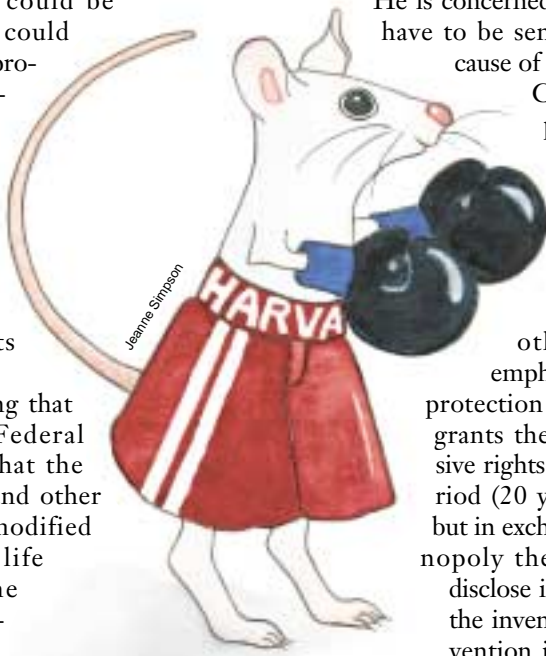


Patenting life: genetically altered mice an invention, court declares

Researchers are hailing a Federal Court of Appeal decision that nonhuman life forms can be patented in Canada, although some doubt that the ruling will have a major effect on their work.

The decision concerns the “oncomouse” developed at Harvard University — a genetically altered mouse that gets cancer very easily, making it an ideal test platform for new therapies. The mouse has been patented for many years in the US. In fact, “transgenic” animals such as the oncomouse can be patented in the US, Japan and many European countries. Until Aug. 3, 2000, however, they could not be patented in Canada. Lower organisms such as bacteria, fungi, yeast and moulds could be patented, as could processes to produce transgenic animals, but an earlier court decision had rejected the patenting of actual plants and animals.

In reversing that ruling, the Federal Court said that the oncomouse and other genetically modified nonhuman life forms fit the Patent Act definition of an invention as a “composition of matter.”¹ This opens the



Knock-out mice: researchers remove or “knock out” a gene to see what happens

door to patenting other transgenic animals used in medical research. Canadian labs have developed dozens of such animals. In basic molecular biology, they are used to study the function of a particular gene by “knocking out” the

gene, usually in a mouse. The resulting “knock-out” mouse strain shows what happens when the gene is absent, suggesting the gene’s actual function. As well, researchers genetically engineer animals to be susceptible to a particular disease in order to study the disease.

“If you develop a useful strain, you should be able to protect your interest in it,” says Dr. Jim Russell, a University of Alberta professor who has created a transgenic rat model of type 2 diabetes. He finds that keeping a new animal strain going is expensive. “The rats must be bred continuously or the strain will be lost. Once lost it is irrecoverable. The court decision may, in the long run, actually help with this.”

He is concerned that his rat may have to be sent to the US because of lack of support in Canada. This was precisely the fate of a previous rat model of type 1 diabetes created in Ottawa.

Russell and other researchers emphasize that patent protection is a trade-off: it grants the inventor exclusive rights for a defined period (20 years in Canada), but in exchange for this monopoly the inventor must disclose information about the invention. And the invention is freely available once the protection period expires. Before the oncomouse decision, Russell was advised to treat his rat strain as a trade secret, like the formula for Coca-Cola, because he couldn’t patent it.

“These days protection is very important,” agrees Dr. Rashmi Kothary, a senior scientist at the Ottawa Hospital Research Institute who develops trans-

genic mouse models of neuromuscular diseases. “Without protection, other laboratories could quickly reproduce the work that you did at great expense and effort without having to compensate you. With the possibility of protecting your work that won’t happen.”

But for researchers who use transgenic mice developed elsewhere, won’t patent protection increase costs and hamper access to lab animals? Most researchers are not concerned. Dr. Barbara Vanderhyden, who runs the transgenic mouse program at the University of Ottawa, says patents are usually related to restrictions on commercial use, and research use of animals in both academic and industrial contexts remains mainly unaffected. Kothary agrees. His lab sometimes uses transgenic animals developed by colleagues elsewhere, which are freely provided in return for an agreement to share research results and to provide recognition for the animal creators in published papers. Even patented, commercially available animals from the US carry only a nominal cost.

