with 25% of the Canadian population projected to be over the age of 65 by 2031, seniors are poised to become more numerous than children—an unprecedented milestone in the country's history. Among the medical issues that are expected to prevail in an aging population is neurovascular health. “I’m going to use atrial fibrillation (AF) as an example,” Dr. Robert Côté, Professor of Neurology, Neurosurgery and Medicine, McGill University, Montreal, told INFO-Cardio. Dr. Côté will address delegates during the Heart and Stroke Foundation of Canada lecture on Sunday entitled “Neurovascular Prevention: A Challenge for All of Us in an Aging Society.”

AF has been established as a major cause of embolic stroke and it is an arrhythmia associated with advancing age. It is commonly accepted that warfarin substantially reduces the risk of AF but as Dr. Côté suggested, its diagnosis and management is often far from optimal. One of the risk factors for stroke is hypertension—perhaps the single most important modifiable risk factor, given that high blood pressure contributes to between 40% and 60% of all strokes.

Patients who experience a transient ischemic attack (TIA) often pass as a genuine emergency, whereas in the presence of significant stenosis is critical following a TIA as the earlier the intervention, the greater the chance subsequent stroke can be prevented. The ABCD2 rule (Lancet 2007;369:283-92) can help distinguish patients who have had a TIA and who are at high risk for subsequent stroke.

Vascular dementia and Alzheimer's disease

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Vascular dementia and Alzheimer’s disease

T he special charm of Montréal is part of the menu as the CCC welcomes delegates from some 19 different cardiovascular (CV) disciplines to a smorgasbord of science and a smashing good time in 2010. “We always have a great turnout for the Montréal meetings,” CCS CEO Anne Ferguson confirms. With its fabulous food and nonpareil nightlife, delegates can be excused for taking some time off as they enjoy the autumn colours of Montréal during the day and take in the exuberant sights and sounds of the evening.

The CCS has joined forces with the Saudi Heart Association for their first ever joint symposium, scheduled for Tuesday morning. “We’ve had a long-standing joint session with the American College of Cardiology,” Ferguson explains, “and we decided to expand that. It was a natural step to go with the Saudi Arabian group because Canada receives quite a few Saudi Arabian trainees every year, who train here and write their Royal College exams and then return home to practice CV medicine there.” On the symposium’s agenda will be discussions surrounding systems by which to deliver state-of-the-art care in ACS; delivery of health care in Canada; a special Saudi project for the assessment of coronary events in their country; and the high incidence of diabetes in Saudi Arabia and its impact on ACS.

The “Healthy Living” initiative featured in last year’s Community Forum in Edmonton has been expanded to what the CCS is now calling the “Prevention Pathway.” Still nestled within the network of booths in the Community Forum, the Pathway is marked throughout the Forum and was initiated in order to raise awareness among all health care professionals of the need for them to take responsibility and promote CV disease prevention as an integral part of their professional practice. Along the Pathway, delegates will be invited to investigate a plethora of Health Check products designed for heart-healthy living along with the many offerings from various organizations that promote a healthful lifestyle. Ferguson reveals, “We’ve also been building an on-line program-at-a-glance over the past few years, and it has now expanded to include all of the participants’ programs.” BlackBerries and iPhones, on your mark!

The Joint CCS/Saudi Heart Association Symposium takes place Tuesday, October 26, 11:00-12:30 (Palais des congrès, Room 520A-C).

Challenges in the management of heart failure combined with novel approaches poised to improve patient outcomes will be discussed by heart failure experts during the Canadian Journal of Cardiology Symposium on Sunday.

Dr. Jonathan Howlett, Clinical Professor of Medicine, University of Calgary, will first discuss the difficult problem of acute decompensated heart failure (ADHF), a common syndrome that necessitates over 100,000 hospitalizations in Canada a year. As he noted in an interview, in-hospital treatment of ADHF has improved over the past few years in Canada, mainly due to improved blood pressure control. On the other hand, the number of patients who are presenting with ADHF both in hospital and in the community setting is increasing. So, too, is the percentage of patients who are presenting with ADHF and preserved ejection fractions.

Unfortunately, there are fewer evidence-based therapies for ADHF accompanied by preserved systolic function, even if such patients are admitted to hospital, the likelihood of them returning to the emergency room within the next 30 days following discharge is high. In-hospital treatment of ADHF has advanced relatively little in recent times as well and no new therapies have yet emerged that significantly improve prognosis, despite multiple attempts. Strategies that may improve the prognosis of patients with ADHF include more accurate diagnosis in the emergency room so that patients who require admission are admitted.

Some short-term interventions may be initiated to reduce hospital time but Dr. Howlett stresses that the real key to improvement rests in the initiation of long-term therapies in hospital to ensure patients receive treatments that can improve prognosis. Transitioning patients from hospital to home again remains a challenge as during this period, patients are inherently unstable, as Dr. Howlett points out, and mortality risk remains high. The establishment of follow-up systems therefore becomes critical in order to protect patients during this transition period from unrecognized deterioration, early readmission and adverse outcomes. “Important gaps remain in the management of ADHF,” Dr. Howlett observes, “and I plan to acquaint people with them.”

The Canadian Journal of Cardiology Symposium takes place Sunday, October 24, 12:00-14:00 (Palais des congrès, Room 520A-C).

Greater value and expanded services for CCS members are the key principles that will guide incoming CCS president Dr. Blair O’Neill throughout the next 24 months of his term.

“We know that the Congress is extremely valuable for members and we have a working group that continues each year to try and improve the offerings at the meeting both in terms of educational initiatives for members, the research presented and the networking opportunities that are available during the meetings,” Dr. O’Neill, Director of Cardiology, University of Alberta and Service Chief, Mazankowski Alberta Heart Institute, tells INFO-CARDIO. As the new president, Dr. O’Neill is sincerely looking forward to further serving CCS members through continued efforts to make the Congress as relevant as possible not only to CCS members but to the many affiliated societies who participate in and contribute to the Congress as well: the Canadian Society of Cardiac Surgeons and the Canadian Heart Rhythm Society are but a handful of societies who shape the meeting each year. Together with the CCS, affiliated societies can serve as a strong advocate for cardiovascular (CV) care across a spectrum of patient needs.

