2006 Canadian Hypertension Education Program Recommendations:

What Are The New Messages?

Hypertension remains a significant health problem—one that is predicted to become a greater global burden in the next 20 years. It is predicted that by 2025, the number of adults worldwide with hypertension will increase by about 60%. The estimated total number of adults with hypertension in 2000 was 972 million. The number of adults with hypertension in 2025 is predicted to increase by about 60% to a total of 1.56 billion.[1] Hence, hypertension is an important public health challenge worldwide. Prevention, detection, treatment and control of this condition should receive high priority. The Canadian Hypertension Education Program (CHEP) has a mandate to improve hypertension management, to develop tools to aid health care professionals and to evaluate the impact of our activities. CHEP continues to provide the most current evidence-based recommendations to Canadian health care workers.

Evidence-based recommendations on behalf of the Canadian Hypertension Education Program

This marks the seventh consecutive year that the Canadian Hypertension Education Program (CHEP) has updated recommendations for the diagnosis, management and treatment of hypertension. This year, CHEP's recommendations focused on adherence to antihypertensive therapy. In addition, based on new and additional evidence, a few changes relating to pharmacological treatment were introduced. Furthermore, CHEP identified that treated hypertensive patients, with masked hypertension (BP controlled in the office but not at home), should monitor home/self BP.

The new key messages identified in the 2006 recommendations

This new messages need to be incorporated into what remain as the older—but still important—considerations for the diagnosis, management and treatment of the patient with hypertension, namely:

- Assess BP in all adults at all appropriate visits
- Expedite the diagnosis of hypertension
- Assess and manage global cardiovascular risk
- Use combinations of antihypertensive medications and lifestyles modifications to achieve recommended targets

Key elements of the 2006 recommendation process

The 2006 Canadian Hypertension Recommendations process incorporated all trials and epidemiological studies published in the past 12 months, which were considered to be relevant for the diagnosis, management and treatment of individuals with hypertension.

The impact of these studies was considered in the context of the cumulative evidence of the past 50 years of major clinical trials in hypertension and in the context of the prior iterations of the evidence-based Canadian Hypertension Recommendations developed over the past 25 years. For the 2006 CHEP Recommendations, the incorporated clinical studies included the:

- Anglo-Scandinavian Cardiac Outcomes Trial-BP Lowering Arm (ASCOT-BPLA),[2-3]
- Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT),[4]

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- Valsartan in Acute Myocardial Infarction Trial (VALIANT),[5]
- Self-measurement of BP at Home in the Elderly: Assessment and Follow-up (SHEAF) study,[6]
- a number of smaller studies, systemic reviews and
- the Cochrane Database.

The new key messages in the 2006 recommendations

Adherence with an antihypertensive prescription can be improved by a multi-pronged approach, including:

1. Assisting your patient to adhere

- Teach patients to take their pills on a regular schedule associated with a routine daily activity (*e.g.*, brushing teeth)
- Simplify medication regimens using long-acting once-daily dosing
- Utilize fixed-dose combination pills
- Utilize unit-of-use packaging (*e.g.*, blister packaging)

2. Getting your patient more involved in their treatment

- Educate patients and patient's families about their disease/treatment regimens verbally and in writing.
- Encourage greater patient responsibility/autonomy in regular monitoring of their BP

3. Improving hypertension management in the office and beyond

- Assess adherence to non-pharmacologic and pharmacologic therapy at every visit
- Encourage adherence to therapy by healthcare practitioner-based telephone contact, particularly over the first three months of therapy
- Coordinate with work-site healthcare providers, if available, to improve hypertension management and monitoring

These recommendations were based on an initial survey of related studies from PsycInfo (including 210 original papers and reviews) and Medline (including 769 original papers and reviews) over the past three years.

Low adherence of patients to prescribed, self-administered antihypertensive drugs is a major problem contributing, in part, to poor control of hypertension. In general, patients who are prescribed self-administered medications typically take less than half the prescribed doses. Efforts to assist patients to follow medication protocols may improve the efficiency of care and enhance the benefits. In Canada, suboptimal control of hypertension is attributed, in part, to patients who stop taking their antihypertensive drugs after one year. Accordingly adherence needs to be stressed and this is a major focus of the 2006 CHEP recommendations.

With the cut-off point between normal and high BP being pushed increasingly downward, particularly for patients with multiple cardiovascular risk factors, most hypertensive patients need more than one antihypertensive agent to reach their target BP. Furthermore, guidelines indicate that low doses of multiple drugs may be even more efficacious than higher doses of fewer drugs.

