American MDs reject moratorium on capital punishment

With capital punishment moving to centre stage in the US election campaign, the American Medical Association has decided not to enter the controversial debate and refused to endorse a call for a national moratorium on executions.

Acting on a resolution from the American Association of Public Health Physicians, delegates attending the AMA's annual House of Delegates meeting in mid-June characterized the death penalty as a legal rather than medical issue. They did endorse more use of "appropriate medical forensic techniques" such as DNA testing in capital cases. Delegate Steven Thorson of Colorado said he feared a temporary moratorium would lead to a permanent ban. That, he said, "wasn't the AMA's business."

The resolution sought a moratorium "until questions concerning the availability of DNA evidence, the quality of legal representation and the harmful impact to the judicial system [through the execution of innocent people]" could be resolved. The resolution stated "that in several states innocent individuals may be executed because medical technology will not be made available in time to prevent their deaths." Although the AMA rejected the moratorium, its existing policy precludes physician participation in executions in any way.

The momentum for death-row reform picked up earlier this year when Governor George Ryan of Illinois suspended executions in that state after concluding that 13 innocent people might have been executed. It grew when other legislators requested reviews of the safeguards provided to inmates throughout their long appeal process, and reached its apogee when Republican presidential nominee George Bush postponed the execution of a convicted killer in June to allow time for DNA testing. One hundred and thirty-one inmates have been put to death during his term as governor of Texas, and Bush has repeatedly said he does not believe any innocent person has been executed in his state. However, he does support expanded use of DNA testing. Bush's opponent for the presidency, Vice-President Al Gore, has affirmed his support for capital punishment and also supports expanded DNA testing.

Canapress

Ronald Carlson of Houston, who witnessed the execution of his sister's murderer, now opposes capital punishment. Here, he protests the execution of Canadian Joseph Faulder in Texas in June 1999.

Since the US Supreme Court reinstated the death penalty in 1976, 643 people have been executed (**www.ojp.usdoj.gov/bjs/cp.htm**). One-third of the executions (218) were carried out in Texas. Shortly after the Bush announcement, a highly publicized research survey from Columbia University revealed that in 4578 appeals of death penalty convictions prior to 1995, 68% of the convictions were overturned because of mistakes by incompetent defence lawyers and other courtroom errors; 7% of those appealing were found to be innocent.

Public support for the death penalty is sliding steadily in the US, from 80% support in a 1994 Gallup poll to 66% support today. There are no surveys on physicians' attitudes toward capital punishment. The AMA policy states that "an individual [physician's] opinion on capital punishment is [a] personal moral decision." — *Milan Korcok*, Florida

Out of country, out of pocket

Nova Scotia will soon make patients from outside the country pay their medical costs before leaving hospital, regardless of whether they're insured. "We will be establishing a policy for full recovery, plus premium," says Health Minister Jamie Muir. That premium is about double the normal cost of a hospital stay. In Halifax, this might total $2400 a day for out-of-country visitors.

Presently, patients from outside Canada are not given a bill. If they are from a country with universal medical coverage, their government is billed directly. If a patient has personal health insurance, the bill is sent to the insurer. Under the new policy, slated to take effect next year, Nova Scotia will become the first province to ask for its money up front. The move is one of many being driven by the province's poor fiscal situation; in an era when most provinces are running budget surpluses, Nova Scotia still faces deficits.

Muir says these patients will not get preferential treatment over Nova Scotians. However, if foreign visitors become ill in Nova Scotia and can't afford to pay, they will still get medical treatment. — *Donalee Moulton*, Halifax

Revised fitness-to-drive guide now available

The CMA's new *Determining Medical Fitness to Drive: A Guide for Physicians*, which took 2 years to revise and is 3 times longer than the previous version, is now available. This new version reflects changes that have taken place in medicine, the transportation industry and the legal system in the last 10 years.

"We feel what we have done is medically responsible and will protect drivers and the public," says Dr. David Irving, chair of the CMA project advisory group assigned to revise the 1991 guide. The new sixth edition, with its emphasis on evidence-based background information, includes a new section on airbags, more supplementary information, and an expanded appendix with evaluative tools. It also has the latest information about elderly drivers, as well as about driving and medical conditions such as epilepsy, sleep apnea and cardiovascular disease.

Irving says his group recognized that elderly drivers are a growing concern. "Their licence is important to them but so is their life and the lives of others," says Irving, an Edmonton cardiologist. Proposed solutions include limiting their driving to local shopping only, and only during daylight, nonrush hours.

