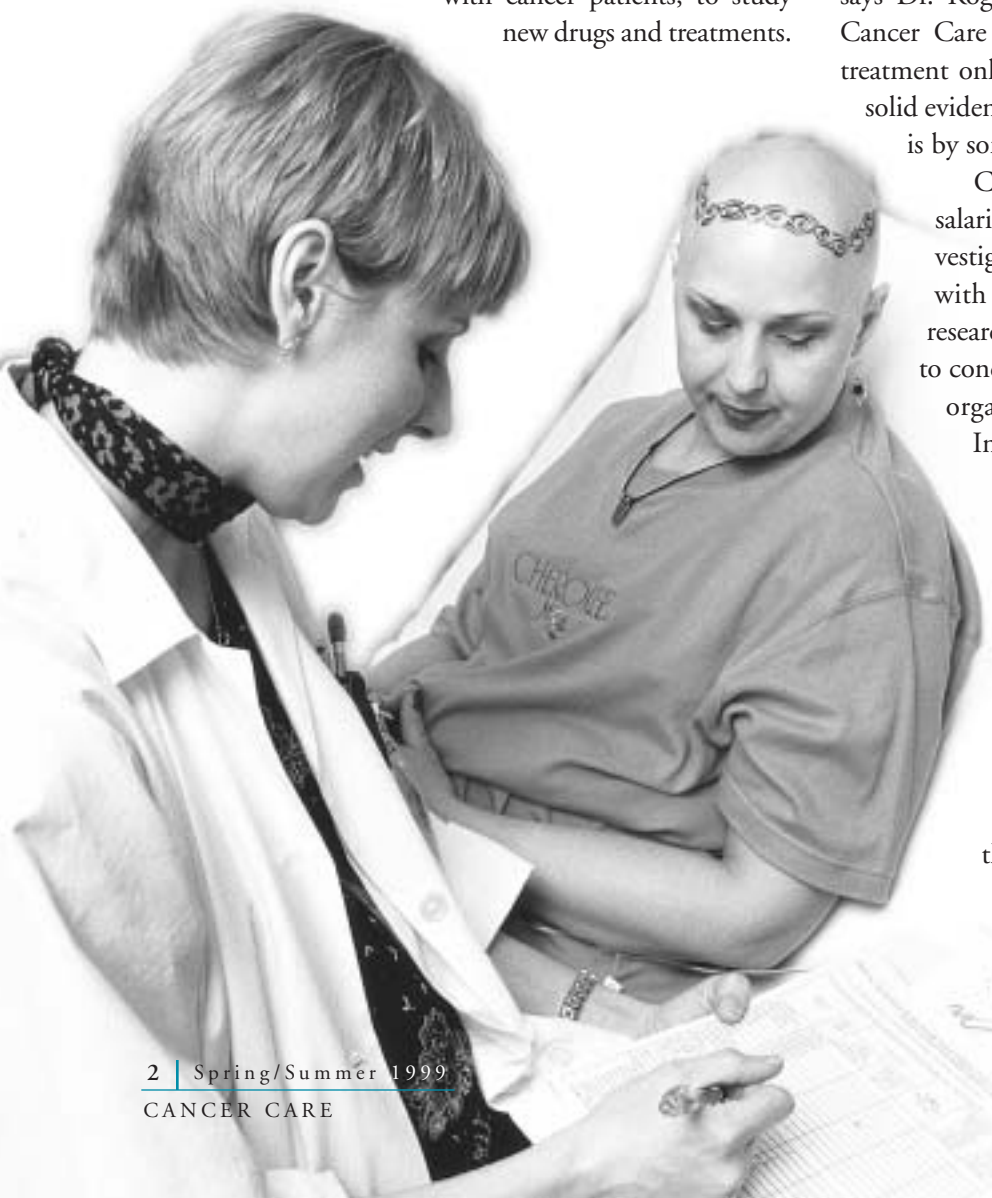
Spring/Summer 1999

CANCER Care

INSIDE

RESEARCH: *Road to* DISCOVERY

Behind every major advance in cancer prevention, screening, and treatment, there lie years of research: Basic science research that is done in the laboratory, and translational research that explores how laboratory discoveries might apply in human beings. Clinical trials with cancer patients, to study new drugs and treatments. And outcomes and health services research to ensure that people with cancer receive consistent, coordinated, and effective care based on the most current knowledge.



