

# CHS Annual Meeting

Montreal,  
October 22-26, 2005

## Reporter

### CHS Satellite Symposium

## The Role of the Renin-angiotensin System in Hypertension and its Treatment

This year's Canadian Hypertension Society (CHS) dinner symposium, entitled "Optimizing Outcomes for the Hypertensive Patient: A Concerted Strategy for Cardiovascular Disease Prevention" and sponsored by Merck Frosst, was aimed at presenting information about the mechanisms for hypertension and cardiovascular disease (CVD) related to angiotensin II (AII) and other components of the renin-angiotensin system (RAS), and discussing the evidence for preventing and treating disease in light of these mechanisms.

Dr. Jacques de Champlain, a Research Professor at the Université de Montréal,

Director of the Autonomic Nervous System Research Group and co-chair of this satellite symposium, began the evening by reviewing the program's learning objectives. He then highlighted the importance of hypertension, pointing out that this condition is responsible for most of the CVDs which cause about one third of the deaths in Canada each year. As such, he continued, treating hypertension is a mechanism by which CV mortality can be efficiently controlled. Specifically, treating hypertension has been shown to reduce the risk of stroke and events related to coronary artery disease (CAD). Nonetheless, Dr. de

Champlain said, there remains room for progress in terms of our understanding of the mechanisms behind hypertension and in terms of the ways we approach hypertension treatment in light of these mechanisms. Among the mechanisms becoming better understood, the important role of the RAS has been highlighted by findings linking it to various disease processes and end-organ damage (e.g., data showing that higher circulating renin levels are associated with increased risk of myocardial infarction [MI], and data linking angiotensin to atherosclerosis, vasoconstriction, vascular and cardiac hypertrophy,

*Continued on page 2*

### CHS/CHEP Joint Symposium

## Adherence: A Key Component of Optimal Hypertension Control

This satellite symposium, entitled "Adherence and Hypertension in 2005," represented the first "train-the-trainers" session planned as part of a collaborative initiative of the Canadian Hypertension Society (CHS) and the Canadian Hypertension Education Program (CHEP) aimed at disseminating the Canadian recommendations for the treatment of hypertension. The symposium was recorded for webcast-

ing by McGill University (available at: [ww2.medicine.mcgill.ca/cme](http://ww2.medicine.mcgill.ca/cme)), and the material presented will be made available on the CHS website ([www.hypertension.ca](http://www.hypertension.ca)) under the "Resource Center" tab.

Dr. Denis Drouin, Associate Director of the CME office at Laval University and Chair of this symposium, began the meeting by reviewing the program's agenda and objectives before presenting his introducto-

ry talk entitled "Why Adherence? The Magnitude of the Problem."

Dr. Drouin presented data from a 1999 study which showed that persistence with antihypertensive therapy declines over time (for all major classes of drugs studied), and other data showing that the addition of a second drug (such as lipid-lowering therapy) results in even lower adherence rates over time than is

*Continued on page 5*



## The Role of the RAS

Continued from page 1

endothelial dysfunction, remodeling of the heart, and kidney dysfunction).

With these types of findings in mind, Dr. de Champlain said, it is clear that a better understanding of the RAS can be an important tool in intervening to help prevent patients from progressing along the well known continuum of CVD.

### New Insights Into Angiotensin II

Dr. Rhian Touyz, the Canada Research Chair in Hypertension at the Kidney Research Centre of the Ottawa Health Research Institute (University of Ottawa), then took the podium to give the evening's first presentation, entitled "What's New in Angiotensin II Signaling, Vascular Re-

Vascular remodeling (*i.e.*, an increased media:lumen ratio) is more than an interesting physiologic observation: it has important pathologic and prognostic implications. Dr. Touyz showed data from an Italian study in which patients had their media:lumen ratio measured and were followed for five years. The investigators found that subjects with more increased ratios had much worse CV outcomes compared to subjects with significantly lower ratios.

