More Canadians need dialysis

The use of dialysis has more than doubled in the past decade, the Canadian Organ Replacement Register reports, with 12 808 Canadians undergoing hemodialysis or peritoneal dialysis in 1998. The national rate of 421.6 cases per million population marks a 107% increase over the past decade. Manitoba had the highest rate, with 625 cases per million people, while British Columbia had the lowest, at 335 per million. Although kidney transplants are the most effective way to treat kidney failure, register spokesperson Dr. Stanley Fenton says "the shortage of organs, along with increasingly older patients who tend to have other health problems, makes transplantation less feasible." About half of the people who start dialysis treatment have chronic conditions such as hypertension and diabetes. The Canadian Institute for Health Information says the growing need for dialysis "reflects an increased incidence of end-stage renal disease among older Canadians."

Three NB MDs in race to head CMA in 2002

Three past presidents of the New Brunswick Medical Society are vying to head the CMA in 2002/03. In the running are Dana Hanson, a Fredericton dermatologist and current speaker for the CMA's General Council, David Marr, a Saint John cardiologist, and Roger Roberge, a Moncton general surgeon. New Brunswick selects the president in 2002 because it is its turn to host the annual meeting. This will mark the sixth time a New Brunswick physician has headed the CMA, which was founded in 1867, and the first time since 1981. The election will take place in October via a mail-in ballot; all society members will be eligible to vote.

Canada's only human milk bank may close

An advocacy group is protesting the possible closure of Canada's last human milk bank by year's end. The bank at the BC Children's Hospital costs about $100 000 a year to operate and provides milk to about 20 infants a year, says Dr. Dorothy Shaw, the hospital's medical program director, diagnostic and ambulatory services.

"It's a significant financial outlay for a small group of babies," says Shaw. "With our deficit, we'd need extremely good evidence to say this is worth while." She says that existing scientific evidence concerning donated milk clearly does not substantiate the need for the bank.

Elisabeth Sterken, a nutritionist who serves as national director of the Infant Feeding Action Coalition (INFACT), says some case studies have demonstrated the value of donated breast milk over infant formula. "Formula is … another stress for the infant," she says.

The milk at the BC milk bank is pooled from volunteer donors, pasteurized and prescribed. It is used within the hospital to feed about 12 patients annually; there are usually 5 patients with specific medical needs, primarily gastrointestinal problems, and another 7 who need the milk because of their mothers' failure to lactate. The remainder goes to children outside the hospital. Few requests for milk come from outside BC. Shaw says there are 7 other milk banks in North America, including 1 in Mexico. — *Barbara Sibbald*, CMAJ

Medical Hall of Fame photo

Drs. John Evans (left), Jack Hirsch and David Sackett were recently inducted into the Canadian Medical Hall of Fame because of their contributions to Canadian medicine. All 3 played major roles in the development of McMaster University's medical school. Three other physicians were honoured with posthumous admission to the hall. Dr. Bernard Belleau was involved in the discovery of lamivudine (3TC), while Dr. G. Malcolm Brown served as president of the Medical Research Council of Canada and Dr. Leonora Howard King was the first Canadian physician to practise in China.

New Brunswick med students off to Newfoundland

The New Brunswick government has purchased a little more medical education for the province's students. Starting this fall, up to 10 spots at Memorial University in St. John's will be earmarked for New Brunswick students.

"Improving accessibility to services for New Brunswickers means having a plan to ensure that New Brunswick is open to doctors," Health and Wellness Minister Dennis Furlong says. "This component of our physician recruitment and retention strategy will provide long-term benefits to people throughout the province."

At present, there is approximately 1 physician for every 600 New Brunswickers. The government's goal is to reduce this to 1:575 by 2003. The national average is 1:541.

The education plan will cost the government nearly $24 000 per medical student annually; the government will also pay travel expenses so students can do their clinical rotations back home. The plan marks a resumption of an earlier arrangement that was cancelled in 1992. New Brunswick also pays for a total of 40 seats a year at Dalhousie University in Halifax and the University of Sherbrooke in Quebec. Charlene Gaudet-Sleep, director of communications with the province's health department, says the additional seats mean that New Brunswick residents have a better chance of entering medical school than Canadians in some other parts of the country, even though the province doesn't have a medical school of its own.

The new spots don't mean the size of Memorial's medical school is growing. Dean Ian Bowmer says spots previously offered to American students for $30 000 per year will now go to the New Brunswick students instead, with first-year enrolment remaining at 56 students. New Brunswick will also pay to provide postgraduate training positions for the students it sponsors.

New Brunswick is not the only province to purchase placements in a medical school. Prince Edward Island buys 2 seats at Memorial, and the Northwest Territories is negotiating to purchase a seat at the University of Alberta. — *Donalee Moulton*, Halifax

No tuition fees for U of T residents

Medical residents at the University of Toronto appear to have won their ongoing battle over tuition fees. The Professional Association of Internes and Residents of Ontario reports that the university will not charge the fee during the 2000/01 academic year. In an update for residents, PAIRO reported that the "zero fee" is likely to continue for the next 4 or 5 years. "As it stands," says PAIRO, "no residents in Ontario will be paying tuition fees for the upcoming year."