"What we're continually trying to achieve is an improvement in the quality of care delivered to patients," says Dr. Roger Deeley, head, Division of Research for Cancer Care Ontario (CCO). "But we should change treatment only when the decision to change is based on solid evidence; and the only way to obtain that evidence is by some form of research activity."

CCO contributes $4.5-million annually to salaries, facilities, and equipment for research investigators, support staff, and trainees associated with its eight regional cancer centres. But researchers must compete for the funds they need to conduct their projects; they submit proposals to organizations such as the National Cancer Institute of Canada, the Medical Research Council, private foundations, and pharmaceutical companies. Then, panels of researchers and public representatives review them; and, if accepted, these projects must be carried out according to rigorous international standards.

"For every dollar that CCO invests in research infrastructure, our researchers bring in from funding agencies at least another $4 to $5," says Dr. Deeley. "I think that's a good return on CCO's investment."

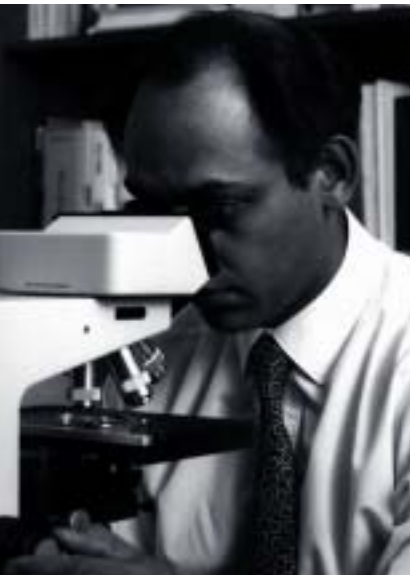
About $2.7-million in annual funding support from CCO also goes to provincial research networks,

groups, and programs, including the research section of the agency's Division of Preventive Oncology, the Ontario Clinical Oncology Group, the Radiation Oncology Research Unit, the Ontario Cancer Genetics Network, the Supportive Cancer Care Research Unit, and the Program in Evidence-Based Care.

CCO's Research Advisory Committee includes researchers from within the agency, outside researchers, and members of the community. The committee provides advice and direction on the future research activities of Cancer Care Ontario and monitors the overall quality of the research program. It also approves initial and renewal appointments, and promotion of career and clinician scientists.

CCO has an extremely high-quality research operation, according to Dr. Deeley. Many researchers have "exceptional international reputations, participate in scientific meetings around the world, and publish their findings in major peer-reviewed journals." They are involved in the full spectrum of research activities spanning all major forms of cancer.

Their studies focus on the causes and prevention of the disease, and new or improved treatments. CCO researchers explore how to best meet the physical, informational, emotional, social, and psychological needs of patients and their families. By analyzing the results of clinical trials and the effectiveness of standard treatments (outcomes research), the Program in Evidence-Based Care develops clinical practice guidelines for the care of cancer patients.



In laboratories across the province, molecular and cellular biologists, pharmacologists, biochemists, and their colleagues study tumour biology to determine the differences between normal cells and cancer cells. What triggers a normal cell to become malignant? Why are some types of cancer cells killed by anticancer drugs, while other cancer cells are resistant? Can tumours be starved to death by attacking the blood vessels that bring them nourishment to grow?