Some of the factors underlying the process of vascular remodeling, Dr. Touyz went on, involve an increase in extracellular matrix deposition, particularly of collagen. She showed images illustrating an increase in collagen in the small arteries of hypertensive animals compared to those of normotensive animals. Similar observations have been made in comparisons of

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modeling and Hypertension?" Dr. Touyz began by reiterating that hypertension is a global problem whose incidence is predicted to increase by about 60% over the next 25 years, and that we have yet to fully understand the fundamental pathophysiologic mechanisms underlying the condition.

Nonetheless, she said, essential hypertension can be understood—in a basic physiologic sense—as an increase in total peripheral resistance due primarily to a decreased arterial radius (brought about by functional or structural factors). Functionally, a vessel can have a decreased lumen diameter if it contracts more or dilates less. Structurally, small and large vessels can be subject to "vascular remodeling" (which can be brought about by a number of factors) which decreases lumen diameter and/or increases media thickness (and therefore increases the media:lumen ratio).

hypertensive to normotensive human arteries. As well, vascular remodeling is associated with a pro-inflammatory process. It has been demonstrated that certain inflammatory mediators, such as ICAM-1 or MCP-1, are markedly increased in the vascular media of hypertensive subjects, and that antihypertensive treatment in these subjects is associated with significant reductions in this inflammatory process.

In light of all these data, Dr. Touyz said, hypertension can be considered to constitute a vascular disease process. This disease process identifies a vascular phenotype in which the vessels undergo functional, structural and mechanical changes, and the RAS plays a critical role in many of these changes.

Until recently, the RAS was understood as being comprised of renin, angiotensinogen, and the production of AII from angiotensin I (AI). It was also

known that AII bound to the AT1 receptor and the AT2 receptor and thereby mediated cellular effects. In 2005, this pathway is known to be much more complex, involving other peptides related to AII, such as AIII and AIV (which may also bind to the AT1 receptor or to specific AT3 or AT4 receptors) and the very important A1-9 and A1-7.

Angiotensin, through its specific receptors, mediates several effects that contribute to vascular remodeling. Basically, it can be said that AT1 receptors are probably the "bad" receptors, as they induce vasoconstriction, inflammation, fibrosis, vascular growth, increased aldosterone secretion and sodium reabsorption. In general, activation of AT2 receptors, as well as activation by A1-7 through its specific receptor (Mas), seems to have opposite effects, inducing vasodilation and inhibition of vascular growth.

There are many very complex signaling processes involved in AII's action related to hypertension. Overall, Dr. Touyz emphasized that in hypertensive subjects, AII—through the AT1 receptor—causes an increase in mobilization of calcium and stimulation of many of the pathways that induce vascular smooth muscle cell (VSMC) hypertrophy, hyperplasia and inflammation. Reactive oxygen species (ROS) have been implicated in controlling many of these pathways. The most important ROS involved in CVD are superoxide anion, hydrogen peroxide and the well known vasodilator, nitric oxide (NO).

Dr. Touyz went on to show that the generation of ROS (particularly superoxide and hydrogen peroxide) is increased in vessels of hypertensive patients compared to normotensive controls. Furthermore, inhibiting the production of ROS is associated with significant attenuation of VSMC growth in the presence of AII. Similarly, it has been shown that the increased collagen (another marker of vascular remodeling) seen in AII-infused mice is markedly reduced when the production of ROS is inhibited. Various pro-inflammatory responses also have been shown to be



reduced through the inhibition of ROS production, further illustrating the role of ROS in AII-induced inflammation.

The mechanisms by which AII induces production of ROS most likely involve the complex enzyme system known as NAD(P)H oxidase. In fact, NAD(P)H oxidase is being considered as a putative therapeutic target for vascular disease in hypertension and atherosclerosis.