Trainees in CV medicine are an equally vital contingent for whom targeted sessions are held each year; as the future of cardiology in this country and elsewhere, attendance by trainees is both valued and necessary. Offering services to its membership means communication and part of what Dr. O’Neill intends to do is find out how members prefer to receive that communication. “People are inundated with information,” he observes, “so the key here is to tailor the communication to what works best for individual members in terms of print, e-mail or social media.”

Two of the city’s most acclaimed caricaturists, Ferg Gadzala and Yves Demers, will be mingling throughout the evening as well and will be there to capture your likeness in exchange for a minimum $5 donation to the Heart and Stroke Foundation of Quebec.

Back by popular demand, the Showmen Orchestra will again be performing to the delight of all. The infectious sounds of this band consist of an 11-piece orchestra—including three singers—whose tunes will beg you to dance the evening away.

Tickets will not be sold at the door so remember to buy your tickets on-line when you register or on-site at the Registration desk from Friday, October 22, until Monday, October 25, during Registration desk hours.

So come, et amuse-vous bien!

Montréal City Night takes place Monday, October 25, 19:30-23:00 (Palais des congrès, Room 710A/B).

City Night features taste of Montréal’s summer festivals

A taste of the wonderful festivals that enliven Montréal every summer will be featured during Monday evening’s “City Night” where music, circus, dance, caricature artists and food will come together in the Palais des congrès.

Sumptuous food has been prepared by “Capitale Traiteur” under the caring eye of chef Wahed Naja. According to Naja, the menu is varied, imaginative, with the utmost care, in the typical Montréal tradition that has made the city a fine dining hub. On the tables will be colourful centrepieces created by grafitti artist Gilbert Alarie from the Momentun Art Gallery; a handful of delegates may be able to leave with one of them if they are lucky.

Cirque Plus performers will bring their considerable talent to the Congress as well. Specializing in high-calibre aerial artistry, the most popular of these acts are “aerial silks” where artists perform stunning figures and cascades within a triangular-shaped structure.

The up-tempo, percussion-driven sound of Kôtou Danse will also be featured. Kôtou Danse takes its name from a triangular-shaped structure. Two of the city’s most acclaimed caricaturists, Ferg Gadzala and Yves Demers, will be mingling throughout the evening as well and will be there to capture your likeness in exchange for a minimum $5 donation to the Heart and Stroke Foundation of Quebec.

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Outgoing CCS president fondly remembers “exciting” initiatives over the past two years

The opportunity to initiate and continue with some “very exciting” initiatives is what outgoing CCS president Dr. Charles Kerr will fondly remember from the past two years of his presidency—a “lifetime experience,” he feels, and an honour to have been elected to the position.

Among the many initiatives undertaken by the CCS during his term as president was the continuing support and delivery of extremely high-quality knowledge translation including the CCC itself as well as multiple symposia. “I’ve been particularly proud of the progress made in the development of guidelines and policy statements,” he added, “and the CCS has taken a leading position in helping guide quality-of-care delivery in Canada.” Dr. Kerr is also proud of the “closed-loop model” for knowledge translation which the Society developed to help disseminate new guidelines. First applied to the management of heart failure in 2005, the same model will again be deployed to help disseminate the new guidelines on atrial fibrillation, to be finalized shortly and published early in the new year.

“As a Society, we have made great strides in issues around advocacy and health policy,” Dr. Kerr observed. This in part has been exemplified by their newly forged collaboration with the Public Health Agency of Canada with whom the CCS will begin to develop a pan-Canadian data dictionary and national cardiac quality indicators.

“The other exciting accomplishment is the enrichment of the trainee’s program,” he added. The Have-a-Heart bursary program has also doubled over the last few years, and the CCS is committed to the provision of ongoing outstanding quality trainee review programs (TRPs), now in place for cardiology, cardiovascular surgery and pediatric cardiology.

“We have continued to partner with our Academy to put a major emphasis on trainee services and education and these TRP programs are funded by our Academy as well,” Dr. Kerr noted.

Lastly, the CCS has become an official affiliate of the European Society of Cardiology. This partnership will potentially open up the way for Canadian specialists to gain access to vital resources of the ESC and take a more active part in its activities.

“I greatly appreciate the enormous help from CCS members, particularly from Council, committee members and staff of the CCS,” Dr. Kerr stated, without whose help none of the exciting initiatives could take place.

Joint CCS/ACC Symposium: Valvular heart disease

Various approaches to valvular heart disease will provide the focus of this year’s joint CCS/ACC symposium taking place on Sunday, Dr. Ian Burwash, Associate Professor of Medicine, University of Ottawa Heart Institute, will tackle the challenging problem of patients with left ventricular systolic dysfunction (LVD) and low-flow, low-gradient aortic stenosis. These patients represent an “especially challenging subset” of patients with aortic stenosis, as he notes in Current Opinion in Cardiology (2007;22:84-91) for a number of reasons, including the fact that it is often difficult to determine whether the aortic stenosis is due to patients with LVD and a reduced transvalvular flow rate. Reduced transvalvular flow can result in an unremarkable, quiet systolic ejection murmur, he states, despite the presence of a severe valve stenosis, so the physical exam can be deceiving.

Another difficulty lies in trying to determine whether the patient has “true” severe aortic stenosis—where the aortic valve is severely stenotic and afterload mismatch exists—or “pseudo-severe” aortic stenosis where the valve area appears to be severely stenotic (although it is not). This is due to inherent limitations in either the valve area equation under low-flow conditions or to an inability of the poorly functioning ventricle to provide sufficient force to open the valve cusps fully.

Fortunately, dobutamine echocardiography can help distinguish true from pseudo-severe aortic stenosis: once distinguished, aortic valve replacement (AVR) should be considered in low-flow, low-gradient aortic stenosis patients with true severe aortic stenosis but avoided in the presence of pseudo-severe aortic stenosis as valve stenosis in these patients is not the primary problem. Dobutamine challenge can also provide information on the presence or absence of LV contractile reserve, an important piece of information, as Dr. Burwash explains, because lack of contractile reserve is a strong predictor of both perioperative mortality and long-term survival in this patient group.