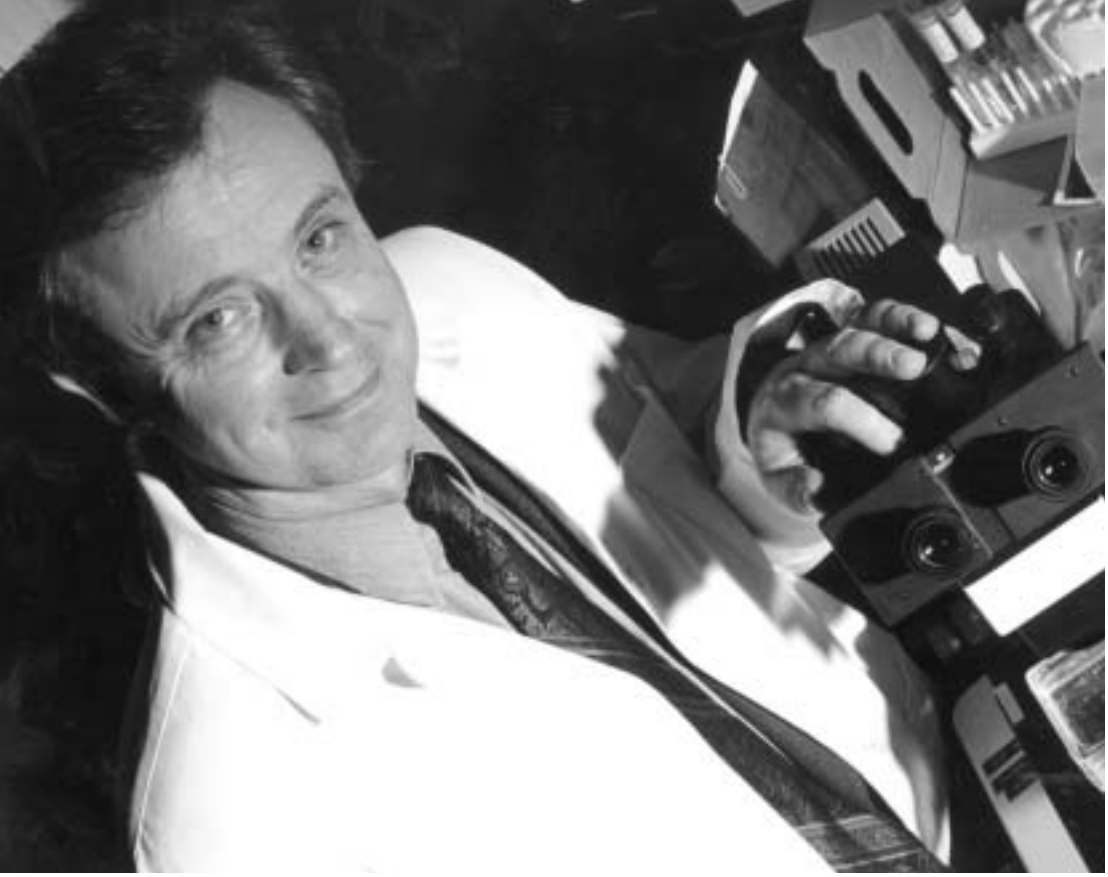
"We have strong research components in all these areas and more," explains Dr. Deeley. "Some of the most fundamental discoveries in the field of drug resistance have been made at CCO-funded research units *(see page 6)* and at Princess Margaret Hospital over the past 10 to 15 years."

Other areas of research interest include the way in which tumour cells respond to radiation and the mechanisms that can make the cells more resistant to this type of therapy. Medical physicists in the regional cancer centres are involved in research that improves the monitoring and delivery of radiation therapy. "We have a very good reputation for innovation in this area," adds Dr. Deeley.

> *"…we should change treatment only when the decision to change is based on solid evidence; and the only way to obtain that evidence is by some form of research activity."*

In the early 1990s, collaboration between a CCO scientist and a medical physicist in London gave the world its first real-time view of how cancer spreads. Using videomicroscopy, a powerful microscope connected to a videocamera and a television monitor, investigators discovered that several previously held beliefs about cancer metastasis (the spread of cancer to other organs or tissues) were inaccurate.