While the negative effects of AII (through the AT1 receptor) are becoming better understood, the possible beneficial effects of angiotensin signaling (vasodilation and inhibition of vascular growth) are also being examined. It has been known for some time that the AT2 receptor plays a role in these processes. In addition, we are beginning to appreciate the role of A1-7, mediating its effects through the receptor Mas (*e.g.*, the increased production of NO) and possibly modulating the AT1-receptor-related effects on AII on NAD(P)H oxidase.

### Prevention and Management of Left Ventricular Dysfunction

The symposium's next speaker was Dr. Malcolm Arnold, Professor of Medicine, Physiology and Pharmacology and Research Director in the Division of Cardiology at the University of Western Ontario, Program Leader of the Circulation Group at the Lawson Health Research Institute, and Chair of the Canadian CHF Clinics Network. Dr. Arnold's presentation, entitled "Improving Heart Failure Outcomes: From the Prevention to the Management of Left Ventricular Dysfunction," began with an overview of the prevalence and implications of heart failure (HF).

Over the past 10 to 12 years, he said, the incidence of—and number of hospital admissions for—HF has continued to increase (*e.g.*, by about 50% in London, Ontario). In various clinical trials of HF, it has been shown that life expectancy is significantly reduced in patients with HF. In fact, real-life patients who are hospitalized for HF and then discharged are known to

have even worse prognoses, illustrating the importance of preventing HF in at-risk patients.

Dr. Arnold presented data showing that various genetic and environmental factors can predispose patients to CV events, and that the earlier in life these first events occur, the smaller an impact pharmacotherapy will have on reducing progression of CVD. Predicting CV events in such

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patients and initiating measures of prevention—based on identified risk factors—is of obvious benefit.

One important risk factor for HF that can be targeted, Dr. Arnold said, is hypertension. In some early placebo-controlled studies, it was shown that reducing systolic BP (from about 180 or 190 mmHg) by approximately 10 mmHg and diastolic BP (from about 100 mmHg) by only 3-4 mmHg resulted in a consistent 40% to 50% reduction in the risk of HF development.

More recently, the focus of clinical trials in hypertensive patients has been on comparing different types of medications in terms of their efficacy. In the ALLHAT trial (whose data continue to be debated), for example, chlorthalidone was shown to be more effective in reducing risk of HF than doxazosin. While this may reflect different properties of the two agents beyond BP effects alone, the message remains that some medications are more effective than others in reducing risk of HF even if each is demonstrated to reduce BP. Similarly, in the VALUE study, a valsartan-based regimen was better than an amlodipine-based regimen in terms of HF risk. Even more recently, in the ASCOT trial, the combination of amlodipine and perindopril was slightly (though not significantly) better

than atenolol and thiazides in reducing incidence of HF.

Another important group of patients to target for aggressive HF prevention is those with systolic dysfunction. In the post-MI SAVE trial, baseline left ventricular ejection fraction (LVEF) was strongly correlated with risk for developing HF (with lower LVEF being associated with higher risk). The SAVE trial also pointed out other risk

factors for HF development, further highlighting which patients require aggressive preventive therapy. Factors strongly correlated with HF risk included age, history of hypertension, history of or new-onset diabetes, presence of audible murmur, and history of prior MI.

The importance of identifying (and then treating) high-risk patients was further illustrated by the SAVE, AIRE and TRACE studies, which showed that ACE inhibitors significantly reduced the risk of death (and of HF) in high-risk post-MI patients. Even in patients without a history of recent MI but with LV dysfunction, the SOLVD-Prevention trial (of patients without documented symptomatic HF and with LVEF < 35%), enalapril showed a trend towards reduced overall death and a trend towards reduced CV death, along with significant reductions in terms of death or HF hospitalization and in terms of death or HF development. In this study, at the end of the planned follow-up (after three years), enalapril was only slightly (and not significantly) better than placebo in terms of survival. After the trial ended, most subjects were prescribed ACE inhibitors. Nonetheless, database follow-up (not part of the trial's planned follow-up) for up to 12 years showed that the absolute mortality difference between the trial's randomized groups grew to 6% (from 4% at five



years and 2% at study end). Findings like this seem to indicate that early treatment of high-risk patients may provide gradual benefit that pays dividends over time.