Dr. David Naylor, the dean of medicine, said the residents "are in a unique situation in that they are at least part-time students." Dr. Kenneth Handelman of the PAIRO board said the decision recognizes "our hybrid nature as teachers, learners and service providers."

The situation is dramatically different from last year, when the university instituted an annual tuition fee of $1950 for residents. It backed away from the proposal after an angry outcry (see *CMAJ* 1999;161[5]:478-9). In 1999, the medical school said it needed the money to help counter government underfunding. Naylor indicates that the final word may not yet have been heard on the issue. "The tuition fee has been set to zero [for 2000/01], but it will be reviewed again in a few years," he says.

The university's undergraduate medical students didn't fare as well as the postgraduates — first-year medical students at the U of T face a fee increase of 27% this year (see *CMAJ* 2000;162[13]:1861). PAIRO calls the latter increase "unjustified." — *Patrick Sullivan*, CMAJ

Manitoba pharmacists get conscience clause

The Manitoba Pharmaceutical Association now allows pharmacists to refuse to provide a prescription if they object to the prescribed drug on moral or religious grounds. Any pharmacist who invokes the conscience clause must still ensure that the customer's needs are met. Some pharmacists object to dispensing drugs like the morning-after pill because of their pro-life beliefs (see *CMAJ* 1999;161[7]:855-6).

"If you have moral or religious beliefs that might interfere with the provision of care, it is your responsibility to enable patient access," says Ron Guse, the association's registrar.

This may be possible in larger centres, but it is unclear how patients in more remote areas that have few pharmacists or pharmacies will be served. In these cases, the amended policy states that the pharmacist must discuss the situation with local prescribers.

The recent amendment to the association's Standards of Practice is "not a new concept to the profession of pharmacy or other health care professions," says Guse. "This is no different from the College of Physicians and Surgeons' Code of Conduct."

The Manitoba Medical Association declined comment on the issue, in part because its Board of Directors had not had an opportunity to consider the matter. — *Jane Stewart*, Winnipeg

Playing chicken with group A streptococcal infection

The case for chickenpox vaccination has been boosted by a recent study showing that children who had contracted chickenpox had a dramatically increased risk of acquiring group A streptococcal (GAS) infection (*Pediatrics* 2000; 105[5]:e60).

The project surveyed invasive GAS infection in Ontario over 5 years, identifying 205 children with the infection. Of the children who had GAS, 15% had had chickenpox in the previous month, representing a 58-fold increased risk of acquiring the infection. In addition, necrotizing fasciitis developed in 4% of the children. The researchers speculate that the GAS bacteria may enter the body when the skin barrier is broken down by chickenpox lesions. Alternatively, the varicella-zoster viral infection may create a predisposing immune aberration.

"The most compelling evidence for chickenpox vaccination is that the economic burden is so high," says Dr. Dele Davies, associate professor of microbiology, infectious diseases and pediatrics at the University of Calgary, and one of the lead researchers. There are more than 300 000 cases in Canada each year, costing millions of dollars. The cost of hospitalizing a patient is more than $7000. "It is not always as mild as people think," explains Davies.

The Canadian Paediatric Society recommends universal vaccination for children at 1 year of age. Varicella vaccine has been available in Canada since 1998; however, at $60 per dose it is the most expensive vaccine available. Another limitation is the need to store it at a temperature of –15°C degrees, unlike most vaccines, which can be kept refrigerated at 2°C to 8°C. (A new chickenpox vaccine that does not require freezing has recently been developed). "Those two things have prevented a wide uptake of the vaccine right away," says Davies. Varicella vaccination is funded by the provincial health plan only in Prince Edward Island, although some other provinces, such as Alberta and Ontario, are planning to introduce funded vaccination. In Alberta, it is available at private clinics.

Davies hopes that his work will help speed up the move to universal vaccination. "Chickenpox is the last preventable childhood illness in Canada, and the most common cause of preventable death. Why should we be content with that situation?" — *Heather Kent*, Vancouver

Newfoundland and Labrador: it's all in the genes

Newfoundland and Labrador is noted for its stark beauty, friendly folk and small gene pool, with the latter making the province an ideal place for genetics research. Now the provincial government is moving to regulate that type of research, likely by forming a provincial research ethics board.

"It is our plan to put in place policies and standards around genetic research later this year," says Health and Community Services Minister Roger Grimes. "There has … been some research by people who studied the DNA of families without following up with them as to the outcome. It is important that the province move forward with policies and standards regarding all genetic research in Newfoundland and Labrador."