The Ontario Clinical Oncology Group (OCOG), formed in 1982 and headquartered in Hamilton, has developed a clinical trials network that includes the province's cancer centres and affiliated community oncology clinics. OCOG promotes clinical research and coordinates Ontario-wide clinical trials involving patients. Studies have included patients with breast, ovarian, prostate, and head and neck cancers, as well as brain tumours. OCOG provides cancer doctors with educational workshops on how to design and carry out clinical trials.



Dr. Roger Deeley is head, Division of Research for Cancer Care Ontario.

Cancer Care Ontario researchers also participate in a variety of large national and international clinical trials. A CCO researcher in Hamilton recently led a national trial that is having a major impact on the management of breast cancer around the world. The study showed that a new intensive chemotherapy regimen is more effective than standard chemotherapy in the treatment of women whose cancer has spread to their lymph nodes (stage II).

CCO's research philosophy involves extensive partnerships with other research and academic organizations. These include teaching hospitals and universities with health science programs. "What CCO has done very successfully in the past is to identify a specific area and try to support the establishment of research networks," says Dr. Deeley. The Ontario Cancer Genetics Network (OCGN) is an example of such a partnership among genetic investigators from several organizations. OCGN has gained international recognition for its studies into the causes, management, and prevention of inherited cancers, including ovarian, breast, and colon cancer, and has attracted substantial American funding from the National Institutes of Health.

CCO's Supportive Cancer Care Research Unit is evaluating the benefits of setting up supportive cancer care networks, involving organizations that provide support services to people with cancer and their families, in each of Cancer Care Ontario's eight regions across the province. A major new initiative planned to begin next year is a network that will enhance the interaction between basic and clinical researchers studying tumours in hormone-responsive organs (the breast, prostate, ovary, and endometrium). A research network to focus on causes of cancer in the environment and workplace is also being considered.

The quality and success of CCO research efforts are in part due to the fact that the agency maintains "exceptional research resources such as the Ontario Cancer Registry, which is among the best in the world," says Dr. Deeley. This registry is a computerized database of information on cases of cancer in Ontario. Information from it can be useful in many types of studies, such as the association between a certain type of cancer and risk factors such as diet, smoking, or sun exposure.

An inventory of all research projects under way at CCO is now being developed. Once complete, this information will be available to the public on the agency's Web site at www.cancercare.on.ca.

Cancer Care Ontario is also in discussion with the president of the Medical Research Council about the creation of a national institute of cancer research, one of a group of potential founding institutes to form the Canadian Institutes of Health Research (CIHR).

"Earlier this year in its budget announcement, the federal government gave a clear indication of its intention to proceed with a Canadian Institutes of Health Research, and announced budgetary provisions that would allow these institutes to be developed," explains Dr. Charles Hollenberg, CCO senior consultant. An interim governing council has been formed to set up CIHR and to advise on the legislation required to establish the organization. Plans call for this initial work to be completed by the fall of 1999.

Faster access to treatment

Since early spring, some Ontario patients with cancer have been offered the opportunity to go elsewhere in the province or to the United States for quicker access to radiation treatment. "This short-term measure was taken to help ensure that patients receive radiation within a medically acceptable time period," explains Dr. Tom McGowan, coordinator of Radiation Oncology for Cancer Care Ontario (CCO).

Recent increases in waiting times in the province are the result of a shortage in radiation professionals, who are "essential to the delivery of radiation therapy for people with cancer," says Dr. McGowan.

Travel, accommodation, and meal costs for all patients who participate in the re-referral program will be covered by CCO.

Patients who can travel without an escort, can live independently, and meet specific medical criteria are eligible to go to other cancer centres. They must be age 21 or over, and have no other major medical problems and no need for an interpreter. The wait for radiation at the cancer centre closest to home must exceed eight weeks, and patients cannot be primary caregivers for small children or disabled adults.

All patients are first assessed by an Ontario oncologist. Patients who are eligible and agree to be re-referred are put in contact with CCO's Central Re-Referral Office, where bookings are made for treatment, travel, and accommodation.