On the other hand, a commercially useful animal can net its creators \$35 000 to \$100 000, estimates Dr. Michel Tremblay, a McGill University researcher who has created 4 transgenic mouse strains, including a knock-out mouse that is resistant to obesity and diabetes. He has patented his mouse model in the US, which is often more important than patenting in Canada. He says the court decision “is just in fact filling a little gap present in Canada.”

Tremblay worked in collaboration with the pharmaceutical company Merck Frosst, but most of the work with transgenic animals is being done in academic settings. “There’s not a ton of companies that are working with transgenic animals,” says Joyce Groote, president of BIOTEC Canada, an association representing the biotechnology industry that counts many Canadian drug companies among its members. “I don’t

think the impact [of the decision] is as high in medical research as it is in other areas." She cites agriculture technology and biomanufacturing as 2 examples.

Although researchers are generally bullish, there are some concerns. Kothary is worried that very broad patents, covering large areas of technology, will limit further research. He cites a technology patented by a large US chemical company that allows researchers to activate a gene in any animal model. Since this applies to more than one animal, or one strain of animal, it means that no other researcher can use the technology freely to create a new animal model.

The Canadian Environmental Law Association is also concerned about the

broad nature of such patents. "What a lot of people don't realize is that Harvard got a patent on all nonhuman mammals" that it can modify in the same way that it has modified the mouse, says Michelle Swenarchuk, a spokesperson for the association. "It applies to all mammals, from a shrew to a whale."

In Canada, the ruling was very clear: patenting does not apply to humans because it is a property-based concept, and humans cannot be considered property. The Environmental Law Association is concerned about considering any form of life as property that can be owned. "This is the commodification of life," says Swenarchuk.

Russell points out that patent pro-

tection only goes part way in solving the key problem with developing transgenic animal models — the lack of financial support. Granting agencies support only the associated research projects, and reviewers often say that industry should support the animal models, a suggestion that Russell finds naïve. He is left wondering whether to feed and breed his expensive rats, or send them to the US, where the rats would be maintained, but would be harder to acquire for Canadian research. — *Carolyn Brown, CMAJ*

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New CMA president-elect from Quebec

Dr. Henry Haddad, a professor of medicine from the University of Sherbrooke, will head the CMA in 2001/02. A former vice-dean at the university, he was named president-elect during the CMA's annual meeting in Saskatoon in August. A 1963 graduate of the University of Ottawa, he is a past president of the Quebec Medical Association and former chief of gastroenterology at the University of Sherbrooke. Haddad's main interests within the CMA have involved physician resources, post-graduate training and issues such as the privacy of health information.

World water crisis in the offing?

The world is facing a critical shortage of fresh water in the next 2 decades, according to a report from the World Commission on Water (www.worldwatercommission.org). The report, *A water-secure world: vision for water, life and the environment*, predicts that the use of water will increase by 40% in the next 20 years due to growing demands from agriculture, industry and urban areas. Today, 1 billion people don't have access to safe water and another 2 billion don't have adequate sanitation. The commission, whose sponsors include the World Bank and UN, was created to recommend ways to achieve "global water security." Many countries will be looking to Canada for help, since it is to fresh water what Saudi Arabia is to oil.

About 70% of the world's available water is now used in agriculture and the remaining 30% is used for households and industry. With population growth, the amount used in agriculture alone is expected to increase by 17%. Industry and cities will also require more. This "gloomy arithmetic" adds up to a burgeoning crisis for all humans, the commission states. Compounding this are existing, and worsening, environmental-degradation problems. For example, 10% of the world's agricultural food production now depends on mined groundwater that is causing a resulting drop in water tables by as much as a metre a year in parts of China, India, Mexico and elsewhere. "Our attitudes on managing water must change," says Ismail Serageldin, the World Bank's vice-president for special programs. — *Barbara Sibbald, CMAJ*