Although Health Canada's Food and Drug Act regulates the establishment and operation of clinical trials, it does not have the authority to regulate genetic studies. Newfoundland and Labrador commissioned Dr. Verna Skanes, former assistant dean of research and graduate studies at Memorial University, to prepare a report on issues arising from the commercialization of this research. She concluded that an ethics board with representatives from the legal community, medical profession and public is necessary. "It seems obvious that the province needs a clearly articulated policy for research ethics review of all human research projects," she says. In preparation for such a policy, the health minister says the department "will review the experiences of countries like Iceland."

The residents of Newfoundland and Labrador descended from approximately 20 000 people, who originally settled in the province in the 1800s. The limited immigration since then makes it easier for medical researchers to trace genetic diseases. — *Donalee Moulton*, Halifax

Rate of HIV infection on rise among Ontario's gay men

After years of steady decline, the rate of HIV infection among gay men in Ontario is on the rise. In a presentation during the 13th International AIDS Conference in South Africa last month, University of Toronto researcher Dr. Liviana Calzavara reported that the rate of HIV diagnosis among the province's gay men has risen from 0.87 per 100 men tested in 1996 to 2.07 in 1999. In an interview published on the U of T Web site, Calzavara said the increase may be due to "safer-sex fatigue. These people have been practising safer sex for over a decade and every once in a while they're going to slip." Most of the increase took place among gay men in Toronto and Ottawa; infection rates among heterosexuals and women have remained stable.

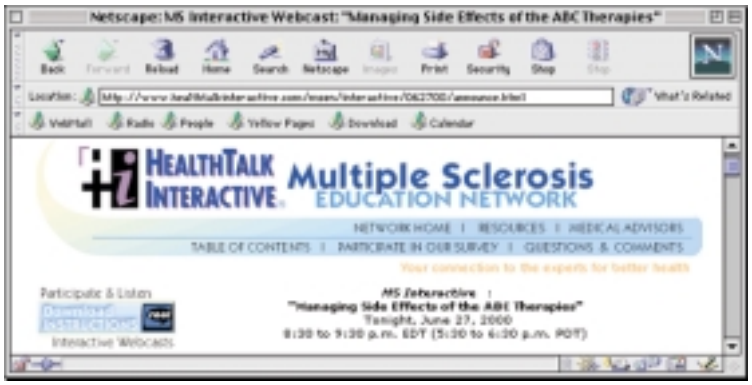
On the Net

Are more online conferences on the way?

Another Internet milestone was reached earlier this year with the first fully interactive Webcast of a biomedical symposium. Participants at the International Cartilage Repair Society (**www.icrs.ch**) gathering were joined electronically by specialists from around the world.

The Webcast of the conference, held in Göteborg, Sweden, included the main conference speeches and panel sessions, poster presentations and live surgery. E-participants were invited to watch using their Web browser and RealPlayer software, and submit questions via email during interactive sessions.

Although no details were available regarding the number of e-participants who logged on, organizers were expecting their servers to be as busy as servers used during other live surgical events. But unlike these other Webcasts, which have been aimed at the public (e.g., **webevents.broadcast.com**, see screen capture of Web site below), the ICRS meeting marked the first major bio-



medical conference to be Webcast.

Although they were first, ICRS officials expect other conferences will soon follow suit. Given the reality of busy schedules and tight travel budgets, the Internet is the perfect solution for physicians needing to attend international gatherings.

"The pressures of modern working life are now such that it is not always possible to set aside time for travelling to congresses," said Dr. Pierre Mainil-Varlet, the ICRS secretary. "Torn between the benefits to be derived from attending such meetings and the time pressures keeping us at home, we are thus forced to make a choice. Our interactive Internet project may now offer a solution for this dilemma."

For those who missed the live conference, the ICRS recorded it and is selling copies of the sessions over the Internet. The cost online ranges from US$20 for single speeches to US$190 for the whole event. A CD-ROM of the conference is also available for US$450. — *Michael OReilly*, mike@oreilly.net

Letter from Durban

Dr. Anthony Jeffery, a family physician from Peterborough, Ont., who treats HIV-infected patients and patients with AIDS, attended the 13th International AIDS Conference in Durban, South Africa, last month. He sent CMAJ *the following email.*

The speech given by the South African president, Thabo Mbeki, was televised live. It disappointed many of us because he did not recant his previous statements and state unequivocally that AIDS is primarily a sexually transmitted disease that is caused by HIV, and that his country is in the midst of an epidemic that dwarfs any plague in history.

Instead, he cited United Nations classification #2595 — "extreme poverty" — as the major cause of death in Africa and the developing world. He said his government is only 6 years old and only so much can be done, etc., and was heckled when he blamed "world indifference" and other factors as the cause of the AIDS epidemic.

Response was swift. The conference's first plenary speaker was Edwin Cameron, a white South African judge who is openly gay and HIV positive. He was unambiguous as he criticized Mbeki's government for its ineptitude in handling the epidemic. Judging from the applause, he echoed the feelings of most attendees when he stated that it is criminal and immoral to allow millions of people to die when the means to save lives and prevent infections are available. Cameron acknowledged that he is alive only because his relative affluence allows him to buy antiretroviral drugs. Most of his poor, black countrymen don't have that luxury.