"Initially, some patients are being re-referred to the Northwestern Ontario Regional Cancer Centre in Thunder Bay. As treatment capacity in Ontario expands, we expect that other cancer centres will also be able to treat patients from outside their regions," says Dr. McGowan. "In addition, cancer centres in Buffalo, Detroit, and Cleveland were selected based on numerous criteria including quality of care, accessibility of accommodation, and reputation. Ontario radiation oncologists visited the U.S. centres, and quality assurance checks were done by CCO physicists." Supportive care — including support groups, and nutrition and social work services — is available for Ontario patients at the U.S. cancer centres. Additional American facilities may be used if needed.

Cancer Care Ontario and Princess Margaret Hospital are working with the provincial government to increase Ontario's radiation treatment capacity. "Incentives are being offered for radiation professionals to work longer hours, radiation professionals are being recruited from outside the province, and new and expanded training programs are being offered for radiation therapists and physicists," says Dr. McGowan. Radiation treatment capacity will also be increased through the expansion of some existing facilities and the development of new cancer centres in Oshawa, Mississauga, and Kitchener.

Adds Dr. McGowan, "We want to ensure that patients who need radiation treatment receive it as quickly as possible — now and in the future."

For more information, call 1 800 263-6750.

Dr. Tom McGowan is coordinator, Radiation Oncology for Cancer Care Ontario.

Dodging *the* bullet: How cancer

When Dr. Susan Cole realized she and her colleagues had identified a new gene that produces a protein which, when present in large amounts, arms cancer cells to resist attack by potent drugs, she knew they had hit the jackpot. It was 2 o'clock one morning in August 1991 when the results of a DNA sequence search made their way from a database in the United States back to her computer screen in Kingston. "It was like winning a lottery," says Dr. Cole, a Cancer Care Ontario senior scientist at the Kingston Regional Cancer Centre and a professor at Queen's University Cancer Research Laboratories.

For years, scientists worldwide have been trying to understand how and why some types of cancer become resistant to anticancer drugs. Cancer cells have the ability to mutate their genes faster than normal cells, and to become a rapidly moving and evasive target.

In 1976, Dr. Victor Ling, an investigator at the Ontario Cancer Institute/Princess Margaret Hospital, discovered p-glycoprotein — a protein that works as a pump to flush anticancer drugs away from some types of malignant cells, leaving the cancer free to grow and spread. "Everybody thought that if we could knock out p-glycoprotein, that would cure drug resistance," explains Dr. Cole.

Dr. Susan Cole and Dr. Ken-ichi Ito, a visiting postdoctoral fellow, examine a DNA sequence related to the MRP gene.

But when she and her team discovered the gene that produced the multidrug resistance protein (MRP), "that changed the thinking completely, and we realized that there was more than one major drug pump.

"You can imagine that a pump on the surface of the cell is like a gatekeeper," she continues. "If the pump is present, a lot less drug gets into the cell. If the drug does not get in, the cancer cell isn't going to die." Her research using human lung cancer cell lines showed that when a lot of MRP is produced in a cancer cell, it successfully pumps away natural-product drugs, a class of anticancer

drugs thought to be among the most useful.

Dr. Cole and colleague Dr. Roger Deeley published these findings in the prestigious journal *Science* in 1992. A landmark paper, it is cited often in other major journals. Drs. Cole and Deeley have supplied more than 120 research labs around the world with biological probes for further study of MRP-related drug resistance, mostly in clinical samples. Several pharmaceutical and biotechnology companies are exploring how to inactivate the MRP drug pump and how to correct or block the incorrect messages sent by the MRP gene.

fights drugs

In the mid-1990s, while continuing to work on MRP, Dr. Cole's team made another important discovery in the field of drug resistance. Using a lung cancer cell line that is free of the two major drug pumps, they discovered why anticancer drugs that make their way into some cancer cells are not killing them.

The team identified mutations in the topo II protein, which is essential for cell division. "If you take out topo II, the cell dies," explains Dr. Cole. "That makes it a very important drug target for cancer."

