

# HYPERTENSION

## Canada



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### CHS President's Report

## Evolution of the Canadian Hypertension Society

By *Richard Lewanczuck*

Since its inception in 1979, the Canadian Hypertension Society (CHS) has undergone a progressive evolution. Established by individuals allied by a common interest in hypertension, the CHS became the professional voice for hypertension in Canada. Traditionally, the CHS has been strongly involved with the promotion of hypertension research and training in Canada. In addition, it promoted standards of clinical care for hypertension. More recently, this latter function has been transferred to an offshoot organization of the CHS: the Canadian Hypertension Education Program (CHEP). This latter organization, which now includes partners from a variety of government and non-government agencies and associations, maintains responsibility for the coordination of the yearly hypertension recommendations. Thus, while the role of the CHS has evolved over the years, I would say our role has undergone more of a maturation rather than an evolution in the past year.

In the past, the CHS "did it all," from promoting research and training, to developing clinical recommendations, to public advocacy. However, with the advent of CHEP and with the appearance of the Canadian Coalition for High Blood Pressure Prevention and Control (now known as Blood Pressure Canada) on the national scene, the CHS has refined its role. Indeed, a significant development in the past

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## President's Report

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year is that all three organizations have developed a clear understanding of their respective roles. Thus, by agreement, Blood Pressure Canada focuses on the public promotion of hypertension prevention, detection and control. CHEP maintains responsibility for coordinating the development of the yearly hypertension recommendations, focusing on health professionals. The CHS, in turn, continues to promote research and training in hypertension, supports CHEP in its clinical role and continues to advocate on behalf of hypertension-related issues in Canada. One can see how this division of responsibilities is complementary and mutually supportive. In fact, as a manifestation of this new-found partnership, all three organizations have agreed to move towards the establishment of a joint office—an event that will likely occur during the current year.

### CHEP: Improving the Health of Canadians

Although CHEP evolved as an offshoot of the CHS, it is now very much an independent, albeit related, organization. It has its own executive, its own steering committee and an independent budget. However, the vast majority of participants in CHEP are CHS members. Thus, the CHS is quite proud of its progeny in the form of CHEP. It should be recalled that the CHS was one of the first organizations in the world to pioneer and introduce evidence-based recommendations into the field of medicine. In keeping with this tradition, CHEP was the first organization to establish a formalized infrastructure to aid in the implementation of such recommendations. Finally, CHEP is also now the first organization to introduce a formal evaluation

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# CHEP: A National Program to Improve the Treatment and Control of Hypertension

By Norman Campbell, Denis Drouin, Finlay McAlister, Jay Onysko, Sheldon Tobe and Rhian Touyz

In the early 1990s, the U.S. had a hypertension treatment and control rate that was almost twice the Canadian rate. Americans with hypertension were also more likely to be aware of their diagnosis and to receive antihypertensive drug therapy. The U.S. has had the National High Blood Pressure Education Program (NHBPEP) for more than 30 years, potentially explaining their superior hypertension awareness, treatment and control rates. The Canadian Hypertension Education Program (CHEP) was developed in 2000, specifically to improve the treatment and control of hypertension in Canada. CHEP is sponsored by the Canadian Hypertension Society (CHS), Blood Pressure Canada, the Public Health Agency of Canada, the Heart and Stroke Foundation of Canada and the College of Family Physicians of Canada.

CHEP has three task forces (Figure 1) with the mandate to:

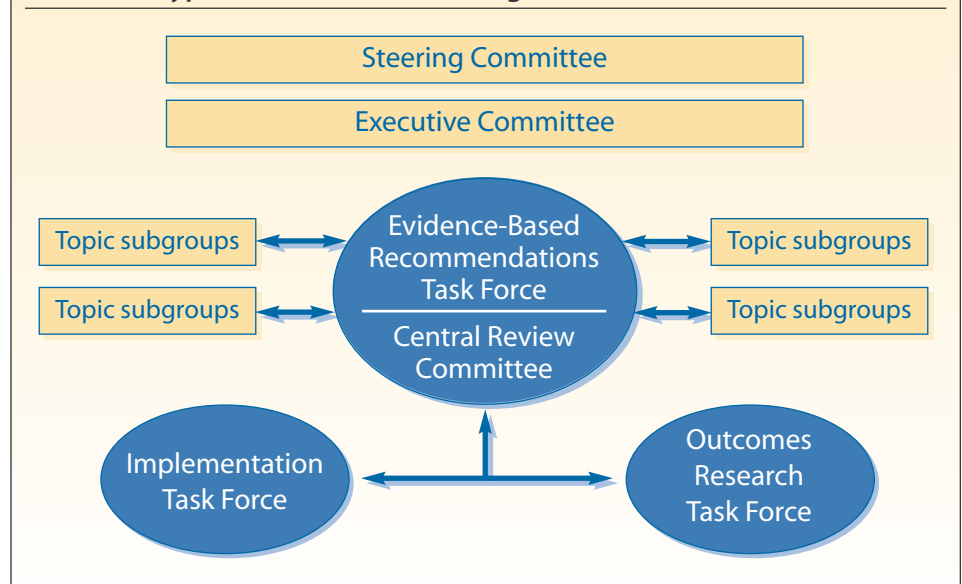
- 1) develop evidence-based management recommendations;
- 2) disseminate and assist the implementation of the recommendations; and
- 3) examine the impact of CHEP on hypertension management and hypertensive complications.