In post-MI patients with atherosclerosis, the CARE trial has also provided insight into predictors of HF risk. In this trial, increased age was again strongly correlated with increased HF risk, as was decreased LVEF. Of note, LVEF was the strongest predictor of HF risk in subjects younger than 70 years, while age was the strongest predictor in those older than 70 years.

In the HOPE study, the vast majority of patients had an LVEF of at least 40%. Baseline characteristics that were identified as clinical predictors of developing HF included (in order of importance): CAD (which more than doubled the likelihood of developing HF), microalbuminuria, diuretic use, LVH, age, diabetes, total cholesterol

events and mortality were not significantly different).

In conclusion, Dr. Arnold observed that there are many opportunities along the CVD continuum at which we can intervene to reduce LV dysfunction and prevent HF. These opportunities may arise upon diagnosis of hypertension, or upon recognition of ECG abnormalities or various risk factors. In any case, the importance of early, aggressive intervention cannot be understated.

### **Preventing and Managing Atrial Fibrillation**

The next presenter was Dr. Kristian Wachtell, Research Associate in the Department of Medicine at Copenhagen County University Hospital in Denmark. Dr. Wachtell's presentation, entitled "Compelling Evidence in the Management

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level, previous coronary artery bypass graft (CABG), previous stroke or transient ischemic attack (TIA), peripheral vascular disease, body weight, heart rate and pulse pressure. Overall, it was observed that patients at higher risk (*e.g.*, those with CAD and those with elevated SBP) derived the greatest benefit from ramipril treatment in terms of decreased HF risk. Of note, patients who developed HF in HOPE had a substantial four-fold increase in risk of CV death compared to those who did not.

Other trials have confirmed the benefit of ACE inhibition in preventing HF. In the EUROPA trial, perindopril treatment significantly reduced the rate of developing HF compared to placebo in patients with CAD. In the PEACE trial, trandolapril reduced the risk of HF compared to placebo (despite the fact that CAD

of Atrial Fibrillation: From Prevalence to Management," was focused on data from the LIFE study regarding atrial fibrillation (AF). First, Dr. Wachtell reminded the audience that AF and hypertension go hand-in-hand (with hypertension most likely being the largest single cause of AF due to its high prevalence), and that AF increases stroke risk while the presence of both conditions places patients at even greater risk of CV events.

Dr. Wachtell went on to point out that guidelines for rate control in AF recommend the use of beta-blockers or non-DHP CCBs, though the impact of these recommendations (on CV morbidity and mortality) remain unclear.

Prior to the LIFE study, other trials had examined the role of inhibiting the RAS in reducing AF. For example, in the

TRACE study, post-MI patients treated with trandolapril had less new-onset AF compared to placebo. In another study, patients with persistent AF experienced longer times in sinus rhythm and more freedom from AF when treated with irbesartan vs. placebo. For each of these studies, it was difficult to assess whether the treatment effects were related to BP differences between the groups.

In the LIFE study, a 25% reduction in risk of fatal and non-fatal stroke was observed with losartan-based therapy compared to atenolol-based therapy. This difference was not explained by the small differences between groups in terms of achieved BP, prompting the investigators to look for other possible mechanisms for losartan's benefit.

LIFE patients with a history of AF treated with losartan experienced a risk reduction for CV mortality of more than 40% compared to atenolol-treated patients—a striking finding in light of the recommendations for the use of atenolol in these patients. Furthermore, about three times more atenolol-treated patients underwent pacemaker implantation compared to losartan-treated patients. In LIFE patients without baseline history of AF, losartan treatment reduced the risk of new-onset AF by 33% compared to atenolol treatment. Of note, even in losartan-treated patients who developed AF, the risk of subsequent CV events was 40% lower compared to atenolol-treated patients who developed AF.