“Unfortunately, there is a frequent misconception that the lack of contractile reserve in low-flow, low-gradient aortic stenosis is a contraindication to AVR,” Dr. Burwash writes. While it is true that patients without contractile reserve have higher operative mortality rates and poorer long-term survival than others, “medical therapy is associated with a dismal 3-year survival of <15%,” he adds. In patients surviving AVR, those with and without contractile reserve preoperatively demonstrated a similar improvement in LV ejection fraction and a similar proportion improved by ≥1 or ≥2 NYHA functional classes, according to the literature.

“...should not be interpreted as an absolute contraindication to AVR,” Dr. Burwash reaffirms, “and strategies to avoid prosthesis-patient mismatch should be carefully considered in patients undergoing AVR to potentially improve the long-term surgical outcome.”

Aortic valve implementation

Dr. John Webb, Medical Director of the Catheterization Laboratory, Director of Interventional Cardiology Research, St. Paul’s Hospital, and Clinical Professor of Medicine, University of British Columbia, and colleagues recently reported on what is now the longest follow-up on transapical aortic valve implantation in humans. Dr. Webb and his team performed the first successful human case of implantation on a beating heart in October 2005. As they report in the Journal of Thoracic and Cardiovascular Surgery (2010;139:1107-13), between October 2005 and February 2009, “71 patients underwent implantation with either a 23- or 26-mm transcatheter bioprosthesis. “All patients with symptomatic aortic stenosis were declined for conventional AVR owing to unacceptable operative risks and were not candidates for transfemoral aortic valve implantation because of poor arterial access,” they noted in their abstract presentation. The mean age of the cohort was 80 years and predicted operative mortality ranged from approximately 20 to 35% by logistic EuroSCORE and by about 12% according to The Society of Thoracic Surgeons Risk Calculators.

The UBC group reported that valves were successfully implanted in all patients, although 12 patients died within 30 days for an overall 30-day mortality rate of 16.9%; 33% in the first 15 patients and 12.5% in the remainder; 10 patients subsequently died. At 24 months, roughly two-thirds of patients were still alive, as were 58% at 36 months’ follow-up. Survival was also higher among patients who survived for at least 30 days post-implantation. NYHA functional class improved significantly, from a preoperative value of 3.3 to a post-operative value at 24 months of 1.8. Both the aortic valve area and mean gradient remained stable at 24 months and late valve-related complications were rare, they reported.

“Our outcome suggests that transapical transcatheter aortic valve implantation provides sustained clinical and hemodynamic benefits for up to 36 months in selected high-risk patients with symptomatic severe aortic stenosis,” investigators concluded.

Early surgery for mitral regurgitation

Among the many controversies in cardiovascular medicine is whether early surgery should be recommended for mitral regurgitation (MR). According to Dr. Maurice Enríquez-Sarano, Director, Valvular Heart Disease Clinic and Professor, Mayo Clinic, Rochester, Minnesota, in an opinion piece co-authored with Dr. Thoralf Sundt (Circulation 2010;121:804-12), surgery is “almost unavoidable” in patients with organic MR.

Studies of patients diagnosed with severe MR in their 60s found mortality rates or the need for cardiac surgery ranged from 10 to 30% per year. Averaging those rates out to approximately 20% a year, “10 years after diagnosis, 90% of patients either have died or have undergone surgery,” the authors write. “Hence the question in both young and older patients is not ‘if’ but ‘when’ surgery should be performed: under duress from the disease or pre-emptively to minimize risk and normalize life expectancy.”

Dr. Enríquez-Sarano and Sundt also argue that rescue surgery for patients who meet class I indications (symptomatic patients or those with an ejection fraction [EF] ≤60% or LV end-systolic dimension ≥40 mm) is associated with excess post-operative mortality and therefore cannot be the preferred surgical indication in organic MR.

On the other hand, patients with no or minimal symptoms before surgery have identical post-operative survival rates to those of the general population while long-term post-operative survival of patients with good EFs is similar to that of the general population as well. “Thus, early surgery (in patients with minimal or no symptoms and EF ≥60%) suppresses the mortality of MR and restores it to that of persons of similar age and sex who never had MR and never had cardiac surgery,” the authors stated. They added that advanced repair centres have the capacity to offer high-quality repair and low operative risk which allows for restorative early mitral surgery.

“Comparative studies favour early surgery,” they confirmed, “and in view of overwhelmingly coherent data obtained worldwide, we consider early surgery the preferred option for treatment of organic MR.”

Dr. Steven Bolling, Director, Multidisciplinary Mitral Valve Clinic and Professor of Surgery, University of Michigan, Ann Arbor, will also discuss therapeutic options and outcomes for the treatment of ischemic and functional MR.

The Joint CCS/ACC Symposium “Hot Topics in Valvular Heart Diseases” takes place Sunday, October 24, 16:30-18:00 (Palais des congrès, Rm. 520AC).
Obesity “front and centre” of public policy session during HSFC session

Obesity will be “front and centre” of a CCC public policy session. Monday morning. ‘Fighting obesity is a top priority for the Heart and Stroke Foundation (HSFC),” states Linda Piazza, Director of Research and Health Policy, HSFC, whose presentation is entitled “Economic Policy, Obesity and Health: A Review of the Evidence.” Obesity is a leading cause of premature death and disability, as Piazza points out, and has a direct effect on a number of chronic diseases including coronary artery disease, stroke and diabetes. Given its prevalence—approximately one-quarter of Canadian adults were considered obese (body mass index ≥30) in 2004, according to Statistics Canada—controlling obesity is going to take a multi-faceted approach, the HSFC believes.

One aspect may lie in offering financial incentives and disincentives to those who supply the population with its food. Agricultural subsidies, for example, could encourage the cultivation of healthy crops over those such as tobacco while pricing policies that favour wholesome foods over fast foods could improve the health of the nation. Such policy interventions, including taxing cigarettes out of the reach of the young, have been shown to be effective in reducing the prevalence of cigarette smoking.