In his speech, Mbeki also indicated that his government has an "AIDS Action Plan" to confront the epidemic, but it includes further "study" to "determine if HIV is the cause of AIDS." This, I think, is what has enraged thousands of scientists who have been working in HIV/AIDS research and treatment for the past 20 years. A group of these scientists has produced a pronouncement called the *Durban Declaration*, in which they spell out why it is known that HIV causes AIDS.

Cameron said the situation in

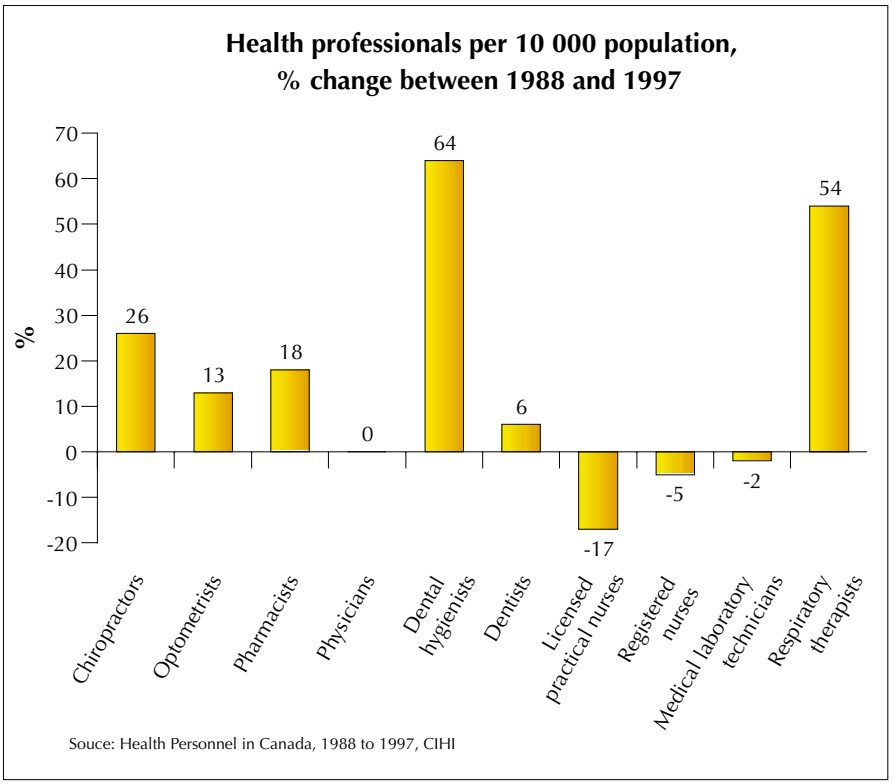
Pulse

Number of health care workers lags behind population growth

A Canadian Institute for Health Information report released in June paints a widely varying picture of trends concerning the number of health care workers in different provinces. While provinces such as Newfoundland and New Brunswick saw gains in the number of health workers per capita between 1988 and 1997 (increases of 22% and 15%, respectively), Ontario, Alberta and British Columbia experienced losses of 8%, 11% and 7%, respectively. Overall, the number of health professionals per 10 000 Canadians fell by 1.7% over the period, from 185 to 182.

Of the 17 occupational groups included in the report, nursing personnel (licensed practical nurses and registered nurses) accounted for 62% of the total. The second largest group was physicians, who accounted for just over 10% of all health personnel in 1997.

The percentage change in the number of health professionals between 1988 and 1997 varied greatly among occupational groups. While the per capita rate for both nurses and physicians decreased during this period, by -8.2% and -0.3% respectively, the number of chiropractors and dental hygienists per 10 000 people increased by 26% and 64% respectively, and the number of occupational therapists more than doubled. — *Lynda Buske*, buskel@cma.ca



South Africa can be likened to "a patient in the emergency ward who is dying." He called on government and the pharmaceutical industry, which he said have been engaged in a form of "collusive paralysis," to provide antiretroviral drugs to those who need them most. The announcement that Boehringer Ingelheim will give free nevirapine to African women to prevent the spread of HIV from mother to child was greeted with the usual cynicism, as other drug companies have made similar promises and failed to follow through. However, given that a recent study revealed that a single dose of nevirapine given to a mother in labour and to the child at birth was as efficacious as the more expensive regimen involving zidovudine, delivery on this promise could prevent many infections.

The AIDS deniers were not taken seriously by many people at the conference, although some here still believed that HIV is not the cause of AIDS. However, most African health care workers have clearly accepted the science that unequivocally links HIV with AIDS, and they have been some of the most vocal critics of government inaction.

There has been an interesting shift in the sense of urgency at this meeting. A few of the old ACT-UP types were here, but they were clearly overshadowed by the enormity of the disaster that is unfolding in sub-Saharan Africa, and there have been few of the protests that captured attention at earlier conferences.

