The future of cardiovascular (CV) medicine must move from treatment of disease to health promotion, state-of-the-art lecturer Dr. Valentin Fuster warned. Otherwise, the cost of continuing to manage it by current strategies will bankrupt every country in the world, including wealthy countries such as Canada. “CV disease (CVD) and stroke are the number one cause of mortality today and 80% of MIs and strokes happen in middle- to low-income countries because four-fifths of the world is low-income,” Dr. Fuster told delegates. Dr. Fuster is Director, Cardiovascular Institute, Mount Sinai Medical Center, New York, and Scientific President, Centro Nacional de Investigaciones Cardiovasculares Carlos III (CNIC) in Madrid. Thus, CVD is a health issue across the world, as Dr. Fuster reaffirmed, and mortality rates from it have remained largely unchanged, even though longevity has been prolonged by approximately six years over the past three decades in high-income countries. In fact, the lion’s share of this increase is attributable to improved treatment of acute coronary syndromes, while only 25% of it is due to prevention—“so we are prolonging life at a very high cost but we are still not preventing disease,” as Dr. Fuster suggested.

Furthermore, over the next three to four decades, CVD will increase not only in high-income countries but by more than 200% in middle- and low-income countries, the key driver behind it being the current epidemic of obesity and its consequences. Researchers are therefore obliged to find an answer to stop the worldwide tsunami of CVD from occurring and the answer must come from more research and development.

As scientific president of the CNIC, Dr. Fuster revealed how the world might acquire future researchers by encouraging them from a very young age. Several years ago, members of the CNIC asked Spanish governments who were the best and the brightest in the land and they delivered some 200 names. Grants were given to a handful of these young students at a time, and they were brought to work in a lab under an investigator. “At the end of their training period, 85% of them said they wanted to become an investigator,” noted Dr. Fuster, “and this is important because 10 years from now, we will have who are all excited to become 200 people investigators.”

Continued Research

Dr. Fuster also reminded delegates that scientists cannot promote health unless they learn how the arteries protect themselves from vascular disease. This will necessitate continued research at a cellular and molecular level; thanks to molecular imaging techniques, certain defense mechanisms are already understood. Having identified many of these mechanisms himself, Dr. Fuster—referred to as a “living legend” in CV medicine by Canadian experts—detailed how traditional risk factors damage the endothelial cells. “Progenitor cells from the bone marrow recognize that there is damage in the endothelium and they work together to try and cover the damaged area,” Dr. Fuster explained. Macrophages also recognize oxidized LDL cholesterol in the arterial wall and they try to deliver it to HDL-C, which then transports LDL cholesterol from the vessel wall back to the liver. But when too much LDL-C enters the
vessel, the macrophages become overloaded and "commit suicide," releasing toxic factors as they do so, tissue factor key among them. The internal elastic lamina breaks down, rendering plaque unstable and ripe for rupture. If that plaque then encounters tissue factor, a thrombus is likely to form and patients will be in the throes of a MI.

The failure of these defense mechanisms is what defines an MI as we see it in 2008," stated Dr. Fuster, and "we have to learn how to enhance all of these defense mechanisms to try and prevent an MI from happening."

One such avenue that appears extremely promising is to boost HDL-C safely. In rabbit models of atherosclerosis, for example, the apoptotic process was stopped by series of injections with the ApoMilano cholesterol subfraction. Others have shown that liposomal glucocorticoids (glucocorticoids attached to a peptide that recognizes inflammation in the vessels wall) completely banished inflammation in that wall, suggesting another pathway by which to circumvent the process leading to MI. "Protecting the health of blood vessels is beginning to be understood through imaging technologies and we are also beginning to understand how the drugs we use work at a molecular level," Dr. Fuster told delegates. "We need a lot of support for research and development to further our knowledge."