Irving and the other 3 members of the advisory group — Drs. Robert Brison, Linda Inkpen and David Smith — began the process in 1998 by consulting with 135 groups and associations ranging from medical specialty bodies to the Canadian Diabetes Association and police organizations. Irving says this inclusive approach yielded "superb recommendations and responses."

These same groups then reviewed the draft guide to ensure it met their concerns. The final draft was then test driven for 6 weeks by 30 general and specialist physicians in rural and urban settings. "We had practically nothing but compliments from them," says Irving. The participating doctors were particularly enthusiastic about the guide's comprehensiveness.

CMA members can order their free copy of the guide by phoning 888 855-2555, or 613 731-8610 x2307. The cost for nonmembers is $34.95, plus taxes and shipping charges. — *Barbara Sibbald*, CMAJ

A stitch in time

In Nova Scotia, an innovative "message quilt" is allowing organ recipients to express their gratitude and donor families to gain a glimpse into the lives they have helped to rebuild. The Organ Procurement Centre at the Queen Elizabeth II Health Sciences Centre in Halifax sponsored the creation of 2 special quilts that are being displayed throughout Nova Scotia. "The most precious gift I ever received has come from a perfect stranger," writes Donald. "Thank you." Heather, on a piece of her satin wedding dress, had these words stitched: "A wedding toast to a young man I never knew who signed a donor card and gave me my Dad to walk down the aisle with me." — *Donalee Moulton*, Halifax

OMA gets involved at federal level

The Ontario Medical Association made its second foray into federal politics in June by urging its members to consider becoming involved in the leadership race of the Canadian Alliance. The new party, which replaced the Reform Party, held its first-round leadership vote June 24. In a June 1 letter to members, surgeon Alan Ryley, chair of the Political Action Committee, said the OMA wanted to encourage doctors to "become involved as the next federal election draws near."

Although a *Globe and Mail* columnist criticized the letter as "partisan," an OMA spokesperson was adamant that the association would have sent the same message if another federal party was having a leadership contest. She also noted that the OMA sent a letter to Toronto-area physicians during the 1997 federal election, urging them to consider supporting 2 candidates — Dr. Carolyn Bennett, a Liberal, and Dr. Bob Frankford, a New Democrat. Ryley says the OMA encourages its members to get involved in politics "as a continuation of our ongoing, nonpartisan participation in municipal, provincial and federal politics." — *Patrick Sullivan*, CMAJ

On the Net

Internet addicts can get online help

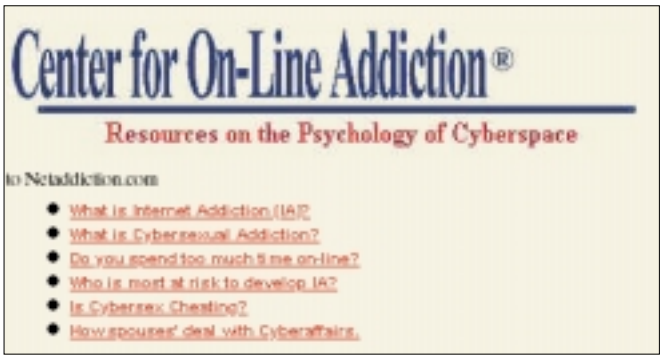
In 1995, psychologist Kimberly Young of the University of Pittsburgh coined the phrase Internet addiction (IA). Six years later, Young has opened the world's only "virtual clinic" to help people deal with their online problems.

Young, who bills herself as "the world's first cyberpsychologist," runs the Center for On-Line Addiction (**www.netaddiction.com**). It includes checklists of warning signs, tips on how to deal with problems and a self-administered assessment test. There is even a "cyberwidows" test aimed at spouses and tests to determine whether you are addicted to cybersex or online gambling.

"Impairment to real-life relationships appears to be the number-one problem caused by Internet addiction," says Young. "Internet addicts gradually spend less time with real people in their lives in exchange for solitary time in front of a computer."

Young's site says IA covers a variety of behaviours and impulse-control problems, including cybersex, cyber-relationships, online gambling and trading, excessive Web surfing and general addiction to computer games or programming.

Once identified as an online addict, people can surf over to Young's virtual clinic, where they can sign up for email, online "chat" or telephone counselling. Have your credit card handy. A patient history is taken — online, of course — and then service commences. The cost runs from US$15 US for a single email response "session" to US$210 for 180 minutes worth of chat or telephone counselling. All major credit cards are accepted.



Although the online clinic does not offer any claims about its success rates, it does highlight the number of times Young's work has been featured in the mass media, in venues ranging from the *New York Times* and *Wall Street Journal* to the BBC and *Good Morning America*. — *Michael OReilly*, mike@oreilly.net

Canadian research facility enters the big leagues

Winnipeg's national research facility received its first shipment of biosafety level-4 viruses, launching it into the elite company of 13 research facilities worldwide that are capable of handling these dangerous pathogens.