The job of the topo II protein is to travel from the cell's cytoplasm (the outer area of the cell) to the nucleus (the centre of the cell), and bind with DNA to allow cell division. When topo II does its job correctly, it forms a target that can be attacked by anticancer drugs, resulting in the death of a malignant cell. But the mutated form of topo II is missing part of its tail, which contains the signal to do its job; therefore, the mutant topo II remains in the cytoplasm. By staying there, it is out of range of the anticancer drugs and the tumour cell becomes drug-resistant.

By identifying the specific causes of drug resistance, Dr. Cole and her team are providing important information to researchers and to pharmaceutical and biotechnology companies. The hope is that their efforts will clear the path for anticancer drugs to be more effective.

Research:

Terry's dream in action

On the wall in Dr. Susan Cole's office is a photograph of Terry Fox running his Marathon of Hope. Down the hall in her main laboratory there's another picture of Terry, who on one real leg and one artificial leg delivered the message about cancer research to people around the world.

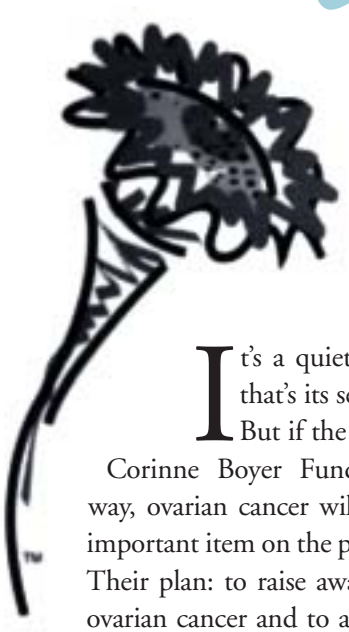
Susan Cole was a PhD student in 1980 when Terry Fox dipped his artificial leg into the Atlantic Ocean and vowed to raise $1 from each Canadian in support of cancer research. She was hooked – by cancer research and by Terry. "He's my hero," she says. "Terry understood that cancer research was important and expensive. He was a believer in research, and that's a statement of hope in the future."

Today, Dr. Cole is a leader in the field of research into drug resistance in cancer. Her work with Drs. Roger Deeley and Barbara Campling is partly financed by a National Cancer Institute of Canada grant with funds provided by The Terry Fox Foundation.

The annual Terry Fox Run has raised over $200-million worldwide in support of innovative cancer research.

The 19th annual Terry Fox Run will take place on September 19. For more information, call 1 888 836-9786 or check the Web site at www.terryfoxrun.org.

SHOUTING *back at the* disease *that* *whispers*



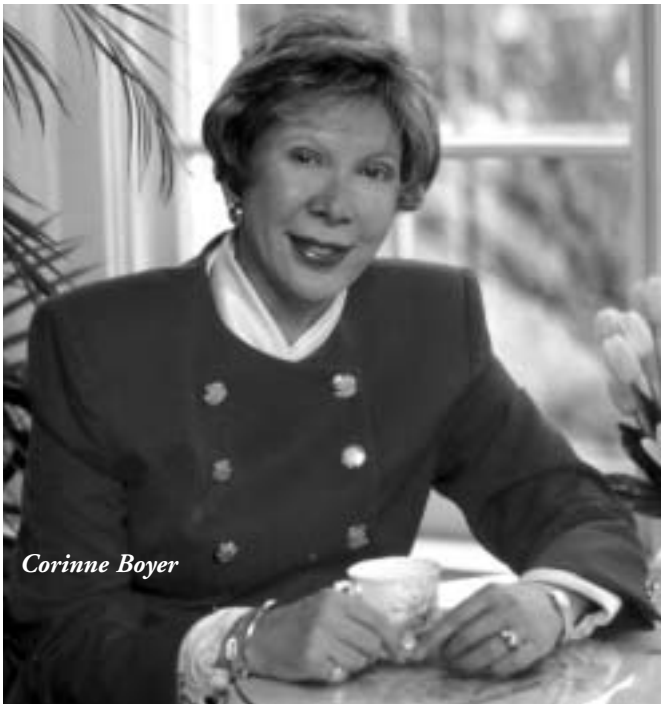
It's a quiet disease, and that's its secret weapon. But if the people at the Corinne Boyer Fund have their way, ovarian cancer will soon be an important item on the public agenda. Their plan: to raise awareness about ovarian cancer and to achieve breakthroughs in prevention, early detection, treatment, and supportive care for women affected by "the disease that whispers."