The HSFC is also interested in assessing the effectiveness such economic policies might have in the fight against obesity. To that end, the HSFC commissioned a rigorous review, led by Guy Faulkner, PhD, Associate Professor, Faculty of Physical Education and Health, University of Toronto, to examine empirical evidence related to the effectiveness of using economic instruments to address obesity. The review found considerable grounds for discussion regarding the manipulation of food and beverage pricing and their ability to affect the nation’s collective weight. The same review also showed that transferring food to the needy through various programs may improve nutrition and birth outcomes but that these efforts can also backfire, as there is some evidence from US studies that programs such as these may contribute to childhood obesity.

And while promotion of physical activity at an economic level may well help control the obesity epidemic, too few studies have been carried out in this area to make clear policy decisions regarding economic incentives and the promotion of physical activity. During the same session, recommendations for further consideration will be presented by Dr. Faulkner while public policy expert Sharon Manson Singer, PhD, will address the question of how organizations can translate results of the review into action.

The Public Policy Session takes place Monday, October 25, 11:00-12:30 (Palais des congrès, Rm. 517A).

INFO-Cardio is published by Medical Education Network Canada Inc. for the annual meeting of the Canadian Cardiovascular Congress. The purpose of INFO-Cardio is to promote events organized by the CCC, and to bring delegates closer together by fostering a sense of community spirit at the meeting. Your comments/suggestions are welcome. Contact us at mednet@mednet.ca or www.mednet.ca
The effort to improve cardiovascular (CV) risk assessment will be a recurring theme over the next few days during the Canadian Cardiovascular Congress (CCC). This includes the Monday-morning release of the results from the Primary Care Audit of Global Risk Management (PARADIGM). The study attempts to assess the accuracy of CV risk stratification in Canada by primary care physicians.

While PARADIGM addresses how screening techniques are being employed at the basic level of primary care, there are multiple subsequent steps vital to changing CV mortality figures. This includes using new strategies to find those at intermediate risk who are being missed by current screening techniques. This particular patient group is the most problematic because they are the most likely to be undertreated.

High-risk patients, such as those with a previous CV event or diabetes, are easily identified and should already be on maximal therapies for established risk factors such as LDL-C or hypertension. Low-risk patients, such as men below the age of 50 and women below the age of 60 without modifiable risk factors, are unlikely to derive immediate benefit from strategies to reduce CV risk. In contrast, many intermediate-risk patients, if properly identified, can be expected to derive major protection from treatment even in the absence of major elevations in conventional risk factors.

One of the best demonstrations of the value of treatment in intermediate-risk patients was generated by JUPITER (Justification for the Use of Statins in Prevention: an Intervention Trial Evaluating Rosuvastatin). JUPITER enrolled men ≥50 years of age and women ≥60 years of age with an LDL-C <3.3 mmol/L, without a history of CV disease and with elevated high-sensitivity C-reactive protein (hsCRP) (≥2.0 mg/L). When compared to placebo, the study agent at 20 mg q.d. achieved a 44% reduction relative to placebo ($P<0.00001$) in a composite primary end point that included CV death, non-fatal myocardial infarction (MI), nonfatal stroke, unstable angina or an arterial revascularization procedure. Partly as a result of that trial, the goal for LDL-C levels is now <2 mmol/L or a ≥50% reduction from baseline in intermediate-risk patients who have an LDL-C of >3.5 mmol/L, if they have a total cholesterol:HDL-C ratio of >5.0, or if they are men older than 50 years or women older than 60 years with an hsCRP level >2.0 mg/L.

It is important to recognize that the intermediate-risk patients who benefited in JUPITER were not candidates for lipid lowering before the study was conducted. Although the proportion of patients with metabolic syndrome was high (41%), the median body mass index of 28.4 kg/m² was only...
two of the most potent statins in patients after an ST-elevation MI (STEMI) underscored this problem. To be presented as a poster on Sunday afternoon, the study demonstrated that only 65.4% of patients were at LDL-C goal.

“A more aggressive approach to lipid management, including the use of higher statin doses, should be encouraged, together with appropriate management of all other risk factors, in order to improve long-term outcomes in STEMI patients,” according to a team of investigators from the Lipid Research Centre at Université Laval, Quebec City, led by Scientific Director Dr. Jean-Pierre Després. According to the researchers, who evaluated 1325 consecutive patients over a 30-month period, the median doses were only 10 mg for rosvuastatin and 40 mg for atorvastatin. Although these agents did not differ for their ability to achieve targets at these doses, large increases in the proportion at target would be expected with either agent at higher doses.

Ultimately, both primary and secondary CV events are preventable. For primary events, the most important step forward, after treating high-risk patients to current guideline-directed goals, is to identify those patients at intermediate risk who are being missed with current screening methods. For secondary events, a major opportunity for further risk reduction is being lost when available options are not used maximally to reach targets. Both expert opinion sessions and new data presented this week will reinforce both concepts.

Summary

The ability to better quantify CV risk through new tools has the potential to substantially reduce the burden of heart disease in Canada. Although the importance of conventional risk screening and treatment to goals cannot be underestimated, a substantial proportion of first CV events occur in middle-aged individuals with unremarkable risk profiles. The ability to introduce relatively simple tools, such as hsCRP screening, to better identify intermediate-risk patients who can anticipate major risk reductions from lipid lowering has important public health implications. The role of screening these patients will be addressed in several scientific forums over the course of the CCC.

Please plan to attend:

SATURDAY, October 23

“Expert Opinions: Advances in Cardiology.” 18:30-21:00, Room 517B, Palais des congrès.
New Anticoagulants a Major Advance in Stroke Prevention

**Montréal** - It is well established that atrial fibrillation (AF) is a major risk factor for stroke. Experts have estimated that approximately 15% of all strokes in the US are attributable to AF and AF increases the risk of ischemic stroke by approximately fivefold. Given that age is also a major risk factor for stroke, stroke prevention in the elderly is of paramount importance. The vitamin K antagonist warfarin is the only currently approved oral anticoagulant for stroke prevention and it works significantly better than ASA. However, warfarin has many shortcomings and it is a difficult drug for patients and physicians to use. New oral anticoagulants including both factor Xa and factor IIa inhibitors are on the horizon and studies thus far indicate they are at least as effective as warfarin and are not associated with any additional bleeding risk. These features suggest that the new oral anticoagulants will likely represent a major advance in stroke prevention.