The increasing complexity of self-administration with the use of multiple drugs and the consequent likelihood for reduction in adherence remains an ongoing problem. Interventions that aim to simplify dosages involve the use of fixed-dose combination pills (*i.e.*, pills that include two or more drugs in fixed proportions in the same formulation) and unit-of-use packaging (*i.e.*, blister packaging of several medications in fixed combination to be taken together). Rational antihypertensive drug combinations are based on their ability to produce additive BP-lowering effects and to reduce the incidence of dose-dependent side-effects.[7]

A recent retrospective analysis of medication adherence by Taylor and Shoheiber[8] compared 2,754

patients who were prescribed a single capsule, fixed-dose combination of amlodipine besylate/ benazepril HCl with 2,978 patients who were prescribed an angiotensin-converting enzyme (ACE) inhibitor and a dihydropyridine calcium channel blocker as separate drugs. Results indicated improved adherence and fewer medical resource requirements for the fixed-dose combination pill group. Therefore, the 2006 CHEP recommendations suggest simplification of the drug regime as a strategy to improve adherence.

A systematic review of randomized controlled trials (RCTs) evaluating the effects of fixed-dose combination pills and unit-of-use packaging[9] concluded that in 12 of 15 trials identified, there were trends indicating improved clinical and/or adherence outcomes. While the trials reviewed were heterogeneous in their settings, the medical conditions being treated and the outcome measures used, three out of the four trials that involved unit-of-use packaging for the treatment of hypertension reported clinically significant reductions in BP. Although interpretation of these findings is limited by the methodological quality of the studies (most were small or had inadequate follow-up time), those with greater methodological rigor were typically associated with larger improvements in measures of adherence and clinical outcomes, including BP reduction.

Looking at patient followup

The proposed revision to the recommendations, in regards to encouraging a role of telephone followups, is primarily based on generalizations from the management of dyslipidemia and is specifically based on the systematic review by Schedlbauer *et al.*[10] In that review, reinforcement and reminders via telephone and postal back-ups were the interventions of interest in three studies selected among 2,380 articles. Weekly phone calls were reported as improving adherence to lovastatin and colestipol in the intervention group, which was judged by prescription refill rate (rate was improved by 24%; 63% in the intervention group vs. 39% in the control group, p-value < 0.05; n = 30).[11] It is notable that telephone and postal reminders in the remaining two RCTs did not result in any significant improvement (79.7% in the intervention group vs. 77.4% in the control group, p-value reported as non significant; n = 4,548;[12] and 88% in the intervention group vs. 82% in the control group, p = 0.32; n = 120).[13] However, the study by Faulkner *et al*[11] was viewed as being of higher quality than the other two (notwithstanding the smaller sample size) and is the primary basis of the proposed revision in the 2006 CHEP recommendations. In addition, studies that predominantly enrolled adherent patients will not be able to improve the adherence of these patients, regardless of the intervention.

New and additional evidence in the pharmacologic treatment of patients with hypertension

Beta-blocker (ß-blocker) therapy is strongly recommended in hypertensive patients of all ages who have specific indications, such as post-MI, angina and congestive heart failure. However, new evidence—based on findings from a recent meta-analysis[14-15]— further supports the use of ß-blockers as a first-line therapy of uncomplicated hypertension in patients younger than 60 years. This recommendation is not new, but is further supported by the new evidence. Trials demonstrate the inferiority of ß-blockers in reducing cardiovascular events in uncomplicated hypertension in older patients, compared to diuretics, angiotensin receptor blockers (ARBs) and calcium channel blockers (CCBs).

Additional antihypertensive drugs should be used if target BP levels are not achieved with standard dose monotherapy (Grade B). Add-on drugs should be chosen from first-line choices, which include a thiazide diuretic or CCB with either an ACE inhibitor, ARB or

ß-blocker (Grade D and/or Grade C for the combination of dihydropyridine CCB and ACE inhibitor). Caution should be exercised in combining a nondihydropyridine CCB and a ß-blocker (Grade D).

This year, the grade of evidence supporting the combination of a dihydropyridine CCB and an ACE inhibitor was increased from a D to a C. This change is based in large part on the results of the ASCOT-BPLA, which showed significantly lower rates of coronary and stroke events in individuals allocated an amlodipine-based combination drug regimen than in those allocated an atenolol-based combination drug regimen.[2-3] This trial was complicated by the use of ß-blockers as initial therapy in a predominantly older study population. Therefore, the design of the trial would be expected to favour the amlodipine-based combination therapy.