Another area under intense investigation is differentiating who will go on to have an actual event and who will not, but who still have the same risk factor profile and the same estimated 10-year CVD risk. "This is a reality that we are all facing with all of our patients whether consciously or unconsciously," Dr. Fuster indicated. The goal, then, is to improve the "diagnostic" yield of the risk factor profile, known to most physicians but not that frequently used, as Dr. Fuster also suggested. One possibility will be genetics. Currently, researchers in different countries are investigating the genome of patients who have sustained an MI and comparing them to those who have not. "This is a very complex disease with a tremendous amount of work is being generated as to where the genes might be located that are important in CVD," Dr. Fuster noted. Molecules against lipoprotein-associated phospholipase A2 have been shown to neutralize high levels of the enzyme and potentially stop disease progression, while treatment with potent statins may also reduce high hsCRP levels, a sign that disease is present if not yet in the realm of traditional risk factors, he added.

The CCS is poised to champion a nationwide initiative to standardize Canadian cardiovascular data in order to provide an opportunity for provinces to compare data and to provide links to other administrative databases, Dr. Ross Davies, University of Ottawa Heart Institute, and chair of the Canadian Cardiovascular data standards workshop held yesterday, is hoping that the CCS will participate in the development of an action plan aimed at developing common Canadian standards for data and data elements. "One of the recommendations coming out of the Canadian Heart Health Strategy is that we need to improve our capacity in terms of data to better manage health care," Dr. Davis told INFO-Cardio. Not that the provinces do not already have some excellent provincial CV databases, he added. These databases are already used to manage wait lists and to help their respective governments with resource allocation. However, as he also pointed out, each of the provinces use different elements in data definitions, "so I think if we move to common data and data elements, it has the potential for great cost savings," he stated."

**Towards standardized CV data**

**John Keith Lecture: Physicians important advocates in pediatric cardiovascular disease risk modification**

Physicians can be important advocates for the kind of lifestyle changes that may prevent an epidemic of heart disease in the future, and they need to start immediately with at-risk children and adolescents.

"The process that leads to a myocardial infarction (MI) or stroke that patients have in adulthood starts in the pediatric age range and if we can identify risk factors for that process in children, hopefully we can intervene to improve long-term risk," states Dr. Stephen Daniels, Professor and Chair, Department of Pediatrics, University of Colorado Denver School of Medicine, and this year's John Keith lecturer. The session will be chaired by Dr. Marc Bélanger, Director of Pediatric Cardiology, McGill University.

Risk factors for cardiovascular disease (CVD) in childhood and adolescence are the same ones that predispose adults to the disease, including hypertension, dyslipidemia, obesity and—perhaps type 2 diabetes, now being seen in adolescents. In the Fels Longitudinal Study, for example (J Pediatr 2008;152:191-200), researchers observed that the first appearance of differences between adults with and without the cardiometabolic syndrome occurred at ages 8 and 13 as these differences related to BMI in boys and girls, respectively, and between the ages of 6 and 13, respectively, as these differences related to waist circumference. Thus, there is no question that children with a BMI and waist circumference exceeding established values in childhood are at increased risk for the cardiometabolic syndrome as adults.

The same study also showed that children with systolic blood pressure above healthy values in childhood are also at increased risk of hypertension as adults. The National Heart, Lung and Blood Institute Growth and Health Study also indicated that girls who were overweight during childhood were 11 to 30 times more likely to be obese in young adulthood, and that being overweight was associated with unhealthy blood pressure levels and dyslipidemia (J Pediatr 2007;150:18-25).

Fortunately, the same risk factors that occur in childhood and adolescence are amenable to risk factor modification. Having explored many facets of risk factor intervention in childhood and adolescence, Dr. Daniels and colleagues reported favourable changes in cardiac geometry as well as systolic and diastolic function before and after weight loss surgery in morbidly obese adolescents. In a study involving 38 adolescents with a preoperative BMI of 60 kg/m² (J Am Coll Cardiol 2008;51:1342-8), the group observed that the prevalence of concentric left ventricular hypertrophy (LVH) improved from 28% preoperatively to only 3% at follow-up, with a post-operative BMI of 40 kg/m². Normal LV geometry also improved from 36% pre-operatively to 79% at follow-up, while both cardiac workload and diastolic function significantly improved with substantial weight loss.