**Montréal** - Il est bien établi que la fibrillation auriculaire (FA) est un facteur de risque majeur d'AVC. De l’avis d’experts, environ 15 % de tous les AVC répertoriés aux États-Unis sont attribuables à la FA, et la FA multiplie le risque d’AVC ischémique par un facteur d’environ 5. L’âge étant également l’un des principaux facteurs de risque d’AVC, la prévention de l’AVC chez le sujet âgé est primordiale. La warfarine, antagoniste de la vitamine K et seul anticoagulant oral actuellement homologué pour la prévention de l’AVC, est significativement plus efficace que l’AAS. La warfarine a toutefois de nombreux inconvénients, et c’est un médicament difficile à utiliser, pour les patients comme pour les médecins. De nouveaux anticoagulants oraux verront le jour sous peu, notamment des inhibiteurs du facteur Xa et du facteur IIa. Les études indiquent à ce jour qu’ils sont au moins aussi efficaces que la warfarine et qu’ils ne sont pas associés à un risque hémorragique supplémentaire. Ces caractéristiques donnent à penser que les nouveaux anticoagulants oraux représenteront probablement une percée dans la prévention de l’AVC.

By Pam Harrison

In her presentation “Predicting and Preventing Stroke in AF: The Benefits and Challenges of Warfarin,” Dr. Elaine Hylek, Associate Professor of Medicine, Boston University School of Medicine, Massachusetts, will likely refer to one of her key clinical findings regarding the use of warfarin in the first year of therapy among elderly patients with atrial fibrillation (AF) (Circulation 2007;115:2689-96). As Dr. Hylek notes in her study, warfarin is frequently underused for stroke prevention, particularly among the elderly who are at the highest risk. At least part of physicians’ reluctance to use warfarin is the perceived bleeding risk.

Based on findings from both randomized trials and observational cohorts, rates of major hemorrhage have been “reassuringly low” but published rates may underestimate bleeding risk in the elderly as few patients over the age of 80 have been enrolled in these trials; similarly, few studies include findings from the initial phase of therapy where the risk of bleeding is reportedly highest. To that end, Dr. Hylek and colleagues enrolled patients aged ≥65 years with AF on newly prescribed warfarin therapy. Warfarin was managed by on-site anticoagulation clinics. Of the 472 patients included in the study, almost one-third were 80 years of age and older and over 90% had at least one risk factor for stroke.

Over a one-year follow-up, the cumulative incidence of major hemorrhage for those 80 years of age and older was 13.1 per 100 person-years, whereas it was only 4.7 per 100 person-years for those under 80. During the first 90 days of warfarin use, age ≥80 years and an INR ≥4.0 were also associated with increased hemorrhagic risk, despite trial-level anticoagulation control. Over one-quarter of patients 80 years of age and older were taken off warfarin within the first year, mostly due to safety concerns. Dr. Hylek also observed that patients at the highest risk of stroke also experienced most of the bleeding, which underscores the complexity of managing these patients.

Understanding Old and New Anticoagulants

In his discussion “Understanding Anticoagulants: The Old and the New,” Dr. Jeffrey Weitz, Professor of Medicine and Biochemistry, McMaster University, Hamilton, Ontario, is likely to review the well documented shortcomings of the vitamin K antagonists, including their slow onset of action and variable dose requirements. In a discussion on anticoagulants with Dr. Graham Turpie, McMaster University, published online (http://www.theheart.org/article/987657.doc), Dr. Weitz noted that the many dietary and drug interactions with the vitamin K antagonists, along with the inconvenience of having to monitor INR, also contribute to the underuse of these agents. An oral anticoagulant that could be given in fixed doses with minimal need for monitoring would thus be a “huge advance,” as he suggested.

Continued
Two such agents—dabigatran, a factor IIa inhibitor, and rivaroxaban and apixaban, both factor Xa inhibitors—are promising such an advance. Both rivaroxaban and apixaban have been evaluated in AF among a number of other settings. The final results of the ROCKET (Rivaroxaban Once daily oral direct Factor Xa inhibition Compared with vitamin K antagonist for the prevention of stroke and Embolism) study will be presented at the American Heart Association meeting in November this year. The main goal of the study, which involved approximately 14,000 patients, will be to compare the efficacy and safety of rivaroxaban to that of warfarin for the prevention of stroke.

Apixaban has similarly been studied in the setting of AF. In AVERROES (Apixaban Versus Acetylsalicylic Acid (ASA) to Prevent Strokes), a total of 5600 patients unsuitable for treatment with a vitamin K antagonist were randomized to apixaban 5 mg b.i.d. or ASA 81 to 324 mg/day. As previously reported by lead investigator Dr. Stuart Connolly, Professor of Medicine, McMaster University, at the European Society of Cardiology meeting earlier this year, the annual rate of stroke or systemic embolism—the primary outcome—was 1.7% per year in the apixaban group vs. 3.9% per year in the ASA group, resulting in a relative risk reduction of 0.45 (P<0.001) in favour of the factor Xa inhibitor (ESC Press Release, August 31, 2010).

Major bleeding rates were similar between the two groups at 1.6% per year with apixaban and 1.4% per year with ASA; hemorrhagic stroke rates were low at 0.2% per year in both treatment groups. There were more minor bleeds (P=0.04) in the apixaban group, but they did not require physician intervention.

**RE-LY trial**

In the RE-LY (Randomized Evaluation of Long-Term Anticoagulation Therapy) trial, dabigatran was similarly shown to be at least as effective as warfarin and it was also safer at lower doses (*N Engl J Med* 2009;361:1139-51). As reported by RE-LY lead investigator Dr. Connolly and colleagues, the study involved 18,113 patients with AF at moderate to high risk for stroke. Patients received either dabigatran 110 or 150 mg b.i.d. or, in an unblinded fashion, adjusted-dose warfarin.