The results of one study suggest that the prognostic value of home BP is better than clinic BP and similar to daytime ambulatory BP

Initial therapy in patients with hypertension who have had a recent ST-elevation MI or non ST-segment elevation myocardial infarction should include both a ß-adrenergic antagonist and an ACE inhibitor. An ARB can be used if the patient is intolerant of an ACE inhibitor. These recommendations are based on findings from the VALIANT trial,[5] which assessed effects of valsartan or captopril (or the combination of the two) in patients with post-MI with heart failure or systolic dysfunction, or both. Total mortality and the combined secondary end point of cardiovascular death (CVD), MI or heart failure were not significantly different in the three groups after 24.7 months of followup. Valsartan was not inferior to captopril in terms of total mortality and cardiovascular death, MI and heart failure. Hence, valsartan can be considered an alternative treatment to ACE inhibitors in these patients.

ACE inhibitors, combined with ARBs, have a positive role in the management of cardiac failure; however, a higher rate of hospitalization for hypotension, hyperkalemia and worsening renal failure has been seen in clinical practice. Careful monitoring is required to ensure patient safety during this combination of therapies.

Home/self measurement of BP

Certain issues appeared to dominate the literature in the area of home/self-measurement in 2004-2005. In 2004, the release of the SHEAF study demonstrated not only the prognostic strength of home BP measuring, but provided, for the first time, data documenting the mortality risk of masked hypertension, which is defined as clinic BP < 140/90 mmHg (three measurements at two office visits) and home BP > 135/85 mmHg (three measurements in the morning and in the evening over two days).[16] More recent analyses of SHEAF data focused on the number of measurements necessary to determine masked hypertension.[17] The SHEAF data provides perhaps the clearest evidence that the risk profile of those with masked hypertension is similar to the risk profile of those with sustained hypertension.

The prognostic significance of home BP measurement was demonstrated again in an 11-year follow-up study of elderly patients.[18] The study results suggest that the prognostic value of home BP is better than clinic BP and is similar to daytime ambulatory BP. Results further demonstrated the importance of the setting for BP measurement (home vs. clinic), strengthening the need to emphasize home rather than self in the terminology used to describe these measurements.

With respect to prognosis, more data from the Ohasama Study[19] show that in addition to the BP measured at home, the home heart rate is a powerful

Table 1

Considerations in the Individualization of Antihypertensive Therapy

Symptoms	Initial therapy	Second-line therapy	Notes and/or cautions
Hypertension without compelling indications for other medications	Thiazide diuretics, beta-blockers (ß-blockers) for patients under 60 years, angiogestin converting enzyme (ACE) inhibitors (in non-African-Americans), angiogestin receptor blockers (ARBs), or long-acting calcium channel blockers (CCBs) (consider acetylsalicylic acid [ASA] and/or statins in selected patients)	Combinations of first-line drugs	Alpha-blockers are not recommended as initial monotherapy. Beta-blockers are not recommended as initial monotherapy in those 60 years of age and older. Hypokalemia should be avoided in those who are prescribed diuretics. ACE inhibitors are not recommended as initial monotherapy in African-Americans. ACE inhibitors and ARBs are contraindicated in pregnancy
Isolated systolic hypertension without compelling indications	Thiazide diuretics, ARBs or long-acting dihydropyridine CCBs	Combinations of first-line drugs	Hypokalemia should be avoided by using potassium-sparing agents in those prescribed diuretics
Diabetes mellitus with nephropathy	ACE inhibitors or ARBs	Addition of one or more of thiazide diuretics, cardio-selective ß-blockers, long-acting CCBs or use of an ARB/ACE inhibitor combination	
Diabetes mellitus without nephropathy	ACE inhibitors, ARBs, thiazide diuretics or dihydropyridine CCB	Combination of first-line drugs or addition of cardioselective ß-blockers	
Angina	ß-blockers (strongly consider adding ACE inhibitors)	Long-acting CCBs	Avoid short-acting nifedipine
Prior MI	ß-blockers and ACE inhibitors (ARBs if ACE inhibitor intolerant)		
Heart failure	ACE inhibitors (ARBs if ACE inhibitor intolerant), ß-blockers, or spironolactone in selected patients	ARBs or hydralazine/isosorbide dinitrate, thiazide or loop diuretics	Avoid nondihydropyridine CCBs. If combining ACE inhibitors and ARBs, monitor for potential adverse events, including hypotension, hyperkalemia and worsening renal function
Past cerebrovascular accident or transient ischemic attack	ACE inhibitor/diuretic combinations		Caution is indicated in deciding whether to lower BP in the acute stroke situation. Pharmacologic agents and routes of administration should be chosen to avoid precipitous falls in BP
Left ventricular hypertrophy	ACE inhibitors, ARBs, CCBs, thiazide diuretics or ß-blockers for patients under 60 years of age		Avoid hydralazine and minoxidil
Peripheral arterial disease	Does not affect treatment recommendations		Avoid ß-blockers with severe disease
Dyslipidemia	Does not affect treatment recommendations		

independent predictor of cardiovascular risk.