Professor Roy Anderson, an epidemiologist from Oxford University, spelled out just how bad things are here. "We're not yet half-way through the epidemic," he said.

At this point there are about 24 million HIV-infected people in sub-Saharan Africa, and there are about 4 million new infections every year. Anderson also warned that new epidemics are already starting in India and China, and those countries must take action now. — *Anthony Jeffery*, Durban

Netherlands set to legalize long-tolerated euthanasia

For 2 decades, mercy killings and assisted suicide involving terminally ill patients have been widely tolerated in the Netherlands, with prosecution of doctors for such acts becoming increasingly rare.

But with contentious legislation introduced last fall likely to be enacted when parliament resumes after its summer break, Holland will actually decriminalize euthanasia under certain criteria, giving the country the least restrictive laws on mercy killing and assisted suicide in the world. The draft legislation permits physicians to assist in the death of terminally ill patients as young as 12.

Although that age may be raised before the final vote, the core of the bill is not likely to change. Doctors' actions in helping patients die would no longer be routinely reviewed by prosecutors but instead by a committee of doctors, lawyers and ethicists. To qualify for assisted suicide or mercy killing, patients' requests must be "durable," they must face "unbearable suffering" and have no "reasonable alternative" to death. The doctor must also consult at least one other independent physician before helping a patient die.

The bill introduces for the first time the possibility of an "advance directive" so that patients may indicate that they wish to die at a certain point in their illness. This opens the door for patients suffering from dementia and Alzheimer's disease to get help to die if they have signed such a directive early in their illness. In the past, such patients have not qualified because they were not considered by some to be suffering "unbearably." Although their condition may cause anguish to their families, they themselves may be unaware of their situation.

Dutch lawmakers and health officials say the new legislation aims to ensure that events during a patient's final hours take place in the open, where they can be scrutinized and regulated.

"If it remains a punishable offence, we will never see the transparency that we are aiming for," said Jacob Visser, a spokesperson for the Medical Ethics Division of the Dutch Ministry of Health, which, along with the country's Ministry of Justice, helped shape the legislation. "To get that [transparency], we must get this out of the criminal system." — *Gil Kezwer*, Toronto

MRI used to detect vCJD

Magnetic resonance imaging may be useful in diagnosing variant Creutzfeldt–Jakob disease (*Lancet* 2000;355: 1412-8). Thirty-six patients with proven vCJD and 57 control subjects underwent MRI. A bilateral pulvinar high signal was seen in the posterior thalamus in 28 of the 36 cases and in none of the 57 controls (sensitivity 78% [95% CI 60%–90%] and specificity 100% [95% CI 94%–100%]). The pulvinar sign may prove useful in the diagnosis of vCJD.

Bioflavonoids linked to childhood leukemia

In a search for environmental causes of infant leukemia Reiner Strick and colleagues have shown in both in vivo and in vitro experiments that bioflavenoids, commonly found in some fruits and vegetables, may induce chromosomal translocation of the *MLL* gene in utero (*Proc Natl Acad Sci USA* 2000;97:4790-5). *MLL* gene translocations occur in about 80% of infants with leukemia.

Potential sperm donors should be tested for HPV

Semen from potential sperm donors should be screened routinely for human papillomavirus (HPV), the virus that causes genital warts and cervical cancer, say Canadian researchers. They are sounding the alarm in light of research showing that the virus can be present even in men with no history of infection and no lesions on their penises, contrary to previous thinking.

In a study involving 85 subjects, University of Saskatchewan researchers detected the virus in sperm samples of 53% of men with past or current infection and in 8% of samples from healthy subjects who had no history of infection. The findings were presented at the recent annual meeting of the American College of Obstetricians and Gynecologists in San Francisco.

Using polymerase chain reaction testing, the researchers also found HPV DNA in the sperm of 11% of men with a history of lesions on their penises, but no visible lesions at the time the test was done, compared with 66% of men who had detectable lesions. The 45 HPV-positive volunteers in the study group had previous or existing lesions, while the control group comprised 40 sperm donors with no signs or history of the disease. The study's findings have generated considerable attention within the medical community, because previously it was thought that HPV was present only in men with genital lesions.

"Clearly, we should be checking for HPV in prospective sperm donors," says Dr. Roger Pierson, with the Department of Obstetrics, Gynecology, and Reproductive Sciences in the University of Saskatchewan College of Medicine. "By excluding those with positive tests, we can prevent transmitting the disease to uninfected sperm recipients." Extrapolating the findings from this small population to all sexually active men, adds Pierson, would suggest it is not only women receiving sperm donations who are at risk of infection.

The researchers also found that standard sperm-washing procedures failed to remove the virus from semen samples. — *Greg Basky*, Saskatoon

Brave new world of e-medicine confronts all MDs, incoming president says

Dr. Peter Barrett's marathon running may prove to be invaluable preparation for the strenuous journey he's about to take as the CMA's new president. The Saskatoon urologist, who runs a couple of marathons a year, is getting set to tackle 2 of the toughest issues ever to face Canadian health care: the ramifications of the information revolution and the sustainability of Canada's medicare system. Barrett assumes the presidency later this month during the CMA annual meeting in Saskatoon.