The Canadian Science Centre for Human and Animal Health received samples of the Ebola, Lassa, Marburg and Hunan viruses from the US Centers for Disease Control and Prevention June 8.

The year-old Winnipeg facility, operated jointly by Health Canada and the Canadian Food Inspection Agency, contains Canada's first biosafety level-4 laboratory and the world's first — and only — facility to combine human and animal health disease research facilities at the highest level of biocontainment. This means that researchers can collaborate as they study established and emerging diseases in human and animal populations. About 220 people now work at the $200-million high-security facility. — *Barbara Sibbald*, CMAJ

A scientific look at what comes naturally

After decades of working in isolation, Canadian researchers and physicians have come together to form the Natural Sourced Medicine Research Network. The organization, the first of its kind in Canada, aims to pool information about the efficacy and safety of natural medicines.

Dr. Tim Lee, professor of immunology at Dalhousie University and director of the research network, says a top priority is to develop a comprehensive database of clinical trials and other research involving natural medicines. This would include methodologic assessment of the research. Lee says "there's no good database that physicians or pharmacists can go to with information that's been reviewed scientifically."

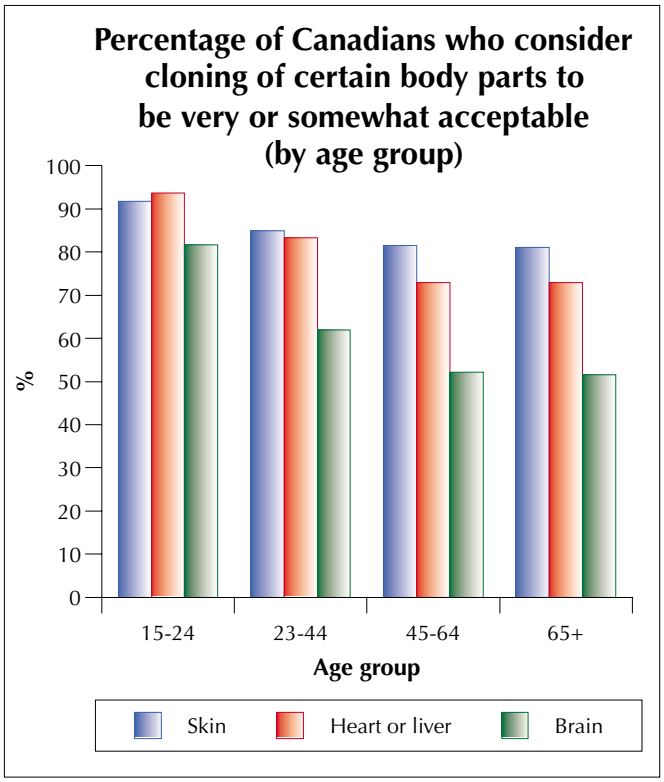
The network, which grew out of a conference sponsored by Health Canada's Office of Natural Health Products, is built on a centre-of-excellence model. "We had 2 choices," says Lee. "Either create a national centre for research in this area or create what would be a virtual centre. This network is the forerunner of a virtual institute in natural-sourced medicine." Although it currently has no funding, the organizers hope to tap into federal funds through the new Office of Natural Health Products. — *Donalee Moulton*, Halifax

Pulse

Most Canadians welcome genetic testing

A recent survey by the financial and managerial firm PricewaterhouseCoopers (*HealthInsider*, Spring 2000) found that most Canadians favour the use of genetic testing for specific medical purposes.

The survey, which tracked attitudes toward a number of biotechnological advances in medicine, found that 93% of those surveyed felt genetic testing would be very or somewhat acceptable if used to diagnose illnesses earlier. Almost as many respondents (91.3%) said it was very or somewhat acceptable to use genetic testing to determine the risk of transmitting a disease to one's children. Using the testing to determine an individual's future risk of acquiring a medical condition was deemed very or somewhat acceptable by 90.6% of respondents. Interestingly, 91.6% of respondents would give their own doctors access to their genetic information, while only 13.6% would grant the same access to government agencies.



Respondents tended to favour genetic engineering if used for specific medical reasons, with 71.2% viewing it as very or somewhat acceptable if used to cure an inherited medical condition, and 81.2% saying it was very or somewhat acceptable when used to decrease the risk of acquiring a specific condition. Canadians view genetic engineering less favourably if it is used for nonmedical reasons: 24.3% said it would be acceptable if used to improve a child's esthetic or physical features, and 17.8% thought it would be acceptable to use it to determine the sex of a child.