At a median follow-up of 2 years, stroke or systemic embolism occurred at a rate of 1.54% per year among patients who received the 110-mg dose, at 1.11% per year in patients receiving the 150-mg dose and at 1.69% per year in warfarin counterparts. Designed as a non-inferiority trial, investigators concluded that both doses of the direct thrombin inhibitor were non-inferior to warfarin (P<0.001). In fact, the higher dose of dabigatran proved to be superior to warfarin, reducing the risk of the primary end point by 34% (P<0.001). Rates of life-threatening bleeding, intracranial bleeding and major or minor bleeding were higher with warfarin than with either dose of dabigatran. Specifically, major bleeding rates were 3.36% per year in the warfarin group, 2.71% per year in the dabigatran 110-mg group and 3.11% per year in the dabigatran 150-mg group.

In his review of the ACTIVE A trial (*N Engl J Med* March 31, 2009, published online), Dr. Connolly will point out that patients considered unsuitable for warfarin were randomized to receive clopidogrel 75 mg/day or placebo on a background of ASA therapy. The primary outcome was a composite of major vascular events including stroke, myocardial infarction (MI), non-central-nervous-system systemic embolism or death from vascular causes. At a median follow-up of 3.6 years, the primary outcome was reduced by 11% with combination clopidogrel/ASA, in large part due to a substantial reduction in stroke. There was also a trend towards a reduction in MI but this did not reach statistical significance. Major bleeding rates were higher in the clopidogrel arm at 2% per year vs. 1.3% per year in the placebo group and fatal hemorrhage rates were slightly though non-significantly higher at 0.3% per year in the clopidogrel arm vs. 0.2% per year in the placebo controls.

**Summary**

Warfarin has been the only available oral anticoagulant for some 65 years and physicians have been waiting a long while for improved anticoagulant alternatives. The emergence of two new classes of oral agents, the factor IIa and the factor Xa inhibitors, offers an opportunity for greater efficacy by improving stroke prevention and causing fewer bleeds. Results from ongoing clinical trials are eagerly awaited.
Looking Ahead in Acute Coronary Syndrome Management

Montréal - Antiplatelet therapy for patients with or recovering from an acute coronary syndrome (ACS) is changing. Here at the CCC, numerous programs over the coming days will explain this evolution, which is based on a series of multinational trials. Of these programs, a breakfast symposium being held on Monday morning deserves attention. ‘ACS Care in Canada: an Evolving Paradigm’ includes several of those involved in the trials that are driving the changes. The program will be a practical analysis. In ACS, decisions must be made rapidly even though the antithrombotic benefits of an antiplatelet regimen are weighed against the risk of life-threatening or fatal bleeds. The previous antiplatelet standard of clopidogrel, administered with ASA, is being replaced by newer antiplatelet agents that have demonstrated a greater relative reduction in major adverse cardiac events. In some cases, this can be achieved without a significant increase in adverse events.

Montréal - Le traitement antiplaquettaires indiqué durant ou après un syndrome coronarien aigu (SCA) est en pleine métamorphose. Dans les jours à venir, de nombreuses activités du congrès porteront sur cette évolution, qui repose sur une série d’essais multinational. Au nombre des activités dignes de mention figure le symposium-déjeuner «La prise en charge du SCA au Canada : un paradigme en évolution» qui aura lieu lundi matin et qui réunira quelques-uns des experts ayant participé aux essais qui sous-tendent les changements. Le symposium prendra la forme d’une analyse pratique. Le SCA impose la prise de décisions rapides, même lorsqu’on doit souper l’activité antithrombotique en regard du risque d’hémorragie mortelle ou potentiellement mortelle. L’association clopidogrel + AAS, antérieurement le traitement antiplaquettaires de référence, fait place peu à peu aux antiplaquettaires de nouvelle génération associés à une réduction plus marquée du risque relatif d’événement cardiaque majeur, mais ce changement n’a pas forcément pour corollaire une augmentation significative des effets indésirables.

By Ted Bosworth

For patients with acute coronary syndrome (ACS), the emergence of novel treatment strategies paired with a focus on improving continuity of care can lead to the optimization of long-term outcomes, including survival.

The best proof of this is that event rates always fall markedly each time a more effective antiplatelet therapy replaces the previous standard. For several years, clopidogrel plus ASA has been the standard, but clopidogrel has now been outperformed by newer antiplatelet agents. Although the greater protection against thrombotic events was accompanied by a greater risk of major bleeding in one study, the benefit:risk ratio still favoured the newer agent in most patient groups. In another study, the newer agent outperformed clopidogrel without significantly increasing clinically significant bleeding.

The clinical relevance of these findings will be evaluated in detail Monday morning. In a program led by Dr. Shamir R. Mehta, Director, Coronary Care Unit, McMaster University Medical Centre, Hamilton, Ontario, the goal is to provide a detailed look at exactly what impact the recent major trials are likely to exert on patient care. According to Dr. Mehta, “The options for preventing thrombotic events in ACS patients are evolving with the introduction of new antiplatelet agents as well as with efforts to address unresolved questions, such as how long to maintain patients on these drugs. The symposium has been developed to provide some practical guidance about where we are now and how this field is likely to evolve in the near future. This should be a useful and practical session for clinicians trying to assimilate a large amount of new information. ACS management is rapidly evolving and is a critically important area for reducing major cardiovascular events.”

What is known about the current antiplatelet options will be summarized by hematologist Dr. John Eikelboom, McMaster University, and Prof. Philippe-Gabriel Steg, Director, Coronary Care Unit, Hôpital Bichat-Claude Bernard, Paris, France. They will provide the background on the importance of the recent trials and how the lessons from those studies are expected to be applied in reducing the risk of thrombotic events.

However, current evidence, including the studies with the newer agents, does not resolve all controversies. Rather, newer strategies raise new issues about how best to manage thrombotic risk in a broad range of clinical situations, such as in patients who receive a percutaneous coronary intervention (PCI) vs. those who require coronary artery bypass grafting (CABG). In particular, patients who receive stents require aggressive antiplatelet therapies for extended periods, but the definition of an aggressive therapy and the specific period of secondary risk prevention with these therapies remain unclear despite the critical importance they may have to patient survival.

In the first of three debates to generate guidance of key unresolved issues, cardiac surgeon Dr. Marc Ruel, Cardiac Surgery Research Chair, Ottawa Heart Institute, Ontario, and Dr. David Fitchett, Director, Cardiac Intensive Care Unit, St. Michael’s Hospital, Toronto, Ontario, will interpret the
evidence in regard to timing of initial antiplatelet therapy. They are expected to provide views that diverge in important ways.