An evaluation of a clinic-based behavioural nutrition intervention which emphasized the Dietary Approaches to Stop Hypertension (DASH)-type diet for adolescents with elevated blood pressure showed that children who followed the DASH program had a greater decrease in total fat as well as systolic blood pressure at three months’ follow-up than those assigned to a routine outpatient hospital-based nutrition care program (J Pediatr 2008;152:494-501).

"Used appropriately and provided children are monitored, antihypertensive drugs are also safe and effective in lowering blood pressure in pediatric patients," Dr. Daniels noted. He added, "It’s not easy, but I think we need to start now and look for risk factors early and follow children over time and health professionals need to interact with families to improve the situation."
Heart and Stroke Foundation's Health Check program helping Canadians shake the salt habit

Late Breakers 2008: focus on myocardial infarction, angina, NT-proBNP, ventricular function

Late breakers once again wind up the CCC meeting as Canadian researchers share the details of important clinical trials in the making. Chaired by Dr. Eva Lonn, Dr. Jean-Claude Tardif and Dr. G. John Mancini on Wednesday at 9:00-10:30, the clinical trials session will feature the following four studies, updating findings based on recent analyses and making delegates privy to information often not available from any other source.

Trail of Efficacy and Safety after Fibrinolysis to Enhance Reperfusion in Acute Myocardial Infarction (TRANSFER-AMI): Six-month outcomes. Study patients consisted of individuals presenting to Canadian non-percutaneous coronary intervention (PCI) centres with STEMI within 12 hours of symptoms onset and with high-risk to drowning. The randomized group received a randomized in-pharmacy strategy of fibrinolysis plus PCI with six hours of fibrinolysis or to standard treatment after fibrinolysis, including rescue PCI as required for ongoing chest pain and >50% resolution of ST-elevation at 60 to 90 minutes. All patents received upfront ASA and antithrombin therapy and upfront use of clopidogrel was strongly encouraged. The primary endpoint was the 30 day composite of death, reinfarction, recurrent ischemia, heart failure or shock. Preliminary 30-day results revealed that the pharmacovascular strategy reduced the primary endpoint by 45% compared with PCI alone. This difference in major bleeding complications between the two treatment arms. The authors promise that six-month outcomes will demonstrate whether the significantly lower rates of ischemic complications seen with the pharmacovascular strategy at 30 days are sustained and translate into lower rates of death or reinfarction at six months.

Safety and Efficacy Study of Integrilin plus Unfractionated Heparin vs. Unfractionated Heparin Alone in Patients with Acute St-Segment Elevation Myocardial Infarction Treated with Percutaneous Coronary Intervention: The ASSIST trial. Over 400 patients presenting with STEMI were randomized within hours 12 hours or less to intravenous epibatidine prior to cardiac catheterization followed by PCI or to treatment with PCI with unfractionated heparin alone. The primary endpoint was a composite of death, reinfarction or recurrent severe ischemia, measured at 30 days. Secondary outcomes included angiographic results before and after PCI, major bleeder rates and left ventricular function. Results at 30 days for both primary and secondary end points will be presented, as well six-month follow-up data. (Abstract 1101)

The ADD-IFI trial. A total of 889 patients with documented CAD and stable angina who were already on atenolol were randomized to receive either sibradine, a novel L L inhibitor that acts specifically on the pacemaker activity of the sinoatrial node, or placebo for four months. Patients underwent treadmill tests at baseline and after four months of treatment. Main outcome measures were changes in total exercise duration, time to limiting angina, time to angina onset and time to 1 mm ST-segment depression. Results at four months indicated that sibradine improved exercise capacity in patients not controlled by standard beta blockade, significantly extending time on all end point measures. Sinus bradycardia was seen in approximately 3% of treated patients vs. 1.6% on placebo, while visual symptoms were reported by 2% of patients in the L group vs. about 1% of placebo patients. (Abstract 1102)