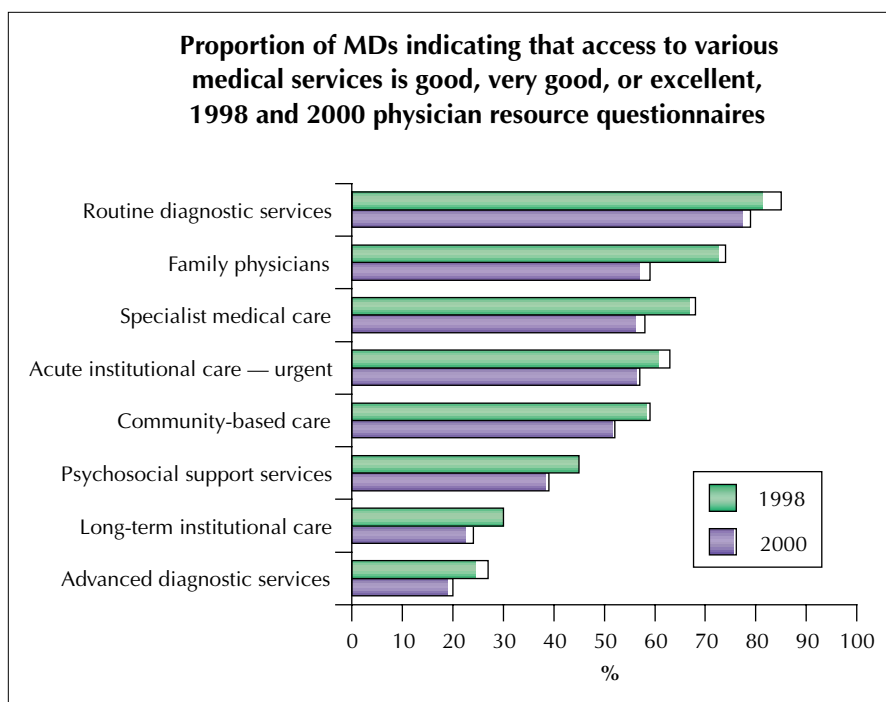


MDs worried about access to care, CMA survey indicates

Access to several medical services remains a problem for some Canadians, results from the CMA's 2000 Physician Resource Questionnaire (PRQ) show. Although 59% of physicians rated access to family physicians in their communities as good, very good or excellent, 35% deemed it fair to poor; 36% also reported that access to specialists is only fair to poor. The PRQ did not ask physicians to rate access to specific specialties, but accompanying comments made by respondents suggest that access to some — such as ophthalmology, orthopedic surgery and psychiatry — is particularly poor.

Physicians seem comfortable with the level of access to routine diagnostic services such as laboratory tests and x-rays, with 79% ranking it as good to excellent and only 14% describing it as fair to poor. However, few physicians think their patients have adequate access to advanced diagnostic tools such as MRIs; only 20% of respondents indicated that availability of these services is good to excellent where they practise. Regional variations were apparent: 69% of physicians in Central Canada consider access fair to poor, compared with 75% in Atlantic Canada and 80% in Western Canada.

The survey also points to problems with the availability of long-term insti-



tutional care. Only 24% of respondents consider it good to excellent, with 64% deeming it fair to poor. One respondent pointed out that a lack of long-term-care beds can have a domino effect: “Long-term-care patients are blocking acute-care beds: dangerous!”

Physicians also appear concerned about psychosocial support services: only 39% indicated that access in their

community is good to excellent, and 52% described it as fair to poor.

The 2000 PRQ was mailed to a random sample of 8000 Canadian physicians; 36.3% responded. Results are considered accurate to within $\pm 1.9\%$, 19 times out of 20. Tables showing the 2000 PRQ results are available online at www.cma.ca/cmaj/vol-163/issue-5/prq. — *Shelley Martin, martis@cma.ca*

An Insider's look at the tobacco industry

The man who inspired the 1999 movie *The Insider* says physicians have a central role to play in the ongoing fight against a savvy tobacco industry. And if they are to battle on equal terms, says Dr. Jeffrey Wigand, they must learn how the tobacco industry operates.