Although Canadians generally feel that the cloning of humans is not very or not at all acceptable (88.3%), they are more receptive to the possibility of cloning human parts for specific medical reasons. Eighty-seven percent of respondents felt that cloning skin for accident victims was very or somewhat acceptable, 84.4% supported cloning a heart or liver for transplantation, while 66.4% would accept the cloning of the human brain for victims of severe brain damage. Younger Canadians were more likely to support the cloning of human parts. — *Shelley Martin*, martis@cma.ca

AMA warns Alberta surgeons about going it alone

The president of the Alberta Medical Association has warned 18 cardiovascular and thoracic surgeons that it will continue to represent all of the province's doctors in negotiations with the province. A May 30 letter from President David Bond was sent to all members after the AMA received resignation letters from the 18 members of its Section of Cardiovascular and Thoracic Surgery. The association was also notified that the surgeons wanted to continue receiving all benefits available to AMA members; although the surgeons would be eligible to pay a nonmember administrative fee that would make them eligible to receive CME and CMPA reimbursements, Bond warned that they would lose benefits such as AMA insurance and the right to invest in MD Management. Dr. Dennis Modry, president of the section, said the resignations were prompted by AMA opposition to Alberta's Bill 11, which would lead to more private surgical services in the province. The request to dissolve the section will be considered by the AMA's Representative Forum Sept. 16. In the meantime, Bond has issued a call for unity. "The profession of medicine, and our cherished autonomy and clinical independence, are best protected and ensured through unity of all physicians, speaking with one voice," he said. — *Patrick Sullivan*, CMAJ

CMPA, OMA try to heal rift over regional rating

As the Canadian Medical Protective Association prepares to hold its annual meeting next month, some doctors are wondering if it is about to be joined on the medicolegal stage by an Ontario Medical Protective Association.

The possible move toward an OMPA is being driven by the CMPA's decision to pursue regional rating, which will see Ontario physicians pay malpractice protection charges that are by far the highest in the country. The rift between the CMPA and Ontario Medical Association is one of the most serious in the history of the CMPA, which turns 100 next year.

It was also the first issue to greet Dr. John Gray, the Ontario FP who stepped into the CMPA's top job — secretary treasurer — in May. Gray has been on the road since then, trying to explain the rationale behind regional rating.

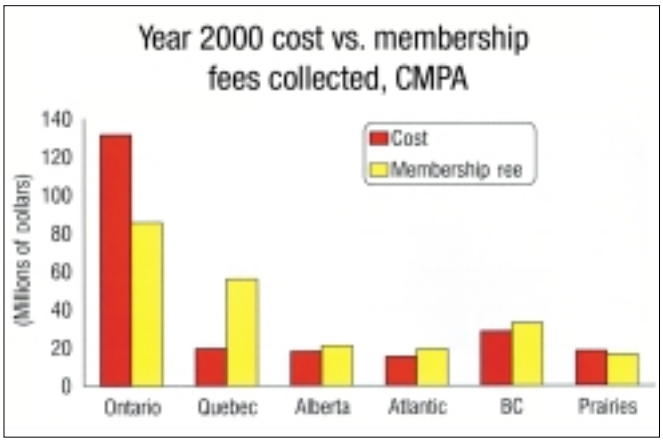
Gray says the issue is relatively simple. The CMPA now pays about $46 million more to provide malpractice protection for Ontario doctors every year than it earns in fees ($130 million vs. $84 million, see chart). In Quebec, revenue from Quebec doctors totals almost $60 million annually, while CMPA costs come to only $20 million. "As the facts become known," says Gray, "there is less opposition."

Under regional rating, Ontario physicians would see an aggregate fee increase of 45%, with increases varying by specialty. (By one estimate, fees for Ontario obstetricians may rise to $65 000 from $30 000.) Quebec doctors would enjoy an aggregate reduction of 63%, while doctors in the rest of Canada would probably see small decreases.

The Ontario government is one of the parties demanding change. It is already paying about $60 million annually to reimburse doctors for their CMPA coverage and would likely have to pay about $40 million more under regional rating. The province currently covers about 72% of physicians' CMPA costs; although doctors are responsible only for the amount they were paying in 1986, they report that reimbursement takes up to 15 months. Dr. John Jeffery, the head of obstetrics at Ontario's Kingston General Hospital, says that with a 45% fee increase, the province's obstetricians would have to perform 12 deliveries a month simply to pay monthly carrying charges on the CMPA premium.