In terms of explaining the mechanisms for losartan's AF-related benefits, the LIFE data were the first to suggest that losartan exhibits anti-arrhythmic properties. These mechanisms have been examined in a number of studies, and may include lowering wall stress, modification of sympathetic tone, diminished atrial fibrosis, modulation of refractoriness, and up-regulation of AT1 receptor polymorphism.

The LIFE study also provided insight into predicting risk of new-onset AF. In a multivariate model, predictors (in order of importance) included age, male gender,

*Continued on page 8*



## Adherence in Hypertension

Continued from page 1

observed with either individual agent. In fact, as Dr. Drouin showed, it has been estimated that, due to improper use, 30% to 50% of prescriptions fail to produce the desired therapeutic results in patients with chronic medical conditions. In the traditional model of overlapping diseases (such as hypertension, dyslipidemia and diabetes) with overlapping associated risk factors (such as age, overweight, smoking, and genetics/gender), non-adherence can be viewed as an underlying risk factor threatening overall disease management.

The consequences of non-adherence, Dr. Drouin continued, can include increased symptoms, failure to meet therapeutic goals or targets, unnecessary investigations, unnecessary treatment adjustments, patient dissatisfaction, physician frustration, and ultimately a major impact on morbidity, mortality and healthcare costs. Based on all of this, adherence must be seen as an important new science, complete with patterns and mechanisms that can be studied and then targeted in order to optimize treatment.

### Defining, Studying and Understanding Adherence

Dr. William Elliot, from the Department of Preventive Medicine at RUSH Medical College in Chicago, was called upon to provide an overview of the issue in a presentation entitled “Basics in Adherence.” He began by pointing out that hypertension control around the world is suboptimal, and that patients are part of the problem and must therefore be part of the solution. In the U.S., he noted, it has been estimated that 10% of each healthcare dollar spent on hypertension is wasted because patients do not take their prescribed medicine. Moreover, the significant impact of non-adherence is illustrated by data such as those from a well known (albeit not focused on hypertension) beta-blocker trial which showed that patients randomized to the active drug who were not adherent (*i.e.*, did not take at least 75% of

their prescribed pills) had a 3.1-fold increased risk of death in the first year compared to adherent subjects. Surprisingly, even among subjects randomized to placebo, non-adherence was associated with a 2.5-fold greater risk of death in the first year compared to adherence.

In discussing the issue of adherence, it is important to define the terms being used. Dr. Elliot defined adherence as the extent to

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which a patient carries out all aspects of the prescribed treatment plan, and persistence as the extent to which a patient continues to take their prescribed pills over the long term. Unfortunately, clinical trial data has been largely unhelpful in tracking these issues, as they most often reflect inflated levels of adherence and compliance because subjects are carefully selected, actively coached by their treating physician, and receive free study medication. In real life, adherence and persistence are known to be major problems in virtually all chronic conditions (including hypertension, dyslipidemia, tuberculosis, HIV/AIDS and asthma).

There are several ways in which adherence can be assessed. Simple solutions include pharmacy records, pill-counting and directly questioning patients. Other methods could include the measurement of serum markers (*e.g.*, uric acid to detect adherence to diuretics) or biomarkers (*e.g.*, heart rate to detect adherence to beta-blockers), or use of the modified Morisky scale. There are also several ways in which short- and long-term adherence can be enhanced, and these are discussed in detail in some of the following presentations.

### Assessing Adherence

Next, Dr. George Fodor, Head of Research at the University of Ottawa's Heart

Institute Prevention and Rehabilitation Centre, presented his talk entitled “Clinical Assessment of Adherence: An International Experience.” His focus was on presenting data from the first phase of the ongoing Austria-Slovakia-Hungary International BP Study, in which blue-collar workers from these countries underwent standardized worksite screening for hypertension and were administered a brief

questionnaire including questions about awareness of and adherence to antihypertensive therapy.