In the second debate, Dr. Mehta is paired with Dr. Deepak L. Bhatt, Chief of Cardiology, Veterans Affairs Boston Healthcare System, Massachusetts, in a discussion of whether reducing ischemic events outweighs the prevention of bleeding when selecting an antiplatelet regimen. Dr. Bhatt is one of the most prolific trialists in antiplatelet medicine. The issue is delicate, because bleeding is considered an iatrogenic event in any given patient, even when the data suggest that this is an acceptable price to pay for a better outcome across a varied population of patients. The debate is likely to be greatly influenced by how a major bleed is defined to ensure that life-threatening ischemic events are being compared against life-threatening bleeding events.

In the third debate, Dr. Shaun G. Goodman, Associate Head of Cardiology, St. Michael’s Hospital, and Dr. Michael P. Love, Director of Revascularization Outcomes Research, Dalhousie University, Halifax, Nova Scotia, will discuss the optimal duration of dual antiplatelet therapy. This is among the most pressing issues. In patients who receive an intracoronary stent, some have argued that dual antiplatelet therapy should be lifelong, but this is not based on outcomes data. Cost efficacy is one argument to choose a much shorter period, but there is concern that follow-up is insufficient to document when dual antiplatelet therapy stops being cost-effective.

The key to the debates and to the optimal delivery of antiplatelet therapy during acute management of ACS will be to understand what the data do and do not reveal. The key studies of the newer agents are PLATO (PLatelet inhibition And PiTient Outcomes), which compared ticagrelor to clopidogrel in an all-comer ACS design, and TRITON-TIMI 38 (TRial to assess Improvement in Therapeutic Outcomes by optimizing platelet inhibitiON), which compared prasugrel to clopidogrel in ACS patients only after they had been scheduled for a PCI.

The relative benefits of ticagrelor and prasugrel over clopidogrel had many parallels, particularly in the primary composite end point of ischemic events. In TRITON-TIMI 38 (Wiviott et al. N Engl J Med 2007;357:2001-15), published two years before PLATO, prasugrel reduced major thrombotic events by a relative 19% ($P<0.001$). Although it was associated with a 32% ($P=0.03$) increase in major bleeding, subsequent analyses found that the benefit:risk ratio still favoured prasugrel except in patients over the age of 75, patients weighing less than 60 kg, and patients with a prior history of cerebrovascular events. In TRITON-TIMI 38, prasugrel was not associated with a mortality benefit.

In PLATO (Wallentin et al. N Engl J Med 2009;361:1045-57), there was a 16% relative reduction ($P<0.001$) in major ischemic events but no relative increase in major bleeding. More importantly, ticagrelor was associated with a 22% relative reduction ($P<0.001$) in all-cause mortality, perhaps the most powerful indicator of a major benefit over the previous standard. There are many potential explanations for the mortality benefit, particularly the ability to provide a greater anti-thrombotic effect without increasing the bleeding risk, which are phenomena that have been tightly linked in the past, but ticagrelor is also the first reversible P2Y$_{12}$ receptor inhibitor. While ticagrelor falls off the receptor so that there is significantly less inhibitory activity 72 hours after the last dose, platelet function after clopidogrel and prasugrel is not restored until new platelets are made. The irreversible inhibition is problematic in patients undergoing unanticipated surgery, including CABG, or with bleeding complications.

**Summary**

Due to large studies that have suggested that newer antiplatelet agents are more effective than clopidogrel in preventing recurrent ischemic events in ACS patients, practice standards are expected to evolve. Among several opportunities to understand this evolution over the coming week, the breakfast symposium on Monday morning may provide some of the best insight in a clinically-relevant context. The summary of evidence will be accompanied by debates on important aspects of the evolving principles of management to establish where treatment is now and where the next areas of potential change can be found.

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**Please plan to attend:**

**MONDAY, October 25**

“ACS Care in Canada: An Evolving Paradigm.” 7:00-9:00, Room 517D, Palais des congrès.

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Smoking as a Modifiable CV Risk Factor: Physicians to Be Encouraged by Evidence-based Tools

Montréal - Tobacco use is an important and well-recognized modifiable risk factor for coronary heart disease. It is also one of the most difficult to control successfully. While lifestyle changes are recommended for many modifiable risk factors, including hypercholesterolemia and hypertension, these risks can also be largely addressed with pharmacologic therapies. Although successful smoking cessation is ultimately dependent on lifestyle changes, there appears to be an under-appreciation for the role of pharmacological therapies to greatly improve the likelihood of treatment success. Well-controlled trials have demonstrated that treatments for smoking can be integrated into the same kind of comprehensive approach taken to treatment of elevated lipids or high blood pressure. Several programs during the CCC will reiterate this message. None is expected to be more directly applicable to clinical practice than one being held Tuesday afternoon at which new CCS guidelines will be released.

Montréal – L’usage du tabac, c’est bien connu, est un important facteur de risque modifiable de maladie coronarienne. C’est aussi l’un des facteurs de risque les plus difficiles à corriger avec succès. Si la modification des habitudes de vie est recommandée dans la prise en charge de nombreux facteurs de risque modifiables, dont l’hypercholestérolémie et l’hypertension, les médicaments jouent aussi un rôle de premier plan. Dans le cas du renoncement au tabac, même si le succès repose en définitive sur la modification des habitudes de vie, il reste que la contribution des traitements médicamenteux à l’amélioration marquée des chances de succès semble sous-estimée. Des essais comparatifs rigoureux ont montré que l’usage d’aides antitabagiques pouvait s’inscrire dans une démarche globale comme celle que l’on utilise déjà pour le traitement de l’hyperlipidémie ou de l’hypertension. Ce message sera réitéré dans plusieurs activités du congrès, mais aucune n’aura de plus grande portée pratique que la présentation, mardi après-midi, des nouvelles recommandations de la Société canadienne de cardiologie.