“[Doctors] are a political power and a group that helps influence policy,” Wigand told *CMAJ*. “They must hold the tobacco industry accountable.”

Wigand, the former head of research for the US tobacco giant Brown & Williamson, is becoming a familiar fixture in Canada. In the spring he addressed the Medical Society of Nova Scotia, and he was recently named a special adviser on smoking issues to federal Health Minister Allan Rock. One of his main responsibilities is to interpret documents unearthed during a series of US lawsuits. He also educates Rock and senior staff about the internal workings of tobacco compa-

nies. Rock says Wigand “gave us the key to some of industry’s language and a thread to follow in fully understanding its internal objectives.”

In addition to his work in Ottawa, Wigand is collaborating with the BC government to help schools enhance awareness of smoking and the industry that promotes it. He is also helping the BC government relaunch its lawsuit against tobacco companies (see *CMAJ* 2000;162[10]:1468). — *Donalee Moulton, Halifax*

On the Net

An interactive approach to treating prostate cancer

A search for prostate cancer information on the Web will turn up more news than you can possibly use. To help people through this confusing maze, Dalhousie University's Department of Urology has created a new site ([www.caprostate](http://www.caprostate.com)



.com) that includes everything from a detailed description of the disease to sets of top-quality related links and definitions. For newly diagnosed patients, it's an ideal place to visit. This site also goes a step further than most by offering a fully interactive online program to help patients identify treatment options according to the stage of their tumour.

Clicking into the site's Treatment Facilitator page pulls up a simple form-based tool (see accompanying illustration). The page asks for a medical history that focuses on prostate cancer issues. It then performs an analysis and presents the patient with a range of individualized treatment options.

"Narrowing down potential treatment options is extremely valuable for patients," says Dr. David Bell, an associate professor in the Department of Urology and the project leader.

"Caprostate.com helps explain why some treatments are not an option for a particular patient and why other options may be beneficial. This is one of the first Internet programs that goes beyond passive education and actually facilitates treatment decision-making."

The Treatment Facilitator presents options based on current clinical research and existing literature. It is careful to point out these are only options and that actual clinical decisions must be made with the help of the patient's physician. As Bell says, the idea is to provide patients with an understanding of the disease so they can begin meaningful discussions with their doctors.

In other words, the Treatment Facilitator is designed to help patients make informed decisions about the difficult path they must follow. — *Michael O'Reilly, mike@oreilly.net*

Supreme Court refuses to hear MD's infertility case

The Supreme Court of Canada has rejected a request by a Halifax couple that was fighting to have the cost of in-vitro fertilization covered by the provincial health care system. This summer the nation's highest court refused to hear the case, effectively bringing the matter to an end.

Last year, in a decision that saved the province more than \$3 million a year, the Supreme Court of Nova Scotia ruled that in-vitro fertilization is not a medically necessary procedure and the provincial government is not required to pay for it.

In that 58-page ruling, Chief Justice Joseph Kennedy argued: "Courts should take care before interfering with an elected government's allocation of limited public funds for social programs or the medical profession's determination of health priorities."

The province was being sued by a Halifax physician and her husband, a lawyer with the Nova Scotia Department of Justice; he argued the case before the Supreme Court. The couple was seeking repayment of more than \$22 000 spent outside the province to have intracytoplasmic sperm injection, a specialized procedure that involves injecting one sperm directly into an egg and implanting it. The Halifax couple has spent more than \$40 000 in their efforts to have a

child. They argued that the government's failure to fund in-vitro fertilization violated their rights under the Canadian Charter of Rights and Freedoms and the Canada Health Act. In his final submission to the court, lawyer Alex Cameron said the hearts of infertile Canadians "are [being] broken" because of the failure to provide funding.

Nova Scotia covers only the cost of tests and doctors' fees incurred in arriving at a diagnosis of infertility. Ontario is the only province to cover the cost of in-vitro fertilization, and it does this only when a woman's fallopian tubes are blocked. In these cases, the government will pay for 3 attempts at conception.