Of the 2,812 subjects screened as part of this study, 841 (30%) were hypertensive (defined as having an SBP  $\geq$  140 mmHg or DBP  $\geq$  90 mmHg, or being treated with antihypertensive drugs). Of these hypertensives, only 43% were treated, and only 54% of these treated hypertensives were adequately controlled. These numbers were similar when broken down into each of the three countries studied. Of note, 57% of hypertensives were newly discovered as such by the study's screening, and only 22% of all hypertensives (*i.e.*, treated and not treated) actually had their hypertension controlled.

Within the short questionnaire, one question asked subjects to select between four statements that described their behavior if they were currently prescribed drugs to lower their BP. The four behaviors described were: 1) strict adherence without missed doses; 2) general adherence with only occasional forgotten doses; 3) occasional forgotten or purposefully missed doses for short periods of time (days); and 4) frequent forgotten or purposefully missed doses for extended periods of time (weeks or months). Overall, 53% of respondents claimed to



be adherent while 47% admitted at least some non-adherence (mostly reporting general adherence with only occasional missed doses).

The main conclusions of this study were that: 1) subjects who reported even occasional lapses in adherence were found to have significantly higher SBP and DBP

human behavior. It is important to identify individual patients' "hot buttons" in order to motivate them to increase their level of physical fitness. A 75-year-old man, for example, may not be motivated by the idea of being able to walk around a track more quickly, but may care about being able to pick up his grandson or carry groceries on

sure," and must therefore be able to assess physical activity in order to target it with various interventions.

Promoting increased physical activity involves an understanding of social cognitive theory, the use of motivational (but non-threatening) interviewing, and helping patients overcome barriers to exercise (such as time constraints, cost factors, low energy level, physical discomfort, and geographic isolation or distance from exercise facilities).

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compared to those reporting strict adherence; and 2) properly formulated questions (using inoffensive wording) can identify non-adherent individuals.

### **Adherence to Exercise**

In the next presentation, entitled "Adherence to Physical Exercise Recommendations: What is the Current State of Knowledge and What is the Effectiveness of Interventions?," Dr. James Stone aimed to review tools for assessing adherence to physical exercise recommendations and interventions that may enhance such adherence. Dr. Stone, Clinical Associate Professor of Medicine at the University of Calgary, Director of Research at the Cardiac Wellness Institute of Calgary and Deputy Secretary General of the World Council on Cardiac Rehabilitation, began by highlighting the importance of exercise as demonstrated by the fact that people with higher fitness levels have the best outcomes. The CHEP and CACR recommendations for physical activity are very similar, each recommending 30 to 60 minutes of moderate or vigorous activity on at least four days each week (CHEP) or on all or almost all days of the week (CACR).

Exercise adherence requires behavior change, and intervening to enhance adherence requires some understanding of

his own. As a healthcare provider, practicing what you preach can also help promote physical activity.

Several studies have shown that there is a survival benefit associated with aerobic fitness. While exercise studies are frequently criticized (*i.e.*, for being retrospective), data also exist from well designed, prospective studies such as the St. James Women's Heart Study, which involved 5,700 women who were followed for an average of nine years. In this study, exercise capacity was correlated with death and MI. As well, studies have shown that interventions can work to improve adherence to exercise programs, and that aggressively treating patients (including strong coaching towards increased exercise) yields improved outcomes.

Useful tools for assessing current activity level and adherence to exercise recommendations include the Duke Activity Status Index, the Patient-centred Assessment and Counselling for Exercise tool, the Physical Activity Scale for the Elderly, and the FANTASTIC assessment tool offered by the Canadian Society for Exercise Physiology. Additionally, the use of pedometers, heart-rate monitors and even running-shoe microchips can help assess patients' activity levels. Ultimately, Dr. Stone pointed out, physicians "can only manage what they mea-

### **The Role of the Pharmacist**

The optimal management of hypertension involves a multi-faceted healthcare approach, and pharmacists can make a major contribution by helping to identify at-risk patients, and by monitoring and enhancing adherence to prescribed medications. This was the basis of the next presentation, entitled "The Role of Pharmacists in Promoting Better Adherence in Hypertension," and given by Dr. Ross Tsuyuki, Professor of Medicine in the Department of Cardiology at the University of Alberta.