The concept of masked hypertension is not new. In general, the term describes the phenomena when clinic BP is normal, but out-of-office readings are in the hypertensive range. Masked hypertension has been variously called: reverse-white coat hypertension or isolated home or isolated ambulatory hypertension, depending on the type of method used to find it. Several of the issues and the history surrounding masked hypertension were discussed in the 2005 subcommittee report.

Important issues still to be resolved centre around how to define masked hypertension in a patient and what method (ambulatory BP or home BP) is most appropriate for making the diagnosis.

The old but still important messages in the 2006 Recommendations[20-21]

1. Measure BP in all adults at all appropriate visits

In the last survey of BP (1985-1992), 43% of adults with high BP were not aware their BP was elevated. This places a large proportion of the Canadian population at preventable risk for cardiovascular disease, due to uncontrolled hypertension. Recent data from the Framingham Study has indicated that over 90% of normotensive participants aged 55 to 65 developed hypertension over the 20 years to 30 years of followup. Forty-six percent of Canadians aged 55 to 65 already have hypertension. It is therefore expected that the vast majority of Canadians will develop hypertension. Measuring the BP of all adults every time they visit your office is an important mechanism to detect hypertension and an opportunity to discuss preventive strategies using lifestyle modification.

2. The diagnosis of hypertension can and should be expedited

A diagnosis of hypertension can be made at an initial hypertension-related visit for patients whose BP is > 140/90 mmHg and with either:

- target organ damage,
- chronic kidney disease or
- diabetes mellitus.

A diagnosis of hypertension can be made if BP is > 180/110 mmHg at a second visit. For patients with BP between 160 mmHg to 179 mmHg/100 mmHg to 109 mmHg (and not already diagnosed based on the criteria above), a diagnosis can be made at a third visit.

Diagnosis can be expedited by home/self measurement of BP. Office-based diagnosis of hypertension has remained the gold standard for the diagnosis of hypertension. However, it is now firmly established that out-of-office modalities for BP measurement are as, or more, effective in assessing the prognostic importance of BP elevations. To be effective, these technologies, including automatic ambulatory BP monitoring and home/self BP monitoring must be used by properly educated practitioners or patients and assumes the use of validated, properly calibrated equipment. However, when available and properly used these modalities are effective and can expedite the diagnosis of hypertension, which would otherwise require up to six visits and six months prior to a diagnosis being made.

3. Assess and manage cardiovascular risk

Over 90% of hypertensive patients have additional cardiovascular risks that require assessment and management. Acetylsalicylic acid should be considered in controlled hypertensive patients. Statins are recommended in hypertensive patients with established cardiovascular disease or the presence of more than three other cardiovascular risks.

4. Lifestyle modifications are the cornerstone of antihypertensive therapy

Lifestyle modifications are safe and inexpensive, can prevent hypertension, can lower BP in hypertensive patients and when combined with drug therapy, may result in better BP control and improved quality of life.

Many of the individual factors, if successfully adopted, may lead to BP changes in the magnitude of that associated with single-drug therapy. Although each factor typically has a modest effect, the combined effects may be substantial. From a public health perspective, even a small reduction in BP should have a significant and beneficial effect on the occurrence of hypertension and its complications.

The lifestyle changes recommended by CHEP to reduce BP to target levels include:

- maintaining a diet that is low in salt and saturated fats and high in fresh fruit and vegetables and low in fat dairy products (DASH diet),
- performing 30 minutes to 60 minutes of exercise, such as walking, jogging, cycling or swimming, four to seven days per week;
- reducing weight in those who are overweight;
- reducing alcohol consumption in those who drink more than two drinks per day and
- the cessation of smoking and living/working in a smoke-free environment to reduce cardiovascular risk.

5. Treat to target

Population surveys demonstrate that small proportions of patients have BP treated to target resulting in suboptimal cardiovascular risk reduction. In particular in high risk patients greater benefits occur with achieving recommended targets. The systolic BP target is the more difficult to achieve in most patients. However, achieving systolic BP targets is important, as systolic BP is at least as important—if not more so—than diastolic BP in determining cardiovascular prognosis.

The current recommended target to reduce BP is:

- < 140 mmHg systolic and < 90 mmHg diastolic BP, in general and
- < 130/80 mmHg in patients with diabetes or chronic kidney disease.

6. Use combinations of medications and lifestyle modification to achieve BP targets

Most patients require two or more drugs to achieve recommended BP targets. Individualization of antihypertensive therapy should always be considered (Table 1). In general, the average reduction in BP, with a single BP lowering medication, is 10/5 mmHg. Combining medications is therefore to be expected in the therapy of hypertension. Using lifestyle modification can reduce the number and doses of medications that are required for BP control and should be recommended for all hypertensive patients. Dx

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