## Recommendations Task Force

The Recommendations Task Force has a highly structured and systematic approach, designed to reduce bias and increase transparency and value, rigor-

Figure 1

### The Organizational Structure of the Canadian Hypertension Education Program



ous research design and patient outcomes. The Task Force has 42 members in 14 subgroups (Figure 1) with assigned topics important to the treatment and control of hypertension. These subgroups draft recommendations based on systematic literature searches performed by a librarian. A committee of experts in evidence-based medicine, the Central Review Committee, reviews all recommendations and evidence to ensure a consistent approach to recommendation development, and negotiates revisions with the subgroups. The evidence and draft recommendations are debated and revised at an annual meeting of the task force and are presented at the Canadian Cardiovascular Congress. The full task force and executive vote on the draft recommenda-

tions and only those recommendations that achieve over 70% support are adopted. The lowest level of support for a recommendation has been more than 80%.

## Implementation Task Force

The implementation of recommendations involves all members of CHEP, as well as many other hypertension and education experts and opinion leaders from across Canada. The membership readdresses contentious issues and new evidence annually. The structured process deters divisive arguments based on the diversity of personal opinions.

The CHEP executive annually determines the key implementation messages to highlight new and important recommendations that are fundamental

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# When Should an ACE Inhibitor be Combined with an ARB?

By Luc Poirier

Angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs) are two classes of antihypertensive agents, commonly used in the treatment of arterial hypertension. Numerous large-scale clinical studies have demonstrated these agents' efficacy in preventing cardiovascular events in various hypertension-related pathologies, particularly with regard to diabetic nephropathy, post-infarction status and heart failure. They now number among the drugs of choice in patients with systolodiastolic or isolated systolic hypertension. In addition, their adverse-event profiles often give them an advantage over other first-line agents used in hypertensive patients.

For all these reasons, some clinicians now advocate combining these

conditions where the concomitant use of an ACE inhibitor and an ARB is justified.

## Mechanism of Action and Theoretical Aspects

ACE inhibitors decrease the production of angiotensin II by blocking the enzyme that converts angiotensin I into angiotensin II. However, despite a sustained reduction in BP, it has clearly been shown that the decrease in angiotensin II levels is only temporary and that this returns to initial levels after a few weeks of treatment. This situation, known as "ACE escape," is amply documented in the literature. Alternative pathways for the production of angiotensin II that do not involve ACE and instead use chymase, cathepsin and a tissue plasminogen activator, take over and enable the synthesis of angiotensin II. It appears that

at the level of the angiotensin I receptor. Thus the ACE escape that causes recovery of angiotensin II synthesis could be countered by adding an ARB that allows direct blockage of the angiotensin I receptor. It would be logical to think that this treatment combination would enable the blockage of both the production and action of angiotensin II and, as a corollary, provide an additive and even synergistic pharmacologic action.

## Additional BP Reduction

Some studies have assessed the efficacy of combining an ARB with an ACE inhibitor in order to obtain a further BP reduction, measured either clinically or via ambulatory BP monitoring. These studies have effectively demonstrated an additional reduction in systolic and diastolic BP vs. the administration of an ARB or an ACE inhibitor alone. However, the results are often inconsistent. Additional reductions were modest and not statistically significant. In addition, certain methodology problems hampered the interpretation of these studies. The use of suboptimal doses of the medication when used as monotherapy and a lack of comparison with treatments recognized as effective (*i.e.*, ARBs or ACE inhibitors with thiazide diuretics) were reported. Therefore, other than the efficacy of such combinations, the studies provide little information on the effectiveness of ACE inhibitor/ARB combinations in hypertensive patients with no associated pathologies. It should be noted

*Theoretically, ARBs allow more complete blockage of the renin-angiotensin system by acting directly at the level of the angiotensin AT1 receptor. Thus the ACE escape that causes recovery of angiotensin II synthesis could be countered by adding an ARB that allows direct blockage of the angiotensin AT1 receptor.*

two classes in order to achieve an additional decrease in blood pressure (BP) when trying to attain target BP levels. When treating hypertension, few situations justify the concomitant use of two agents from the same pharmacologic class, or which share a similar mechanism of action. This article will therefore attempt to highlight clinical

these alternative pathways are particularly active in pathological conditions that trigger high levels of oxidative stress, particularly when diabetes or proinflammatory vascular processes are present.