Effect of rosiglitazone on left ventricular systolic and diastolic function and on NT-proBNP level of patients with type 2 diabetes mellitus. The DREAM trial. DREAM was a placebo-controlled trial of rosiglitazone in patients with impaired glucose tolerance, impaired fasting glucose or both but without CVD at baseline. Echocardiograms were obtained in a subset of participants after a median of three years post-study entry and NT proBNP was measured at baseline and again after three years. Three years’ post-randomization, patients receiving rosiglitazone had higher left ventricular (LV) end-systolic and end-diastolic volumes, LV mass indices, left atrial volume indices and advanced LV diastolic dysfunction, but LV ejection fraction and wall motion scores did not differ between the two treatment groups. NT proBNP also increased significantly more in the rosiglitazone group, likely due to fluid retention.

Q: How would you compare this congress with other cardiology meetings in other countries?

Dr. William Faris, Ottawa Heart Institute: I think this one has a uniquely Canadian flavour in terms of the quality of the presentations, the quality of the science and the quality of the teaching. It’s right up there with the important international meetings and at the same time, you can access the meeting more easily, so I find I come to the CCC quite regularly whereas my attendance at international meetings has become more sporadic. This meeting challenges international meetings in terms of quality, and it has the added attraction where Canadians can meet their mentors when they were in training, and their peers with whom they’ve trained and who’ve now populated the country from coast to coast, and it’s a chance to catch up with their professional and personal lives.

Dr. Charles Kerr, incoming CCS President: It’s difficult to compare them, as they are quite different in their emphasis and amount of content. However, Canadians are extremely well known internationally for collaborative Canada-wide research—we have some of the best clinical trials and the best collaborations demonstrated around the world and are leaders in that area, and a lot of this stems from the ability of a congress like this to bring people together. It is also great to see our junior members commence their academic careers. I recall very vividly my first experience presenting a scientific abstract at a CCS meeting in Quebec City in 1979; it was a very important event for me and I presented many abstracts over those first three to four years which prepared me for my entire research career. So I think it’s the combination of the Canadian nature of the meeting, the intimacy of it, the ability to collaborate, the opportunities for Canadian investigators to get together, and particularly for our young and up-and-coming stars to get a start to their careers.

Dr. David Fitchett, University of Toronto: This is a national meeting in a country of about 30 million people so you can’t compare it to an international meeting like the AHA or the ACC. However, it’s very good representation of the cardiology research and the cardiology community in Canada so it has enormous importance for our development. New ideas are developed within the country—we are not a branch plant of the US—we have our own clinical trials, we have our own ideas and we have our own version of doing things even guidelines need to be adapted to the way we practice which is often very difficult to US practice. So the CCC is an immensely important meeting for Canadian cardiology.
Helping cardiac patients quit: Smoking cessation starts with a new attitude

The most important service physicians can offer their cardiac patients is to help them quit smoking. But in order to do that more effectively, they are going to have to drop old attitudes about smokers and take a more direct, helpful and non-judgmental approach, as Dr. Andrew Pipe, Professor of Medicine, University of Ottawa, will argue in his session on smoking cessation on Tuesday.

As Dr. Pipe told INFO-CARDIO, “The prevailing dogma from the mid- to late-20th century is that smoking is a habit; it’s a lifestyle choice, that everybody should be able to quit if they really want to.”

The reality, however, is that smoking—and more importantly, a patient’s ability to stop smoking—is really a biologic issue that is governed by genetics and in part by atavistic impulses from the brain that make patients feel uncomfortable if they try to quit. As Dr. Pipe explains, there are variations in people’s ability to quit smoking. These variations are reflective of an individual’s genetic predisposition to become addicted, to maintain behaviours that result in recidivism, as well as in their ability to become successful non-smokers.

In addition, “most smokers need to maintain a certain level of nicotine in the blood and because nicotine ultimately stimulates dopamine release in the brain, the need to smoke is really a reflection of disordered brain function, structure and neurochemistry,” Dr. Pipe observes. Even well-informed, intelligent smokers determined to quit find it difficult to ignore signals from the brain stem that essentially tell a smoker, “If you don’t bathe me in nicotine every 15 to 20 minutes, I’m going to make you very uncomfortable.”