"My fear is that we will have two-tier medicine, not financially but in terms of information," he warns. The wealthy and educated, armed with information from the Internet, will bypass conventional barriers to gain access to health care services. Less fortunate Canadians will not have this knowledge — or power.

"We're going to have to bring them into this world somehow and empower them," says Barrett, a former Saskatchewan Medical Association president who has served on the CMA board since 1998.

He is also convinced that physicians have to start using their "e-resources to the max." Barrett says physicians need peer-reviewed, useful information in a "manageable, edible format. They don't need a whole journal to look through, they need a summary of the key things in that journal that would change how they practise medicine or improve how they practise medicine.

"Within 4 or 5 years, *CMAJ*, like all other journals, will no longer be available in paper form."

Dr. Peter Barrett: one more mountain to climb

Barrett's other major challenge involves the sustainability of Canada's health care system, which he says cannot endure by accepting the status quo. He advocates a grassroots approach, with solutions emerging through a "dialogue among Canadians." Physicians and politicians can contribute and present the options, he says, but the system's end users have to decide what constitutes the publicly funded system. "Are we spending money on the right things? Maybe, maybe not."

Most important, he said, is stable, accountable funding for health care, which includes reinvestment, particularly in human resources and technology.

Barrett says he is tackling these issues for the most personal of reasons: his 2 new grandchildren. "We have to leave something for them. We can't gobble it all up now and leave them in the same situation as [developing] countries."

Barrett and his wife, Susan, a special education teacher, have 3 grown children — Jennifer, Jonathan and Andrew. The couple moved to Saskatoon from Toronto in 1975 after Barrett finished his residency in urology at the University of Toronto, where he also earned his medical degree. They were looking for new frontiers and planned to stay a few years. "We both love it," says Barrett, who was born in Kingston, Ont. "I have the best of both [academic and clinical] worlds here."

He is a clinical professor of surgery at the University of Saskatchewan and his group practice of 7 urologists serves the entire province and is internationally renowned for its expertise in minimally invasive surgery — one of Barrett's enduring interests.

He'd only been practising for 5 years when he caught the political bug. "My wife started getting mad about my complaining at home and told me to get off my butt and change it if I didn't like it," he recalls. He became president of the Saskatoon City Hospital medical staff and then held several administrative positions.

Provincially, he served the Saskatchewan Medical Association in many roles before becoming president in 1993. After that, he took a few years off to concentrate on making his practice a leader in minimally invasive surgery. "People now know about us in other parts of the world, but they don't know about us in Canada," he says.

Gradually, he slid back into politics as deputy speaker for the SMA's Representative Assembly in 1997 and as a member of the CMA's Political Action Committee in 1998. Within 6 months he was on the CMA Board of Directors. He was already travelling to Ottawa regularly to visit his parents. "The SMA said let us pay your way," he laughs.

Barrett keeps his humour up and stress down by backpacking through the Rockies with friends, fishing at his cabin in Northern Saskatchewan and running. Last year he ran his personal best in the National Capital Marathon, finishing in 3 hours and 17 minutes and placing fourth in his age group.

Through it all, his abiding philosophy remains simple. "If you're not involved in helping change things, then you're probably part of the problem." — *Barbara Sibbald*, CMAJ

Clinical Update

Inhaled corticosteroids and COPD

Burge PS, Calverley PMA, Jones PW, Spencer S, Anderson JA, Maslen TK, on behalf of the ISOLDE study investigators. Randomised, double blind, placebo controlled study of fluticasone propionate in patients with moderate to severe chronic obstructive pulmonary disease: the ISOLDE trial. *BMJ* 2000;320:1297-303.

Background

Although inhaled corticosteroid therapy has been well validated as the mainstay for the pharmacological management of asthma,[1] its role in the treatment of chronic obstructive pulmonary disease (COPD) remains less certain.

Question

What is the effect of long-term inhaled corticosteroid therapy on lung function, frequency of exacerbations and health status in patients with moderate to severe COPD?

Design

In this double-blind clinical trial, conducted in 18 hospitals in the United Kingdom, 751 patients with nonasthmatic COPD were randomly assigned to receive either fluticasone, 500 µg twice daily, or placebo. All subjects were given a 14-day course of prednisolone, 0.6 mg/kg daily, before randomization. Bronchodilator therapy with salbutamol or ipratropium bromide, or both, was continued during the trial, and the use of theophyllines and nasal and ophthalmic corticosteroids was also allowed. Subjects were seen quarterly for 3 years to measure their forced expiratory volume in 1 second (FEV_1) and to record self-reported exacerbations, and every 6 months to measure their health status and serum cortisol levels. Exacerbations were defined as worsening respiratory symptoms requiring orally administered corticosteroids or antibiotics, or both, and health status was measured using the St. George's Respiratory Questionnaire, a disease-specific instrument. Subjects were withdrawn if they reported more than 2 exacerbations in 3 months that required treatment with corticosteroids.