Dr. André Lalonde, executive vice-president of the Society of Obstetricians and Gynaecologists of Canada, says the SOGC considers infertility an illness that deserves publicly funded treatment. However, he acknowledges that because of the technological advances being made in treating infertility and the associated costs, provincial governments face difficult financial choices. "The SOGC believes that a Canadian consensus should be developed to determine what reasonable fertility treatment should be paid by government, given the limited budgets that are available." — *Donalee Moulton, Halifax*

Desperate government begs Yellowknife's MDs to stay

Physicians in Yellowknife are the latest to benefit as desperate governments continue upping the ante in a bid to keep rural or remote doctors on the job.

In August, the Yellowknife Health and Social Services Board assumed the overhead and operating costs of the city's 4 medical clinics — an expense estimated to consume 40% of the 18 physicians' gross incomes.

The health board then offered the doctors a contract with salary, incentives and benefits that total as much as \$285 000 annually (see sidebar). By making the move, the NWT hopes to achieve some of the same stability it acquired by putting the 40 physicians practising outside Yellowknife on contract.

"We were up against the wall," Dr. David King, president of the Northwest Territories Medical Association, says of the recruiting situation.

Yellowknife, which has 17 000 residents, was down to only 14 physicians in the summer of 1999, and until recently the territory has depended on locums to provide up to half of its physician workforce.

According to the Society of Rural Physicians of Canada (SRPC), the number of rural physicians in Canada declined by 15% between 1994 and 1998. A CMA report to Health Canada in April 1999 pointed out that even in the unlikely event that nothing changes, the rural physician supply will drop by 18% in the next 21 years.

But Dr. John Wootton, executive director of Health Canada's Rural Health Office, says salaries and incentives alone aren't enough. Just look at Quebec, he says, which has had salaried physicians in its community clinics for 20 years and yet still has a shortfall. Wootton points to the need for technological links and a consistent level of infrastructure, including diagnostic, therapeutic and transportation tools, for all rural areas. The key to recruitment and retention, Wootton says, is flexibility to address local needs.

Dr. David O'Neil, the SRPC president, agrees. "Every rural area has dif-

ferent needs and different distances to tertiary services or cultural resources." Sometimes all that's needed is a transportation allowance or a turn-key office. Other times, the physicians need everything from housing to spousal-employment assistance. He admits, though, that alternative payment plans are particularly useful when patient volume is unpredictable or low.

Salaries and other financial incentives are the cornerstone of most rural recruitment and retention plans across Canada. For example, Prince Edward Island's new rural physicians get a \$20 000 moving grant for providing a 2-year commitment. This summer, Quebec began offering fee-for-service bonuses of 15% to 30% (depending on years of service) and 40% bonuses to specialists. Ontario offers a range of incentives, including salaries and bonuses of \$25 000. Saskatchewan physicians are offered salaries of up to \$140 000 to start, plus benefits such as subsidized housing and a practice-establishment grant of \$18 000.

But Alberta is ahead of everyone by a decade, says O'Neil, who practises in

Trochu, Alta. It offers paid locums, CME, enrichment training, bonuses for on-call work, and more. "You have to make the environment attractive for them," O'Neil says. Next year, Alberta will also offer incentives to 40 medical students to enter a 2-year rural residency program.

Meanwhile, British Columbia may have the most work to do on rural initiatives. This summer, rural physicians in some areas withdrew services and resigned hospital privileges to protest antiquated equipment, inconsistent on-call rates for specialists and the lack of incentives to lure much-needed physicians.

At its annual meeting in Saskatoon in August, the CMA adopted a policy to ensure "reasonable access to uniform, high quality medical care" in rural and remote areas. It contains 28 recommendations touching on the training, compensation, and work and lifestyle issues of these physicians.

"We've got to make the practice enjoyable," maintains O'Neil. "That's probably as important as the money." — *Barbara Sibbald, CMAJ*

Salary, sweet salary

Family physicians in Yellowknife are being enticed to stay in town with a newly introduced salary and benefits package. Depending on their on-call arrangements, the Yellowknife Health and Social Services Board is offering salaries ranging from \$130 000 to \$180 000, plus up to \$12 000 extra a year for emergency department shifts, cash bonuses for being on call and an annual retention bonus of \$5000. Benefits include full dental and health coverage plus 15 weeks' maternity leave, 4 weeks' holidays a year and an impressive pension plan that adds 15% to the value of the base salary. The government will also assume the overhead costs of physicians who sign on. All told, each doctor will cost the health board up to \$285 000 a year.