Theoretically, ARBs allow more complete blockage of the renin-angiotensin system by acting directly



that the Canadian guidelines for the treatment of hypertension recommend the administration of combined medications with complementary effects. Because of its high cost and the lack of conclusive data showing increased efficacy when compared with other cost-effective combinations, it would be logical to advocate the use of an ACE inhibitor/ARB combination only as a last resort (*i.e.*, in patients where target BP levels cannot be achieved despite optimal antihypertensive polypharmacotherapy).

#### **Additional Albumin Level Reduction**

Several studies have clearly shown a direct relationship between BP levels and cardiovascular morbidity/mortality. In diabetic patients presenting with chronic kidney failure, the literature clearly shows the benefits of strictly maintaining BP below 130/80 mmHg. The presence of microalbuminuria (30 to 300 mg/day) or an equivalent albumin-creatinine ratio in hypertensive patients with diabetes is also a major predictor of progression towards macroalbuminuria and overt kidney disease. Albuminuria is also a potent indicator of cardiovascular morbidity/mortality. Therefore, it appears advisable to reduce serum albumin levels to the greatest extent possible in order to lower cardiovascular and renal risks in all patients.

Many studies have assessed the benefits of the various classes of antihypertensive agents in reducing albuminuria. It has now been clearly demonstrated that blocking the renin-angiotensin system protects the kidneys. Thus, ACE inhibitors and ARBs are proven drugs of choice in hypertensive patients with diabetes. As they target the renin-angiotensin system, they

cause a greater reduction in albuminuria levels than other antihypertensive agents (*i.e.*, diuretics, beta-blockers, calcium channel blockers, etc.), with a comparable decrease in BP.

Several studies carried out in patient populations with type 2 diabetes and hypertension have shown that controlling BP is vitally important with regard to the occurrence of macrovascular complications (*i.e.*, myocardial infarction, stroke, kidney failure). To achieve this, it would appear more effective to

*In diabetic patients presenting with chronic kidney failure, the literature clearly shows the benefits of strictly maintaining BP below 130/80 mmHg.*

maximize the quality of the drug combinations used for the greatest possible reduction in BP and achievement of the 130/80 mmHg therapeutic target.

Studies using an ARB and ACE inhibitor combination have been carried out. The Candesartan and Lisinopril Microalbuminuria (CALM) study is one of the most important. This study evaluated the effects on the reduction of albuminuria of candesartan (an ARB) combined with lisinopril (an ACE inhibitor) vs. one of these agents individually. Results revealed a significant decrease in clinical BP levels vs. the ACE inhibitor or ARB alone. The ARB/ACE inhibitor combination also showed a significant decrease (50%) in the albumin-creatinine ratio vs. candesartan (24%) but not vs. lisinopril (39%). However, the study was not able to show whether the additional benefits were due to greater blockage of the renin-angiotensin system or the greater reduction in BP levels. More recently, the CALM II study has been published, comparing the administration of 40 mg lisinopril with a combination of 20 mg lisinopril and

16 mg candesartan on ambulatory BP and albumin-creatinine ratio of 75 hypertensive patients with diabetes. The study failed to confirm the benefits of the ACE inhibitor/ARB combination, and the combined therapy did not bring about any additional reduction in either ambulatory BP levels or the albumin-creatinine ratio compared to optimal dosage levels of the ACE inhibitor alone. The additional decrease in ambulatory BP and the reduction of the albumin-creatinine

ratio associated with the use of an ACE inhibitor/ARB combination are often modest and not significant when compared with optimal-dose monotherapy.