Dr. Tsuyuki pointed out that, in his view, promoting adherence is an integral part of the overall hypertension-management strategy to which pharmacists can contribute (and therefore not necessarily separated into secondary interventions but rather incorporated into the general measures taken to ensure optimal management). He also pointed out that patients tend to see their pharmacist more often than their family physician (due to the need to refill prescriptions and greater accessibility), and that pharmacists may see patients who do not see their family physician. Often, he continued, pharmacists are the only healthcare providers to know every medication a patient is taking.

One of the fundamental things pharmacists can do to optimize the management of hypertension is identify patients at risk for hypertension (*e.g.*, those with diabetes or CHD), based on their prescribed medications. As well, pharmacists can improve hypertension treatment and control by pro-



viding patient education, reviewing the treatment regimen, referring—and making recommendations to—the patient’s physician, and monitoring/promoting adherence.

In terms of adherence, the pharmacist’s role can be divided into: 1) patient education; 2) simplification of the regimen; and 3) patient monitoring. Patient education includes reinforcing the need for the medication, involving the family and/or caregivers, explaining the benefits and risk of the medication, and determining/addressing any barriers to adherence. Simplifying the patient’s regimen can include the use of once-daily drugs and combination drugs, discontinuation of unnecessary drugs, cost considerations, recommendations for scheduling medications, and the use of dosettes. Patient monitoring can involve regular BP measurement, encouraging regular visits, looking for adverse effects, encouraging the use of home BP monitors, and refill monitoring.

Several studies have shown that, when pharmacists are actively involved in the treatment plan of hypertensive patients, there is improved BP control, better medication selection, better adherence, reduced drug interactions and reduced costs. As well, the large SCRIP study (not a hypertension study) showed improved cholesterol risk management in patients randomized to pharmacist intervention vs. usual care. The ongoing SCRIP-Hypertension study will examine the effect of a community-based multidisciplinary screening and intervention program (including screening and follow-up with a pharmacist and nurse) vs. usual care on BP control in patients with diabetes and hypertension.

### The Role of the Physician

Dr. Alain Milot, from the Internal Medicine Department at the *Centre Hospitalier Universitaire de Québec* (Saint-François d’Assise Hospital), picked up where Dr. Tsuyuki left off, with a presentation entitled “What Physicians Can Do to Enhance Adherence in Hypertension.” He began by reiterating the problem of non-adherence, pointing out that it

is a major barrier to adequate control of hypertension in Canada and that an estimated 50% to 70% of hypertensive patients adhere to their prescribed therapy.

The barriers to adherence can be broken into factors relating to: 1) the evidence; 2) the healthcare provider; 3) the patient; and 4) the healthcare setting. Evidence-related barriers can include inconsistency between trials and recommendations, uncertainty of clinical significance or applicability, and lack of an implementation strategy. Provider-related barriers can include lack of awareness or knowledge, lack of time, lack of outcome expectancy, and failure to communicate effectively with the patient. Patient-related barriers can include lack of awareness or

and for how long lifestyle modification and medication are needed, how to take the medication, and how to deal with side effects or missed doses. Written materials can play an important role, and should be provided to patients and their family/caregivers. Finally, system-based means of improving adherence can include increasing the frequency of visits for patients who do not achieve therapeutic targets, the use of a reminder system and coordinating nurses, providing services in the form of specialized clinics, and the use of pill organizers (e.g., dosettes).

As these interventions and their surrounding issues might be difficult for physicians to tackle on their own in the course of a 15-minute patient visit, the

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knowledge, lack of motivation, lack of self-efficacy, and over-emphasis on potential side effects. Setting-related barriers can include an emphasis on acute symptoms rather than chronic disease, lack of time, lack of human and material resources, and lack of training of healthcare workers. There are things physicians can do to overcome some of these barriers. As a starting point, adherence should be assessed initially and repeatedly in all patients. No single measure is universally effective, so interventions should be individualized and multiple.