By Ted Bosworth

It is difficult to generate more concern by citing the health risks of smoking because they are so well known. Although the proportion of adults who smoke in Canada has declined from approximately 35% in 1985 to less than 20% in the most recent survey, those who continue to buy cigarettes do so despite a warning on the package that the habit is lethal. The ability of those addicted to cigarettes to ignore this message and the overwhelming evidence of harm is the reason that many clinicians only devote modest time to inducing patients to quit. However, this ignores the fact that many smokers want to quit and that there are evidence-based strategies to apply.

The specific evidence-based strategies will be described in detail in new CCS guidelines and position statements to be released on Tuesday afternoon by Dr. Mark Eisenberg, Director, Cardiovascular Health Services Research Group, Jewish General Hospital, Montréal, and Dr. Andrew Pipe, Medical Director, Minto Prevention and Rehabilitation Centre, University of Ottawa Heart Institute. One of the most important roles of the guidelines is to reinforce the concept that smoking is treatable and that the same type of rigor is needed in addressing this risk factor as applied to other modifiable risk factors.

Evidence-based smoking cessation guidelines were first introduced more than a decade ago. One of the first was developed by a consortium of medical specialist organizations in the UK (Raw et al. BMJ 1999;318:182-5) in recognition that the risk of smoking extends to a broad array of organ systems. In Canada, there are also numerous organizations other than the CCS interested in reducing smoking rates. The Canada Lung Association (CLA) is among those that advocate pharmacologic therapy as part of the strategy for smoking cessation.

“Quit-smoking medicines can reduce your nicotine withdrawal symptoms, reduce your urge to smoke and boost your chances of quitting.” the CLA has stated in a patient-education Web site (www.lung.ca/protect-protegez/tobacco-tabagisme/quitte/medicines-medicaments_e.php). It notes that 3 medications have been specifically approved by Health Canada for smoking cessation. For each of these—varenicline, nicotine replacement and bupropion—the mechanisms and practical applications are described.

Past guidelines have stressed individualization of therapy based on specific patient characteristics, and new data to be presented this week at the CCC suggest that the available pharmacologic agents may not be interchangeable for successful quit rates. In an oral presentation scheduled for Sunday, Dr. Robert D. Reid, Associate Director, Minto Prevention and Rehabilitation Centre, will present data from a direct pilot comparison of varenicline and a transdermal nicotine patch in patients with CHD. According to Dr. Reid, there are few comparative studies in secondary prevention or other well-defined subgroups at risk. Data from this pilot study are being collected to direct a much larger study expected to generate more definitive answers about which strategies to consider first.

Nicotine replacement is based on providing diminishing amounts of nicotine as patients are weaned from their addiction and is one of the oldest approaches to smoking cessation;
varenicline and bupropion avoid nicotine altogether. The α2β4 nicotinic acetylcholine receptor partial agonist varenicline reduces the rewarding properties of nicotine. Bupropion, initially developed as an antidepressant, has several effects that may reduce cravings, such as weak antagonism of nicotinic receptors, although its mechanism is less well-understood.

In one of the most frequently cited studies of smoking cessation, both varenicline and bupropion were found effective relative to placebo for smoking cessation as measured by continuous abstinence from cigarette smoking over the final 4 weeks of a 12-week trial (Jorenby et al. JAMA 2006;296:56-63). In that multicentre study, 1027 patients were randomized. On the basis of the primary end point, 43.9% of those treated with varenicline, 29.8% of those treated with bupropion and 17.6% of those treated with placebo were treated successfully. Relative to placebo, the odds ratio (OR) of success was 3.85 for varenicline (P<0.001) and 1.9 for bupropion (P<0.001).

When comparing pharmacologic therapies, however, the context of the supportive program is important. Although drug therapy provides an important framework for success, pharmacologic therapy alone is widely acknowledged to be insufficient. A variety of evidence suggests that smoking is not only driven by nicotine addiction but specific triggers, such as use of coffee or alcohol, which establish cravings. A prescription for pharmacologic therapy is unlikely to be successful without arming patients with strategies to manage cravings and avoid the triggers. This phenomenon is likely to be recognized in the new guidelines which, again, have been aided by substantial progress in defining components of successful programs that can be reproduced by others.

Indeed, this is the subject of another oral presentation by researchers at the Minto Prevention and Rehabilitation Centre. The data for this study, which evaluate the Ottawa Model for Smoking Cessation (OMSC), are scheduled for presentation directly after the oral presentation by Dr. Reid on Sunday. The OMSC has now been exported to 70 cardiac care centres in Canada—an important step forward because “most hospitals in Canada are still without systems and protocols to adequately identify and treat admitted tobacco-users,” according to the Minto centre researchers. Evidence that a systematic approach can be employed to improve quit rates is important information for physicians counselling patients, particularly those who have tried and failed to quit previously.

For motivated patients, cardiologists and primary care physicians may be able to provide an adequate framework for successful cessation of smoking with pharmacologic therapy and tools for lifestyle changes, but clinicians should become familiar with referral services. Even patients who are anxious to quit smoking may have difficulty coping with the multiple components of biochemical and behavioural forces that drive addiction. Many patients may fail multiple smoking cessation attempts before succeeding, but these failures may often be part of a process. While a systematic approach is appropriate, clinicians should not be discouraged by an initial failure.

There is a large amount of data available with which to convince smokers to quit. In aging patients consulting with a cardiologist, there may be a willingness to hear messages that were ignored at a younger age. Canadian data suggest that quit rates increase with age, perhaps as patients recognize their mortality. While the risks of CHD and lung cancer associated with cigarette smoking may be enough to attract the patient’s attention, one of the most potent messages is that smokers live shorter lives. On average, male smokers die 13 years earlier and females die 14 years earlier than individuals of their gender who do not smoke, according to data collected from the U.S. National Heart, Lung, and Blood Institute (Anthonisen et al. Ann Intern Med 2005;142:233-9).

Summary

New CCS guidelines for smoking cessation to be released Tuesday afternoon are expected to aid clinicians in pursuing a systematic approach to control of one of the most important modifiable risk factors for cardiovascular disease. Smoking cessation cannot be reduced to a pharmacologic prescription, but drug therapy can provide an important framework for successful quit rates as demonstrated in controlled trials. Application of evidence-based principles may help bring the type of rigor to smoking cessation that is now employed for other modifiable risk factors, such as lipid or blood pressure control.