Results

The subjects were predominantly male (74%), and the mean age was 64 years. The mean number of cigarette pack-years was 44 at the time of randomization; about 40% of the subjects smoked throughout the trial. The mean FEV_1 was 1.4 L (50% predicted), in keeping with moderate to severe COPD. Each group demonstrated a slight improvement in FEV_1 (by about 60 mL) after taking prednisolone. In the placebo group, however, the mean FEV_1 fell within 3 months to pre-prednisolone levels and remained at least 70 mL lower than in the fluticasone group at each 3-month interval throughout the study period ($p < 0.001$). In the fluticasone group, there was no correlation between prednisolone response and subsequent response to inhaled corticosteroid therapy. Over the study period, the rate of FEV_1 decline did not differ between the fluticasone and placebo groups (50 v. 59 mL/yr respectively, $p = 0.16$). However, patients receiving fluticasone experienced 25% fewer exacerbations (0.99 v. 1.32 per year, $p = 0.026$) and a significantly slower decline in health status ($p = 0.004$). Withdrawal rates were high in both groups (fluticasone 43%, placebo 53%), but withdrawals related to respiratory disease (chiefly exacerbations of COPD) were significantly more frequent in the placebo group (25% v. 19%, $p = 0.034$). Rates of adverse events were comparable, with a slightly higher incidence of hoarseness, throat irritation and oropharyngeal candidiasis in the fluticasone group. Although serum cortisol levels were slightly decreased in that group as compared with the placebo group ($p < 0.032$), the levels were no more than 5% below the lower limit of normal at any time.

Commentary

Results from this trial were similar to those from 2 previously published studies of long-term use of inhaled corticosteroid therapy for COPD: it showed a modest improvement in FEV_1 but no effect on the rate of FEV_1 decline.[2,3] However, this study differed from the others because, in addition to assessing physiologic end points, it measured exacerbation rates and quality of life. Although the study's chief limitation was the high withdrawal rates in both groups, it is conceivable that the higher rate of withdrawal in the placebo arm may have led to an underestimate of treatment effect.

Practice implications

Although this study confirms that long-term inhaled corticosteroid therapy does not alter the rate of decline of FEV_1 in COPD, it does provide evidence of modest clinical benefit in terms of health status and frequency of exacerbations. These findings add a measure of justification for what is fast becoming widespread practice in the management of patients with this common condition. — *Donald Farquhar*

The Clinical Update section is edited by Dr. Donald Farquhar, head of the Division of Internal Medicine, Queen's University, Kingston, Ont. The updates are written by members of the division.

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ACE inhibitors and high-risk patients

Heart Outcomes Prevention Evaluation Study Investigators. Effects of an angiotensin-converting-enzyme inhibitor, ramipril, on cardiovascular events in high-risk patients. *N Engl J Med* 2000;342:145-53.

Background

Angiotensin-converting-enzyme (ACE) inhibitors lower morbidity and mortality among patients with congestive heart failure. In addition to a reduction in afterload, ACE inhibitors have a protective effect on the vasculature, which may lead to a reduction in cardiovascular events in high-risk patients without a history of left ventricular dysfunction.[1]

Question

Do ACE inhibitors lower the incidence of cardiovascular events and death among high-risk patients who do not have a history of congestive heart failure?

Design

A double-blind, multicentre, randomized controlled trial was conducted to compare the effects of ramipril to placebo in 9297 patients over the age of 55 who were at high risk for cardiovascular events. Eligible patients included those with coronary artery disease, stroke, peripheral vascular disease or a history of diabetes mellitus plus another cardiovascular risk factor. Exclusion criteria included congestive heart failure, overt nephropathy or a history of myocardial infarction or stroke within 4 weeks of the study. The primary study outcome was the combination of myocardial infarction, stroke or death from any cardiovascular event.

Results

Almost half of the subjects were older than 65, and just over one-quarter were women. Most patients (80%) had a history of coronary artery disease, about half were hypertensive (46.8%), and many (38.5%) had diabetes mellitus.

A chart audit found that more than half of the patients had had their ventricular function assessed before the study. Of this group, 8.1% had a low ejection fraction without a clinical history of congestive heart failure.

The study was designed to continue for 5 years, but it was stopped early because of the beneficial effects of ramipril on the primary outcome. The primary end point occurred in 14.0% of the patients in the treatment group, as compared with 17.8% in the placebo group.

This result was consistent in both men and women and in all predefined subgroups, including patients with diabetes, hypertension and left ventricular dysfunction. Treatment with ramipril was associated with significant reductions in secondary end points such as cardiac arrest, congestive heart failure, revascularization procedures and death from any cause. The incidence of new diagnoses of diabetes was significantly lower in the ramipril group than in the placebo group (102 v. 155 patients).