Gray says regional rating points to the need for tort reform. Why, for instance, is the average medicolegal settlement in Ontario 156% higher than in Quebec ($172 000 vs. $67 000)? "Perhaps it's a cultural difference," says Gray, with Quebecers "looking to the courts less than they do in Ontario."

OMA President Albert Schumacher says the association would prefer to have Ontario doctors remain with the CMPA, but "we have to explore all our options." He says frustration has been growing over certain aspects of CMPA policy. For instance, the CMPA "hasn't gone that extra step" of covering Ontario doctors who see American patients.



Schumacher says that's a major issue in border areas like Windsor, where he practises, because American patients are a major source of income for doctors in certain specialties. "Basically, we've been told not to see these patients. There's a market of 5 million people here [Americans living near the border] but the CMPA is not too interested. It only wants to insure [under] medicare."

The OMA also wants the CMPA to do a better job promoting risk management. "This is a bone of contention," says Schumacher. Gray, a past president of the OMA, admits that the CMPA must "become more aggressive" in this area.

The OMA also thinks the CMPA should be actively pursuing tort reform. "Basically," says Schumacher, "they've just sat back and said, 'We don't care who pays [the CMPA fees].' " However, tort reform involves political lobbying, and this may prove difficult for a tradition-bound organization like the CMPA. "We have always had a single focus [of representing members] and a reputation of integrity," says Gray. "We do not get political."

Gray and Schumacher have both received many letters from doctors telling them to "work things out." Will they? "I'm cautiously optimistic," says Schumacher, who adds that Gray's arrival at the CMPA will help. "I think liaison with the CMPA will be better because he's there."

Gray, whose annual CMPA fee was $50 when he joined in 1972, acknowledges that Ontario doctors account for about 40% of CMPA membership, but says the organization "could survive without Ontario, absolutely."

However, he too is confident that an agreement can be reached. "The members need to hear firsthand about regional rating," he says. "If they do, I think an understanding will develop that this was the way we had to go."

Ontario doctors appeared to make their feelings clear during the OMA annual meeting in May, when they passed a motion stating that a referendum of the membership must be held if the OMA recommends an alternative to CMPA coverage for Ontario's doctors. — *Patrick Sullivan*, CMAJ

Health workers take to streets to reduce impact of homelessness

A few years ago, the steep increase in the HIV infection rate among injection drug users prompted Vancouver's Lookout Emergency Aid Society to begin admitting some of the epidemic's sickest victims. "We admitted people we thought were going to die soon," says society worker David Richardson. The society began setting aside 5 of its 39 tenancy beds for homeless and HIV-positive drug users. Today, 2 of the first 5 tenants are dead, but the other 3 have moved on to more independent living. "Miracles can happen with stable housing, proper medication, decent meals and some people around who care," explains Richardson (see page 161).

The society's successes are noteworthy, but for too many sick, homeless people in cities like Vancouver and Toronto the things that can turn their lives around — stable housing, people who care — can prove elusive.

Canapress

"Getting access to a doctor, to medical care, is one piece [of caring for the homeless sick], but it's actually the easiest piece," says Kathy Hardill, a street nurse with Toronto's Regent Park Community Health Centre. She spends much of her time helping homeless people gain access to the drug benefit cards they need to fill prescriptions. In Ontario, welfare recipients are entitled to prescription drugs with only a small copayment. However, getting on the welfare rolls can be a major hurdle for the homeless, and drug coverage isn't always automatic. "The process is not what you'd call streamlined," says Hardill.

Hardill met with one homeless woman who, unable to fill a prescription for antibiotics for a urinary tract infection, was hospitalized with pyelonephritis. "From a purely economic point of view it makes more sense to improve accessibility to the drugs," Hardill says. Ontario's community health centres, many of which are located in marginalized communities, can pay for some drugs in emergencies, but their resources are being stretched thin as the ranks of the most needy swell.

"Patients should never be discharged from hospital with prescriptions they can't fill," says Hardill. "We want medical staff to routinely ask if they can fill their prescriptions, or if they can afford the [recommended] over-the-counter drugs."

In downtown Vancouver, access to prescription drugs by homeless people is a bit easier than in Ontario. Welfare payments are a formal precondition for access to the provincial drug plan, Pharmacare, but the rules are eased a little for needy clients of the Downtown Community Health Clinic and the BC Centre for Disease Control's Street Nurse Program. The downtown clinic operates a community pharmacy that provides prescription and over-the-counter drugs to patients who have seen clinic doctors and are waiting to receive welfare or disability payments.

