotensive individuals.<sup>15</sup>

Patient compliance is still a major challenge and should be addressed by health-care professionals at each medical visit.

### *Recommendations Process*

There were 105 recommendations produced and 38 eligible voters (subgroup, central review committee and steering committee membership). For 22 recommendations there was no disagreement, 74 recommendations had one vote in disagreement, seven recommendations had two votes in disagreement and two recommendations had three votes in disagreement. The recommendation that had

## 2001 Recommendations

Table 5


### Additive Hypotensive Effect

For additive hypotensive effect in dual therapy, combine an agent from column 1 with any in column 2\*:

Column 1	Column 2
Low-dose thiazide diuretic Long-acting dihydropyridine Calcium channel blocker	Beta blocker Angiotensin converting enzyme inhibitor**

\* Dual combination of agents within column 1 and within column 2 have less than additive hypotensive effect, but may be indicated in specific settings (*i.e.*, column 2 drugs in patients following myocardial infarction.)

\*\* Angiotensin receptor blockers (ARBs) are an alternative initial choice in patients with diabetes and nephropathy.

the greatest disagreement was voted against by 8% of eligible voters. It is important to note that individuals involved in the recommendations process, or in a subgroup, may have personally opposed specific recommendations. Acknowledgement of an individual's contribution to the hypertension recommendations process, therefore, does not indicate personal support for any specific recommendation. 

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Table 6

## Considerations in the Individualization of Antihypertensive Therapy

Risk Factor/Disease	Initial Therapy	Second Step Therapy	Notes/Cautions*
Uncomplicated hypertension	Low-dose thiazide-like diuretics, beta blockers, ACE** inhibitors or long-acting dihydropyridine CCB***	Combinations of first-line drugs. See Table 5.	Alpha blockers are not recommended as initial therapy. Beta blockers are not recommended as initial therapy in those > age 60. Hypokalemia should be avoided by using K**** sparing agents in those prescribed diuretics
Isolated systolic hypertension	Low-dose thiazide-like diuretics, or long-acting dihydropyridine CCB	_____	Hypokalemia should be avoided by using K sparing agents in those prescribed diuretics
Diabetes mellitus with nephropathy	ACE inhibitors (alternatively, angiotensin II receptor blockers)	One or more of low-dose thiazide-like diuretics, cardioselective beta blockers, long-acting CCBs	If the serum creatinine is > 150 µmol/L, a loop diuretic should be used as a replacement for a low-dose thiazide diuretic if volume control is required
Diabetes mellitus without nephropathy	ACE inhibitors	One or more of angiotensin II receptor blockers, low-dose thiazide-like diuretics, cardioselective beta blockers, long-acting CCBs	_____
Diabetes mellitus without nephropathy, with systolic hypertension	ACE inhibitors (alternatively, low-dose thiazide diuretics, long-acting dihydropyridine CCBs)	_____	_____
Angina	Beta blockers (consider ACE inhibitors as add-on therapy)	Long-acting CCBs	_____
Prior myocardial infarction	Beta blockers and/or ACE inhibitors	Combinations of additional agents	_____
Systolic dysfunction	ACE inhibitors (thiazide or loop diuretics, beta blockers, spironolactone as additive therapy)	Angiotensin II receptor blockers, hydralazine/isosorbide dinitrate, Amlopidine	Avoid non-dihydropyridine CCBs (diltiazem, verapamil)
Past cerebrovascular accident or TIA*****	Strongly consider blood pressure reduction after the acute phase	_____	Blood pressure reduction reduces recurrent cerebrovascular events
Renal disease	ACE inhibitors (diuretics as additive therapy)	Combinations of additional agents	ACE inhibitors if bilateral renal artery stenosis
Left ventricular hypertrophy	Does not affect initial treatment recommendations	Does not affect initial treatment recommendations	Avoid hydralazine and minoxidil
Peripheral arterial disease	Does not affect initial treatment recommendations	Does not affect initial treatment recommendations	Beta blockers (with severe disease)
Dyslipidemia	Does not affect initial treatment recommendations	Does not affect initial treatment recommendations	_____

Short-acting CCBs are not recommended in the treatment of hypertension.

\* When using two drugs specifically to lower blood pressure, use Table 5 to maximize the hypotensive effect.

\*\* Angiotensin converting enzyme \*\*\* Calcium channel blocker \*\*\*\* Potassium \*\*\*\*\* Transient ischemic attack

### Case Discussion

Pharmacotherapy to reduce BP is indicated. The choice is a low dose thiazide-like diuretic, an angiotensin converting enzyme (ACE) inhibitor, or a long-acting dihydropyridine calcium channel blocker (CCB).

Beta blockers are less effective in those > age 60 and should not be used as first-line therapy. A low dose thiazide-like diuretic is selected. Potassium should be watched carefully as hypokalemia is associated with higher morbidity. A potassium-sparing diuretic combination could be selected to help prevent hypokalemia.

In order to achieve a BP target < 140/90 mmHg, additional agents are likely required. Using Table 5 to assist in the choice of therapy, an ACE inhibitor is selected as the second agent. The potassium sparing component of a combination diuretic may need to be discontinued to avoid hyperkalemia. Because Mr. John's BP is still 138/94 mmHg, a third agent is required. Either a beta blocker or CCB is a reasonable third-line agent to add to this regime.

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