"It's a lot," admits Al Woods, the health board's CEO, "but we need them and we have to be competitive."

By late August, 7 of the town's 18 physicians had already signed on.

"The only way to free up your life and gain control is to go on contract," says Woods. "This is an attractive package for us when we recruit. Other [provinces] could use it [as a model] but we hope they don't until we get our numbers up."

Physicians who opt to remain on the fee-for-service system will pay 10% of hospital billings and 30% of clinic billings to cover overhead costs (see www.yhssb.org).

Communities plead with college over suspension of FP

Some 4000 residents of a rural area in Nova Scotia have signed a petition urging the provincial college not to suspend a local physician who had a romantic relationship with a patient.

Dr. William Hunter Blair, 60, lost his medical licence for a year and must undergo an independent psychiatric assessment at a sexual behaviours clinic. He is also banned from practising psychotherapy.

But the 39-year-old former patient and the 4000 residents of Barrington and Clarks Harbour, 200 km south of Halifax, strongly disagree with the decision. They say the relationship involves consenting adults and that Blair, who has practised in the area for 18 years, did not begin a sexual relationship with Joanna Hyde until after the doctor-patient relationship had ended. The relationship was reported to the college by a colleague of Blair's.

The Nova Scotia Medical Act has strict rules against sexual relationships between physicians and patients, even if the doctor-patient relationship has ended. This is particularly true when psychotherapy is involved.

Hyde was not impressed by those rules. "I will not have a governing body from the land of Oz telling me that my emotions and my affections for someone are somehow misplaced or unhealthy," Hyde said.

This is the first time in the college's history of such cases that a patient has come forward publicly to state that she has no complaint against a doctor charged with professional misconduct. In the last 5 cases of sexual misconduct before the college, the physicians' licences were suspended for at least 18 months.

In support of Blair, and in an effort not to lose 1 of only 3 family physicians in a catchment area of 10 000 people, local residents presented the petition to Dr. Cameron Little, registrar of the College of Physicians and Surgeons of Nova Scotia.

Little said the college is sympathetic, but the community's concern about a physician shortage is best addressed by the Department of Health. As for the petition, he said all physicians must be held to the same standard: "You can't have one person slapped on the wrist when for the same thing someone else's licence is removed." — *Donalee Moulton, Halifax*

Pulse

The greying of Canada's medical workforce continues

The Canadian Institute for Health Information reports that the average age of Canadian physicians rose over the last 5 years, from 46.3 years in 1995 to 47.2 years in 1999. The proportion of physicians aged 50 to 59 also increased, from 19.6% in 1995 to 22.8% in 1999. The number of physicians younger than 40 fell during the same period, from 33% of the total to 28.1%.

Although the overall number of physicians relative to the population has remained stable over the last 5 years at about 185 physicians per 100 000 population, the proportion of family physicians relative to the supply of specialists is decreasing. The number of family physicians per 100 000 population dropped by 3.1% between 1995 and 1999, while the number of specialist physicians per 100 000 population rose by 3.4%.

The number of physicians emigrating from Canada continues to decline from the peak levels reached in the mid-1990s, with 585 physicians moving abroad during 1999 and 343 returning. The proportion of specialists migrating (69%) far exceeded that of family physicians (31%), although this has not always been the case. From the mid-1980s to the mid-1990s, the proportion of emigrating family physicians was consistently higher than that of specialists.

The average age of physicians leaving the country was 40, while the average age of those returning to active practice in Canada was 41. — *Lynda Buske, buskel@cma.ca*



Average age of Canada's MDs is on the rise

Ontario to train 40 more medical students

Ontario has joined the parade of provinces increasing medical school enrolment. On Aug. 23 it announced a 7.5% boost in enrolment, bringing the provincial total to 572 first-year places. Alberta, Quebec and British Columbia made similar announcements earlier in the year. Ontario's 40 new slots will be spread among all 5 of its medical schools. The University of Toronto will get the most, 13, while McMaster will get 8 and the University of Western Ontario and University of Ottawa will each get 7. Queen's will get 5 additional places. The new spaces will cost the province \$976 000 a year and will help replace some of the roughly 75 spots cut in Ontario in the early 1990s; all of those cuts were made at the University of Toronto.