"We operate on the premise that some people are caught between a rock and a hard place," says pharmacist Cathy Cormier. Clinic staff help clients navigate through the application maze, and most people are covered by a drug plan within 3 months. The pharmacy fills between 150 and 200 prescriptions a day, she said, and up to 25% of the people receiving them are not covered by Pharmacare.

Hardill says Toronto's street nurses have argued without success for a community pharmacy that provides medication for people waiting for drug cards. Even if they do get their drugs, chaotic circumstances can make it hard for the homeless to take them properly. One of her clients, an elderly homeless man with multiple chronic ailments, has coverage for his prescription drugs, but diarrhea is a troubling side effect of his medication. His usual shelter has beds for 100 people but only 2 bathrooms; he doesn't bother to take his drugs when he stays there.

Meanwhile, emergency housing is hardest to find for the sickest people, says Hardill. "If someone is chronically ill or disabled — say they are blind or incontinent — I call a shelter to find them a bed. I describe their condition. I'm told, 'No, we just can't deal with someone who is not self-managing.' The shelter staff are stretched to the max."

Another homeless client has a serious mental illness and a significant physical disability. He can be difficult and combative, and hence is unwelcome at emergency shelters. "We just don't have enough appropriately staffed emergency beds to respond to the crisis — 3 staff to 100 people is pretty typical." In the space of a few weeks, her client was hit by a car, causing a neck fracture. Shortly after his release, he was beaten so badly that he spent 3 days in hospital as a surgical patient. "It is very stressful looking after [people like] him," says Hardill, a nurse practitioner with 12 years' experience as a street nurse. "Community health has become about the basics of survival." — *Ann Silversides*, Toronto

Clinical Update

The dyspepsia dilemma

Talley NJ, Vakil N, Ballard ED II, Fennerty MB. Absence of benefit of eradicating *Helicobacter pylori* in patients with nonulcer dyspepsia. *N Engl J Med* 1999;341(15):1106-11.

Background

Dyspepsia is one of the most frequent presenting complaints in primary care practice. More than 50% of affected patients do not have an ulcer, but as many as 30% may have *Helicobacter pylori* infection, indisputably the main cause of peptic ulcer. Various expert groups have issued recommendations, largely on the basis of consensus (i.e., no direct evidence), for and against therapy to eradicate *H. pylori*.

Question

Should patients with dyspepsia and positive test results for *H. pylori* be treated for eradication of the bacterium?

Design

A randomized controlled trial involving 170 patients with nonulcer dyspepsia (confirmed by endoscopy) and *H. pylori* infection were randomly assigned to receive triple therapy for eradication of the bacterium (omeprazole 20 mg, amoxicillin 1000 mg and clarithromycin 500 mg, twice daily for 14 days); 167 control subjects with the same condition were given identical-appearing placebos. Successful treatment was defined as the absence of symptoms or only mild pain or discomfort. The study was undertaken at multiple centres in the United States.

Results

At 12 months 46% of the subjects in the treatment group and 50% of those in the placebo group reported either no discomfort or no more than mild pain or discomfort in the upper abdomen during the 7 days preceding the assessment. The mean rate of antacid use was similar in both groups at 12 months. Urea breath test results 4–6 weeks after termination of active treatment indicated that 90% of the patients in the treatment group had negative results for *H. pylori*, as compared with 2% of those in the placebo group. In a subset of patients with chronic gastritis diagnosed during their entry gastroscopy, 86% of those in the treatment group no longer had the problem, as compared with 8% of those receiving placebos. When endoscopy was performed after 12 months, duodenal ulcer was found in 2% of the treated patients and 4% of the control subjects ($p = 0.22$).

Commentary

This was a carefully conducted, randomized, double-blind, placebo-controlled clinical trial. The primary outcome measure (symptom relief) is relevant. The authors also documented the presence of peptic ulcer at the final visit, did pill counts of antacid use and collected a variety of other measures of patient well-being that are not reported here. The study was multicentred; although the precise number of centres was not stated, each centre enrolled 6 patients on average. It is unclear whether patients in this study were similar to those seen in a primary care practice.

Implications for practice

Patients with moderate pain or discomfort in the upper abdomen (dyspepsia) who do not present with warning signs of more serious disease (age less than 50 or signs of blood loss) may have *H. pylori* infection. This study shows that the eradication of *H. pylori* does not convey a health benefit. The implication is that patients presenting with moderate upper abdominal discomfort but without warning signs do not require testing for *H. pylori* infection and should be managed with conventional therapy. A recent meta-analysis supports this recommendation.[1] — *John Hoey*, CMAJ

Reference

1. Danesh J, Pounder RE. Eradication of *Helicobacter pylori* and non-ulcer dyspepsia. *Lancet* 2000;355:766-7.

Breast cancer and distant metastatic disease

Braun S, Pantel K, Müller P, Janni W, Hepp F, Kentenich CRM et al. Cytokeratin-positive cells in the bone marrow and survival of patients with stage I, II, or III breast cancer. *N Engl J Med* 2000;342(8):525-33.