#### **Additional Protection Against Heart Failure**

The Valsartan Heart Failure Trial (Val-HeFT) and CHARM-added studies, conducted in heart-failure patients who had already been treated with an ACE inhibitor, evaluated the additive effects of valsartan and candesartan, two ARBs, respectively. The Val-HeFT study showed that adding an ARB to a treatment regimen that already included an ACE inhibitor and a beta-blocker increased total morbidity/mortality events. These surprising results were not, however, duplicated in the CHARM-added study where a candesartan/ACE inhibitor combination significantly lowered the primary endpoint. Finally, the Valsartan in Acute Myocardial Infarction (VALIANT) study in post-infarction heart-failure patients did not demonstrate any benefit for the combina-

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## CHEP

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to reducing morbidity and mortality in hypertensive patients. Generally, a theme is also selected to highlight a new change or an important CHEP initiative. The dissemination process has involved publishing full scientific manuscripts in the *Canadian Journal of Cardiology*, a variety of summaries tailored to the audience, short handouts, posters, pocket cards, advertisements, education kits, text books, slide sets and workshops. Summaries of the

The CHEP Implementation Task Force was revised this year to have specific subgroups of nurses, family physicians, pharmacists, a stroke neurologist and an exercise physiologist to specifically aid dissemination to those healthcare professions. Other subgroups will be added in the future. The subgroups will identify discipline-specific issues and tailor the implementation material. The subgroups will also identify and disseminate to the healthcare professional schools and training programs, national and provincial organizations, as well as to websites and written publications for their specific discipline. In

- 2) cross-sectional national questionnaire surveys on awareness of hypertension, treatment of hypertension and the gap between awareness and treatment of hypertension;
- 3) provincial administrative databases to track hypertension diagnosis, hypertension treatment and complications for hypertension; and
- 4) national prescriptions of antihypertensive drugs.

The Task Force also communicates with Statistics Canada regarding the Canadian Health Measures Survey, which will be conducted from 2006 to 2008 to determine the prevalence of hypertension as well as the hypertension treatment and control rate.

*The CHEP executive annually determines the key implementation messages to highlight new and important recommendations that are fundamental to reducing morbidity and mortality in hypertensive patients.*

*The evidence and draft recommendations are debated and revised at an annual meeting of the task force and are presented at the Canadian Cardiovascular Congress. The full task force and executive vote on the draft recommendations and only those recommendations that achieve over 70% support are adopted. The lowest level of support for a recommendation has been more than 80%.*

recommendations are published in up to 15 multi-disciplinary journals each year. Many pharmaceutical companies have developed educational material based on the recommendations and “train the trainer” sessions where local opinion leaders learn to provide workshops in the latest CHEP recommendations. CHEP endorses only those programs that are completely consistent with the recommendations. The CHS website ([www.hypertension.ca](http://www.hypertension.ca)) houses the recommendations and a number of dissemination tools.

In addition, CHEP is actively seeking formal partnership arrangements with professional societies to help aid the dissemination process.

### Outcomes Research Task Force

An Outcomes Research Task Force is developing a surveillance program for hypertension and is evaluating the impact of the CHEP program. The task force has four subgroups to examine:

- 1) the incidence of hospitalization for acute stroke, acute myocardial infarction and heart failure;

### Conclusion

CHEP is a dynamic program that changes annually based on previous years' experience. To meet the challenge of hypertension treatment and control, CHEP is growing and currently has 72 members. CHEP aids healthcare professionals by providing credible, widely disseminated, up-to-date recommendations in multiple formats to suit individual learning needs. CHEP material is available on the CHS website at [www.hypertension.ca](http://www.hypertension.ca).

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process to assess the effect of its recommendations and their implementation on the health of Canadians. Due to these international milestones, the CHS was extremely pleased to nominate CHEP for a Canadian Institutes of Health Research (CIHR) Knowledge Translation Award this year. As described by the CIHR, this award “honors and supports teams or organizations that make an outstanding contribution to the health of Canadians or to the health system through exemplary knowledge translation.” We can think of no more appropriate organization for such an award than CHEP, and are confident that they will be highly ranked for this award.

### CHS: Hypertension Research and Beyond

As mentioned above, the CHS continues to support hypertension research in Canada. This is done in a number of ways. While the CHS does not directly fund research, the Society does fund research training. The CHS, in partnership the CIHR, Rx&D, and a number of industry sponsors, provides a variety of trainee support awards, ranging from the student to the post-doctoral to junior investigator-level investigators. Over the years, many of the recipients of such awards have gone on to highly productive careers in hypertension research. A second way in which the CHS supports research is through its sponsorship of the annual scientific meeting. This meeting allows for hypertension researchers across the country to share their findings, to network and to exchange ideas. In addition, there is an emphasis on providing “how to” workshops and other events for trainees at this meeting. Finally, the CHS works

with funding agencies to help determine priorities and to promote hypertension research in Canada.

Recently, the CHS executive had an exciting meeting with members of the Institute of Circulatory and Respiratory Health (ICRH) of the CIHR. At this meeting, we were able to confirm our mutual ongoing commitment to the trainee award programs and to streamline and expand the opportunities for the applicants to such programs.