Dr. Jeff Turnbull, vice-dean of education at the University of Ottawa, says the final go-ahead for the increases wasn't received until Aug. 23, but the medical school had let people on its waiting list know that an increase was probable. "We certainly hope that more increases are in the offing and we've been given preliminary indications that this is the case," he said. He added that the increase, while good news for the 7 additional students accepted at the U of O, remains "a small drop in the bucket." — *Patrick Sullivan, CMAJ*

Clinical Update

A new treatment option for severe heart failure

Pitt B, Zannad F, Remme WJ, Cody R, Castaigne A, Perez A, et al. The effect of spironolactone on morbidity and mortality in patients with severe heart failure. Randomized Aldactone Evaluation Study Investigators. *N Engl J Med* 1999;341:709-17.

Background

Over the past decade significant advances have been made in the treatment of congestive heart failure (CHF). Despite the reduction in morbidity and mortality conferred by angiotensin-converting-enzyme (ACE) inhibitors and β -blockers, the burden of illness from CHF remains high. Although ACE inhibitors inhibit the renin-angiotensin-aldosterone system, complete suppression of aldosterone production does not occur.¹ Given the deleterious effects of aldosterone, which include salt and water retention, sympathetic activation and vascular fibrosis, aldosterone-receptor blockade with spironolactone may be beneficial in patients with CHF.²

Question

Does the addition of spironolactone to a standard treatment regimen for heart failure reduce morbidity and mortality among patients with severe CHF?

Design

In this study 1663 patients with severe CHF (New York Heart Association [NYHA] functional class III or IV) were randomly assigned to receive placebo or spironolactone (starting dose 25 mg) in a double-blind fashion. At the time of study entry almost all patients were taking ACE inhibitors and loop diuretics, and most were taking digoxin. Impor-

tant exclusion criteria included an elevated creatinine level ($> 221 \mu\text{mol/L}$) or a potassium level above 5 mmol/L at baseline. Patients were monitored for hyperkalemia and rising creatinine levels 1 week after starting therapy, every 4 weeks for the first 12 weeks, and every 3 to 6 months thereafter. Spironolactone therapy was stopped if the creatinine level reached 354 $\mu\text{mol/L}$. The primary end point was death from any cause. Secondary end points included admission to hospital because of cardiac causes and change in NYHA functional class. Data were analyzed using the intention-to-treat principle.

Results

The baseline characteristics of the patients were similar in both groups. Over two-thirds were classified as NYHA functional class III. The average daily dose of ACE inhibitor was 15 mg of enalapril or lisinopril, or 63 mg of captopril. Ischemia was the cause of CHF in just over half of the patients. After 2 years of follow-up, the mean daily dose of spironolactone in the treatment arm was 26 mg.

The study was stopped after a mean follow-up of 24 months because the death rate was significantly lower in the spironolactone group than in the placebo group (35% v. 46% respectively; relative risk 0.70, 95% confidence interval [CI] 0.60–0.82; $p < 0.001$). The number of hospital admissions because of cardiac causes was also significantly lower in the spironolactone group than in the placebo group (515 v. 753; relative risk 0.70; 95% CI 0.59–0.82; $p < 0.001$). Fewer patients in the placebo group than in the spironolactone group showed improvement in functional class. Serious hyperkalemia (potassium level above 6.0 mmol/L) occurred in 10

patients in the placebo group and 14 patients in the spironolactone group (difference not significant, $p = 0.42$). Gynecomastia or breast pain was reported in 10% of men taking spironolactone, although few of them (1.2%) stopped taking the drug for this reason.

Commentary

The patients in this study had advanced heart failure, as demonstrated by their high mortality rate. The addition of spironolactone, at doses that have little diuretic effect, resulted in significant reductions in mortality and hospital admissions and improved functional status of patients with CHF. There were surprisingly few episodes of serious hyperkalemia. This is attributable to the use of spironolactone in low dose and strict adherence to exclusion criteria.