Dr. Pipe confirms, “If you are addicted to nicotine, your brain stem will trump higher levels of cognitive function every time.”

There are variations, especially those with symptomatic smoking-related diseases, absolutely understand that smoking has toxic consequences. To bombard them with didactic messages that smoking kills has little impact: “Patients don’t want to be preached to or lectured to,” as Dr. Pipe stresses.

Systematic Fashion

To really help patients stop smoking, physicians need to approach the problem in a systematic fashion. First, they need to document a patient’s smoking history and status. This does not mean, as Dr. Pipe emphasizes, that physicians simply ask a patient whether or not they smoke, because they are in the hospital for cardiac crises, they will likely not have smoked for at least a while and they may be proud of the fact that they can say, albeit disingenuously, that they do not smoke. Rather, physicians need to ask them: Have you used any tobacco products in the past six months? If yes, in the last seven days? Then and only then will physicians get an accurate reflection of a patient’s smoking status,” states Dr. Pipe.

Physicians also need to offer each smoker personalized, unambiguous and non-judgmental advice and assistance to help them quit. “We also need to make sure that health professionals and institutions have the wherewithal to deliver specific assistance, most typically pharmacotherapy,” he added. For example, a physician may approach a patient who has just survived a heart attack with a statement such as, “Since you’ve had this heart attack, the most important thing we can do is to help you stop smoking and I’m going to give you every assistance I can to help you quit.”

While still in hospital, physicians also need to be mindful that smokers are likely going through nicotine withdrawal. “Instead of complaining that Mr. X is being difficult, we have to recognize that Mr. X might be a 2.5-pack-a-day smoker and he’s been in the hospital for 90 minutes without a cigarette and he’s just very uncomfortable because of nicotine withdrawal,” Dr. Pipe notes.

By providing patients with a nicotine patch—and making sure it is appropriately dosed (a 21-mg nicotine patch is not sufficient for a 2.5-pack-a-day smoker)—patients may realize that they can go without smoking and still be completely comfortable. This will facilitate a patient’s cooperation with their treatment and enhance the likelihood of smoking cessation. It is also important for physicians to realize that today’s smokers are “hardened smokers,” likely more addicted and therefore less likely to be able to quit without assistance. Nicotine replacement therapy is particularly effective against symptoms of immediate withdrawal, as are both bupropion and varenicline. The latter targets nicotine receptors directly and will reduce cravings as well.

At the same time, physicians need to recognize that many smokers suffer from comorbid psychiatric disorders being among the most common. Smoking helps alleviate symptoms of depression, as Dr. Pipe pointed out, and when smokers quit, depressive symptoms may re-emerge. If on previous attempts to quit smoking patients note that they felt more depressed (and in fact went back to smoking because they hated the way they felt), “you can at least anticipate these symptoms and not attribute them to any of the smoking cessation aids,” Dr. Pipe indicated. (Despite being an antidepressant, bupropion does not help with depressive symptoms any more effectively than other smoking aids.)

“The other thing that many people fail to understand is that when you stop smoking, metabolism of a number of compounds can change quite dramatically, one of the most important being caffeine,” Dr. Pipe remarks. Physicians are accustomed to drinking four cups of coffee a day, four cups may feel like eight cups when they quit and being over-caffeinated will only contribute to their edginess. Patients therefore need to be counselled to moderate caffeine intake (colas, coffee and chocolate included).

They also need to appreciate that weight gain, although prevalent on quitting smoking, is not as dramatic as many smokers fear, and that the benefits of smoking cessation are both more dramatic and more rapid than any other single intervention they could embrace. If they are still unconvinced, tell them that they would have to gain between 35 and 45 kg to equal the risk they incur if they continue to smoke.

“The focus is first, let’s help you stop smoking, and then we can focus more specifically on helping you lose weight if that has become a significant issue,” Dr. Pipe concluded.