Perhaps even more exciting was a broad-reaching strategic discussion on

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priority and new areas for hypertension research. The executive was greatly encouraged by the ICRH/CIHR's openness to obtain input on in this area from our Society. Perhaps most exciting in the realm of research, however, is the soon-to-be announced awardee of the National Chair for High Blood Pressure Prevention and Control. This initiative was formally announced at last year's annual CHS business meeting and by the time this article is read, the awardee should have been announced. The award is co-sponsored by the CHS, the CIHR, and Sanofi-Aventis and will serve as a focal point from which national population-based research or strategies may be developed.

May 14 of this year marked World Hypertension Day. On May 10, mem-

bers of the CHS executive, along with representatives from the CIHR, Blood Pressure Canada, the Heart and Stroke Foundation, and other organizations participated in a press conference and blood-pressure-measurement clinic on Parliament Hill. The Minister of Health, Ujjal Dosanjh, spoke about the significance of hypertension at the press conference, which was attended by a number of MPs and senators. Overall, the event was a great success, thanks to the efforts of Arun Chockalingam from the CIHR, a well-known and longstanding

member of our Society. Based on this year's success, even greater things are planned for next year.

### The Future of the CHS

Finally, what can one predict for the future of the CHS? With an increasing national emphasis on chronic disease management, cardiovascular prevention and healthcare delivery, I think the future looks busy. The CHS will be increasingly called upon to participate in national forums dealing with hypertension research as well as with the practicalities of hypertension prevention and control. Indeed the CHS was invited this year to send a representative to a joint Federal/Western Provinces initiative to establish chronic disease management “infrastructure”



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(no, this is not a mis-spelling) for the areas of hypertension, diabetes and chronic kidney disease—three areas obviously seen as priorities by various levels of government. Thus we are, and will continue to be, indebted to the huge number of CHS members who voluntarily provide their time in the

service of the various missions of the CHS. Up until this year, although basic hypertension research and training has always been strong in Canada, with many up and coming young investigators, the same couldn't be said for clinical hypertension researchers or practitioners. However, the prominence that hypertension now receives as a preventable risk factor for both cardiovascular and cerebrovascular disease should lead to a renewed interest from

younger clinicians and clinical trainees in the field of hypertension. Thus, as you read this article, I will be nearing the end of my presidency of the CHS, but am very satisfied that the future of the Society is assured, bright and in good hands.

*Richard Lewanczuk, MD, FRCPC, PhD  
President, Canadian Hypertension Society*

## ACE Inhibitors and ARBs

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tion therapy. Therefore, the place of ACE inhibitor/ARB combinations in

*... it appears that an ACE inhibitor/ARB combination should be reserved for hypertensive diabetic patients when a further reduction in albuminuria is desired or in patients with heart failure when trying to improve the functional class. This combined therapy could also be used in patients when the therapeutic target is not achieved, despite optimal antihypertensive polypharmacotherapy.*

heart-failure patients remains to be clarified, despite the CHARM-added study results which might indicate a benefit in patients already receiving ACE inhibitors.

## Conclusion

At present, the cardinal message in the management of arterial hypertension is to achieve therapeutic target values. It is important to lower BP levels below 130/80 mmHg, par-

ticularly in diabetic patients with or without kidney disease. To reach this goal, cost-effective drug combinations of at least three antihypertensive agents often have to be

administered. Therefore, it appears that an ACE inhibitor/ARB combination should be reserved for hypertensive diabetic patients when a further reduction in albuminuria is desired or in patients with heart failure when trying to improve the functional class. This combined therapy could also be used in patients when the therapeutic target is not achieved, despite optimal antihypertensive polypharmacotherapy.

However, the Ongoing Telmisartan Alone and in Combination with Ramipril Global Endpoint Trial (ONTARGET) will be looking at the benefits of ACE-inhibitor/ARB combinations from a different angle. This study, with morbidity/mortality objectives, will assess the effects of both these drugs used singly or in combination in a high-risk cardiovascular population similar to that in the HOPE study (*i.e.*, more than 23,000 patients with a history of coronary disease, stroke, peripheral vascular disease, or diabetes with target-organ involvement).

## Suggested Reading

1. Finnegan PM, Gleason BL. Combination ACE Inhibitors and Angiotensin II Receptor Blockers for Hypertension. *Ann Pharmacother* 2003; 37:886-9.

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Readers of Hypertension Canada are invited to visit the CHS homepage at [www.hypertension.ca](http://www.hypertension.ca) and submit suggestions on its improvement.