Interventions related to pharmacotherapy include reducing the number of daily doses and the number of pills per dose (e.g., through the use of combination agents), avoiding switches, using better-tolerated agents, and minimizing costs. In terms of patient communication/education, it is important to inform patients about the purpose of the prescribed treatment, why

notion of a therapeutic alliance has been proposed. In establishing such an alliance, physicians should recruit the patient (and their family/caregivers) to do their part in adhering to and monitoring the effects of prescribed therapy, and should recruit other healthcare allies such as pharmacists, nurses and/or dietitians.

### CHEP Adherence Recommendations

The symposium’s final presentation, entitled “The 2006 CHEP Recommendations: Focus on the Nonadherence Epidemic,” was given by Dr. Ross Feldman, from the Robarts Research Institute at the University of Western Ontario and Chair of CHEP’s Adherence subcommittee of the Recommendations Task Force. Dr. Feldman began by reviewing the process by which CHEP develops and updates its recommendations on adherence, pointing out that the recommendations include only those supported by



## The Role of the RAS

Continued from page 4

SBP, and ECG LVH. It should be noted, however, that randomization to losartan was still associated with a 33% lower rate of new-onset AF compared to atenolol, independent of these risk factors. The

LIFE data also showed that systolic function is a very strong predictor of new-onset AF, and that reducing left atrial size (*i.e.*, removing the presence of left atrial dilatation) yields an 80% risk reduction in new-onset AF.

In conclusion, Dr. Wachtell reiterated that afterload reduction with losartan appears to provide better outcomes than

the heart-rate reducing properties associated with atenolol, and that the anti-arrhythmic properties of losartan are probably more important than the electrical properties that have been investigated previously. Furthermore, he added, lower heart rate might not provide protection against AF, particularly in patients with normal baseline heart rates.

## Adherence in Hypertension

Continued from page 7

clinical-trial evidence that reached CHEP's standards for inclusion. He showed that the "headlines" for 2006 focus on simplified dosage regimens and improved reminder systems, and then—in keeping with CHEP tradition—went on to outline the recommendations which are "old but still important" followed by those which are new for this year. The new recommendations he showed remained to be ratified at the time of the presentation.

The recommendations carried over from previous years include:

- 1) Simplifying medication regimens to once-daily dosing;
- 2) Utilizing electronic medication compliance aids;
- 3) Tailoring pill-taking to fit patients' daily habits;

- 4) Encouraging greater patient responsibility/autonomy in monitoring their BP and adjusting their prescriptions;
- 5) Coordinating with work-site healthcare providers to improve monitoring of adherence with pharmacologic and lifestyle-modification prescriptions;
- 6) Educating patients and their families about their disease/treatment; and
- 7) Assessing adherence to pharmacologic and nonpharmacologic therapy at every visit.

The new recommendations pending ratification at the time of Dr. Feldman's presentation included:

- 8) Encouraging compliance with therapy by healthcare-practitioner-based telephone contact, particularly over the first three months of therapy;
- 9) Utilizing fixed-dose combination pills; and

- 10) Utilizing unit-of-use packaging.

In support of the first of these three new recommendations, Dr. Feldman presented data showing that telephone contact improved compliance to and effectiveness of lipid-lowering therapy. The use of fixed-dose combination pills, he explained, is a further extension of the effort to simplify dosing, and has been shown to increase adherence and possibly enhance therapeutic effect. Finally, unit-of-use packaging involves the use of blister packaging (*i.e.*, in which several medications are packaged in a fixed combination to be taken together) or dosette-type packaging. Of note, unit-of-use packaging was shown to be effective in enhancing adherence, but only when combined with patient education. This finding underscores the fact that no single intervention is likely to be 100% effective, and that a multi-pronged approach to adherence enhancement is required.

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