Practice implications

The absolute risk reduction of 11% means that only 9 patients with severe CHF need to be treated with low-dose spironolactone for 2 years to prevent 1 death. Patients with pre-existing hyperkalemia or significant renal impairment, however, are ineligible for this treatment. When initiating spironolactone therapy, physicians must monitor potassium and creatinine levels closely. — *Kathryn A. Myers*

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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Public Health

West Nile fever heads north

Epidemiology

West Nile fever is a mosquito-borne illness that can cause encephalitis or meningitis in 1% to 10% of cases.^{1,2} It is named after the West Nile region of Uganda, where it was first isolated in 1937. The virus usually circulates in a bird-mosquito-bird cycle that can spill over into humans. Outbreaks in humans have occurred in at least 17 countries in Africa and Europe. The 1996/97 outbreak of West Nile fever in and near Bucharest, Romania, which has a climate similar to Canada's, resulted in more than 500 clinical cases and a case-fatality rate approaching 10%.² An outbreak of viral encephalitis in New York City in 1999 that involved 62 people and resulted in 7 deaths was the first recognized introduction of the virus into North America.^{3,4} The virus was probably transported in a person who recently returned from an endemic region, in an imported, infected bird or in an infected mosquito.



Canada's front line of defence against the West Nile virus: sentinel chickens.

To estimate the public health impact of the outbreak in New York City, a seroprevalence survey of residents of North Queens, New York, was conducted in the fall of 1999. Of the 677 residents tested, 19 people (2.6% of the

population older than 5 years) showed evidence of previous infection,¹ suggesting that most human infections are asymptomatic. Elderly people appear to be more susceptible to severe neurological disease.³

Last summer New York City implemented a mosquito control and abatement plan that included mosquito surveillance, the elimination of breeding sites and pesticide spraying to kill adult mosquitoes and larvae. In January and February 2000, researchers found low but detectable levels of the virus in 3 of 69 mosquito breeding pools in New York City, suggesting that the virus was able to survive the winter. Subsequently, 38 mosquito breeding pools in New York state and 1 in Connecticut tested positive for the virus.⁵

On Aug. 4, 2000, the New York City Department of Health reported another case of infection in a 78-year-old man from south Richmond county on Staten Island, an area where the virus was not detected in 1999. As of Aug. 7, 188 birds infected with the virus had been identified in New York, New Jersey, Massachusetts and Connecticut, indicating an expanding zone of epizootic transmission of the virus.⁵ To date, the virus has not been detected in Canada.

Clinical management

Symptoms appear 3 to 12 days after a person has been bitten by an infected mosquito. Symptoms range from mild fever and headache, occasionally accompanied by a maculopapular rash that expands from the trunk to the extremities, to severe headache, fever, stiff neck, muscle weakness and disorientation.⁴ Many people remain asymptomatic. Diagnosis is based on a serum IgM result. Physicians who think a patient may be infected should phone their public health units for advice on

laboratory testing. Treatment is symptomatic; there is no vaccine.

Prevention

There are 4 components to prevention: surveillance, individual risk reduction, mosquito larval mapping and control, and adult mosquito control.⁵ Health Canada is working with the provinces and territories and with private industry to establish sentinel chicken surveillance. Coops have been placed in strategic locations from Saskatchewan to Atlantic Canada and tested weekly for the presence of West Nile virus. Wild birds, domestic animals and mosquito populations are also being monitored. Physicians are asked to report all cases of suspected viral encephalitis to their public health unit. Health Canada is currently establishing surveillance programs at selected hospitals in designated high-risk areas.

Individual risk can be reduced by using appropriate clothing and repellents and by eliminating mosquito breeding grounds, such as stagnant pools of standing water. Health Canada is coordinating the development of guidelines for mosquito abatement that include guidance on the use of pesticides.

Further information is available at www.nationalatlas.gov/virusmap.html, where maps are updated weekly with data from the US West Nile virus surveillance system. — *Erica Weir, CMAJ*

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