Background

Many women with breast cancer that appears localized to the breast or to the breast and regional lymph nodes are believed to have undetectable distant metastases at the time of initial staging. Because of this, current recommendations are that systemic chemotherapy be given to all women with regional node involvement and to those with no node involvement but a primary lesion greater than 1 or 2 cm in diameter. However, the improvement in outcome with chemotherapy is slight. In women

with a primary tumour of 1 cm or less, systemic therapy reduces the rate of distant metastases from 10% to 7%. Although this is a risk reduction of 40%, it means, in effect, that an average of only 3 women on average in every 100 actually benefit from the therapy.[1] Thus, many women may needlessly undergo chemotherapy. However, if distant metastatic disease could be detected at the time of initial cancer diagnosis, the precision of prognostic stratification might be improved. A new technique to detect bone marrow micrometastatic lesions is now available.

Question

What proportion of women presenting with stage I, II or III breast cancer have distant metastatic disease?

Design

Bone marrow aspirates from the upper iliac crests were obtained from 743 consecutive patients admitted to a breast clinic in Germany; 552 had been newly diagnosed with stage I, II or III breast cancer and 191 patients with nonmalignant disease (mainly of the breast). The patients were followed for several years, thus providing some information on the test's usefulness in categorizing women into meaningful risk groups.

Results

Using an immunocytochemical technique to detect an antigen on cytokeratin peptides (a specific marker of epithelial cancer cells in bone marrow), 36% of the women with breast cancer tested positive, compared with only 1% of women without breast cancer. During a median follow-up period of 38 months, women with marrow-detectable cytokeratins were much more likely to die of cancer-related causes than women without the markers (relative risk 4.17; 95% confidence interval 2.51–6.94; $p < 0.001$). There were 301 women with no detectable lymph-node metastastes. Cytokeratin markers were found in the bone marrow of 23% of women with tumours smaller than 0.5 cm and 35% of those with tumours 0.5 to 1.0 cm. Of the 100 patients with node-negative tumours and evidence of micrometastases, 14 died of cancer-related causes over the follow-up period, compared with only 2 of the 201 women without micrometastases.

Commentary

This is a carefully conducted study of a large cohort of women. The testing for cytokeratins was done independently from the clinical staging. However, follow-up was relatively short, especially for a disease such as breast cancer.

Clinical implications

In a related editorial,[1] Barbara Smith comments that it is now important to proceed with trials of therapy because the follow-up is relatively short for breast cancer. Nonetheless, the survival curves extending to 48 months show a continuous divergence of survival and disease-free survival between groups with and without micrometastases. Smith feels that it is premature to recommend cytokeratin tests to patients with disease limited to the breast who wish to avoid chemotherapy. — *John Hoey*, CMAJ

Reference

1. Smith BL. Approaches to breast-cancer screening. *N Engl J Med* 2000;342(8):580-1.

Amok enzymes damage tissues during heart attack

A team of University of Alberta researchers has discovered a cause of the tissue damage that occurs during heart attacks and, in the process, added a wrinkle to current thought on the role of bacterial infections in heart disease (*Circulation* 2000;101:1833).

Led by Dr. Richard Schulz, an Alberta Heritage researcher, the team has come up with striking evidence that the enzyme matrix metalloproteinase-2 (MMP) is responsible for some injuries to heart tissues in the seconds following the onset of a heart attack. What's more, the authors say a novel side effect of tetracycline-class antibiotics that inhibits the action of MMPs must be taken into consideration by researchers probing the involvement of bacteria in heart attacks.

Schulz likens the role of MMPs to a bulldozer parked in your garage — the garage being one of your cardiac muscle cells. In an experimental model of heart attack in rat hearts, the researchers discovered that MMPs, commonly associated with wound healing, were responsible for injury. Beginning mere seconds after the onset of a heart attack, MMPs run amok. It is, Schulz says, as if someone was driving the bulldozer around inside the garage, causing tremendous damage.

They discovered that tetracycline-class antibiotics block the action of MMPs during heart attacks and reduce damage. The drugs can be modified to inhibit only MMPs, so that their use for nonbacterial conditions such as this would not add to the problem of bacterial resistance to antibiotic drugs.