Commentary

This large, randomized study documents the beneficial effects of ACE inhibitors in patients at high risk for cardiovascular events. The results were consistent across subgroups, and benefit extended to a number of secondary outcomes. Ramipril was well tolerated, with cough resulting in discontinuation of the medication in 7.3 % of patients.

The intriguing reduction in the incidence of diabetes corresponds to observations in the Captopril Prevention Project study of antihypertensive therapy.[2]

Practice implications

When given ramipril therapy, high-risk patients over age 55 with normal left ventricular function have a reduced rate of myocardial infarction, stroke and death from cardiovascular causes. Ramipril, started at a dose of 2.5 mg/d and titrated over 1 month to a dose of 10 mg/d, is well tolerated. Whether the findings of this study can be extended to angiotensin II receptor inhibitors is unknown.

The reduction in the incidence of diabetes among patients taking the ACE inhibitor is an important observation that merits further investigation. — *Kathryn A. Myers*

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Public Health

Wife assault in Canada

Epidemiology

Only a minority of spousal assaults come to the attention of Canada's judicial and medical systems. In a 1993 national telephone survey of 12 300 women, 29% of respondents who had ever married reported that they had been subjected to violence — they had been pushed, grabbed, shoved, slapped, sexually assaulted, hit with an object or had a gun or knife used against them — by their partner at some point in the relationship.[1] This proportion is comparable to results of national surveys in the US (25%), Australia (23%) and England and Wales (23%).[2]

Only 25% of the Canadian respondents who had experienced assault had reported an incident of violence to the police.[1] They were more likely to make a report if their children witnessed the incident, if a weapon was used or if they feared for their lives. However, 57% of women who were injured, 51% of women who were assaulted more than 10 times and almost 50% of the women who feared for their lives did not call the police.[1]

According to the records of 179 police forces in 6 provinces, common assault (an assault that doesn't involve a weapon or cause serious injury) represented 74% of domestic violence incidents reported in 1997.[2] More serious forms of assault (assault with a weapon, assault causing bodily harm or aggravated assault) accounted for 14% of the incidents, while criminal harassment (stalking) comprised 7%. The vast majority of victims (96%) suffered either no injuries or minor injuries that required either no professional attention or at most first aid. This suggests that physicians who rely on characteristic patterns such as centrally distributed injuries, defensive injuries of the forearm and bruises in various stages of healing to identify victims of abuse are likely missing most cases.

Clinical management

Domestic violence can be a diagnostic challenge because victims present with ambiguous signs and symptoms such as dental trauma, chronic pelvic pain, eating disorders, lack of prenatal care and delays in seeking help. Although physicians may be uncomfortable introducing the subject of abuse, most victims report that they hope the clinician will ask whether they have been abused and, if asked in a caring manner, would be prepared to discuss it.[3]

Routine gynecologic, obstetric and pediatric visits provide opportunities for screening. In a recent pilot study to introduce domestic-violence screening during well-baby visits in a pediatrician's clinic, 47 (31%) of 154 women screened revealed a history of domestic violence at some point in their lives.[4] Before routine screening was introduced, only 1 report of domestic violence had been made in the previous 4 years.

Screening should be done in private and introduced with a general question: "We are concerned about the health effects of domestic violence, so we now ask a few questions of all our patients." Two simple screening questions — "Do you ever feel unsafe at home?" and "Has anyone at home hit you or tried to injure you in any way?" — have a sensitivity of 71% and a specificity of 85%.[3] Doctors might also ask "Has anyone ever threatened you or tried to control you?" or "Have you ever felt afraid of your partner?" Women should also be made aware that abuse takes many forms.[5]

When patients admit to being abused, the physician needs to identify and clearly document the relevant history and physical findings, refer the patient to appropriate community and advocacy services, and assess whether the patient is at immediate risk upon leaving the premises. A handbook to help physicians deal with the issue and the judicial system's responses to it has recently been published.[6]

Prevention

Many risk factors are associated with wife assault. Predictors include the couple's young age (18–24 years), living in a common-law relationship, chronic unemployment of the male partner, the witnessing of violence as a child and the presence of emotional abuse. Women who have recently separated from their partners or who are pregnant are at increased risk.[1]

Spousal assault is a complex issue that requires a collaboration between government, community, legal, health and police services. In Canada, gains were made in 1983 with the implementation of Bill C-127, which allowed officers to make an arrest when they had *reasonable and probable grounds* to believe an assault had been committed. Before, officers had to witness the assault or the resulting bodily harm to make an arrest.[2] Thus, rather than leaving the scene without laying charges, the law now allows officers to intervene at an earlier stage and possibly prevent later escalations of the violence.

For further information, contact the National Clearinghouse on Family Violence, Health Canada, tel 800 267-1291; **www.hc-sc.gc.ca/nc-cn**. — *Erica Weir*, CMAJ

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