"The question now is for those people who are susceptible to heart attacks — for example, patients with a previous history or angina — whether this class of inhibitors could be used as a prophylactic measure." Other research has drawn links between bacteria and heart attacks. Schulz's team hasn't disproved any connection, but he says its findings cannot be ignored.

"The bacteria angle needs a lot more research," he says. "It really captures the imagination of researchers. People are saying 'Maybe we will find a bacteria that causes some forms of heart attack,' and they may be right. But we are just saying there are novel protective elements of tetracyclines that you have to consider." — *Richard Cairney*, Devon, Alta.

Public Health

Escherichia coli O157:H7

Epidemiology

Escherichia coli O157:H7 is one of hundreds of strains of the gram-negative bacillus *E. coli*. Most strains are harmless, colonizing the intestines of healthy humans and animals, where they suppress the growth of pathogenic bacterial species and synthesize appreciable amounts of vitamin K and vitamin B complex. But a few strains cause gastroenteritis in humans by 4 mechanisms: adherence to small-bowel mucosa, direct invasion of mucosal cells, disruption of the microvillous brush border and toxin release. The class enterohemorrhagic *E. coli*, which includes *E. coli* O157:H7, produces hemorrhagic colitis by elaborating one or more cytotoxins closely related to the *Shigella* toxin. These toxins, variably called Shiga's toxins or verotoxins, damage intestinal epithelium and appear to possess neurotoxic and enterotoxic properties.[1]

E. coli O157:H7 was not recognized as a human pathogen until 1982, when the serotype was identified in stool specimens from American patients with bloody diarrhea.[2] Since then at least 65 outbreaks of the infection have been reported,[3] most recently in Walkerton, Ont., where at least 7 residents died after drinking contaminated municipal water.[4] Most outbreaks occur after people eat undercooked ground beef that is likely contaminated during slaughtering and subsequent meat processing. Outbreaks have also been caused by unpasteurized milk and similar products.[3]

Clinical management

The incubation period to onset of diarrhea is 1–8 days. Young children may continue to excrete the bacteria for more than 3 weeks after infection, but prolonged asymptomatic infection with *E. coli* O157 is unusual.[5] Infection is typically characterized by severe abdominal cramping and diarrhea that is initially watery and may become bloody; occasionally vomiting occurs. Fever is either low grade or absent. The illness is usually self-limiting and lasts for 8 days on average. Many sporadic cases likely go unrecognized.

Hemolytic uremic syndrome (HUS) develops in about 8% of patients, with very young and elderly patients being most susceptible. HUS is characterized by the sudden onset of hemolytic anemia, with fragmentation of red blood cells, thrombocytopenia and acute renal failure. It is believed to be caused by the systemic absorption of Shiga's toxins and the resultant direct effects of the toxins on endothelial and renal tubular epithelial cells. A recent case series reported that the region of colon affected differed between patients with hemorrhagic colitis in whom HUS developed and patients without HUS, which suggests that different mechanisms of injury and absorption are involved.[6] Occasionally, thrombotic thrombocytopenic purpura develops in elderly patients and they display 2 additional symptoms: fever and neurologic deficits. Clinicians considering a diagnosis of *E. coli* O157:H7 infection should specifically request a stool culture of the isolate because some laboratories do not screen for it routinely.

Fluid and electrolyte replacement is the cornerstone of therapy. In a recent prospective study[7] children treated with antibiotics were at greater risk of HUS than children who were not treated (relative risk 14.3). Physicians are advised to withhold antibiotic treatment until the results of a stool culture identify a pathogen and rule out *E. coli* O157:H7 infection.[4]

There is no specific treatment for HUS. Health Canada, through its Special Access Program, approved the sale of the drug Synsorb PK, which is currently in phase III clinical trials, to the hospital in Walkerton. The drug is designed to prevent the progression to HUS in children who have recently been infected by *E. coli* O157:H7 by binding the Shiga's toxins in the lumen of the gastrointestinal tract.[8]

Prevention

Preventing this infection is difficult because the organisms colonize the intestines of healthy cattle and other food animals. They are also resistant to acidic conditions, dehydration and high salt concentrations.[4] Irradiation dramatically reduces the risk of foodborne infection from *E. coli* O157:H7.[4] In the future a toxoid vaccine may be available, but for now vigilant public health control is paramount. Preventive strategies include[9]

- cooking all ground beef thoroughly;
- thoroughly washing hands, surfaces and utensils that may have been contaminated by uncooked meat;
- limiting milk consumption to pasteurized products;
- frequently washing hands of people who are infected; and
- drinking municipal water that has been treated with adequate levels of disinfectants. — *Erica Weir*, CMAJ

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