An action plan for ovarian cancer is being developed over the summer. It is the result of Ovarian Cancer Forum '99, a national meeting held this spring in Toronto with researchers, health care providers, and women living with the disease.

"Ovarian cancer is a disease with dismal survival rates that haven't improved in decades," says Elisabeth Ross, executive director of the Corinne Boyer Fund. "That's because its symptoms are so quiet and muddy that it doesn't usually get diagnosed until the disease is in its late stages."

"I'm one of the women with ovarian cancer who's lucky," adds Dianne Macfarlane, co-chair of the Corinne Boyer Fund. In 1995, at age 52, she was diagnosed with an early stage of the disease and was treated with surgery, radiation therapy, and chemotherapy. She remains healthy today. But in the last year, ovarian cancer has claimed the lives of five friends from her support group — "all magnificent women," she says.

In 1995, it also took the life of Corinne Boyer, whose husband Patrick — a former parliamentarian, a journalist, lawyer, and member of the Board of Cancer Care Ontario — founded the fund a year later in his wife's honour. For 17 years, Corinne Boyer lived with cancer — first, a malignant melanoma; later,



Corinne Boyer

Dianne Macfarlane, a survivor of ovarian cancer, is co-chair of the Corinne Boyer Fund.

breast cancer; and then, ovarian cancer. She worked diligently through the Genesis Foundation to raise awareness and funds for research into women's cancers.

When ovarian cancer is caught and treated early, the survival rate is 85 to 90 percent. But 60 to 70 percent of women diagnosed have late-stage disease and die within five years, which means that ovarian cancer has one of the highest death rates for any malignancy. About 2,500 Canadian women are diagnosed each year; 1,400 die annually. By focusing efforts around early detection of ovarian cancer, many lives could be saved.

Because the ovaries are buried deep in the abdomen, many health professionals and women living with ovarian cancer believe that a rectal–vaginal internal examination should be a part of every woman's annual physical. (A Pap test checks for cervical cancer, not ovarian cancer.)

> *"Ovarian cancer is a disease with dismal survival rates that haven't improved in decades."*

Symptoms of ovarian cancer include abdominal discomfort, painless swelling in the abdomen, loss of appetite, nausea, weight loss, frequent urination, and constipation. A woman who experiences any or some of these symptoms for more than two to three weeks should see her doctor. Women with symptoms or who are at increased risk of the disease can have a CA125 blood test and a transvaginal ultrasound. These tests are not specifically for ovarian cancer, but they can be helpful. Reliable screening tests for ovarian cancer are being sought.

Risk factors for ovarian cancer include a family history of the disease; a history of infertility; never having had children; early menstruation; a history of breast, endometrial, or colorectal cancer; late menopause; and obesity. Oral contraceptives taken for more than five years can reduce the incidence of ovarian cancer by 50 percent; with more than 10 years on the pill, the incidence drops another 25 percent. A diet low in total calories and fat is also recommended.

Educating women about these facts is just part of the role of the Corinne Boyer Fund. The organization recently provided $1-million to create an endowed chair in ovarian cancer research at the University of Ottawa's Faculty of Medicine. "Corinne's fight is now ours," says Patrick Boyer. "We will not give up until a breakthrough is achieved."

This spring, the fund also committed $120,000 for the first phase of a national tumour bank network to store tissue for research purposes. Other activities include the formation of a consumer action group; Lunch and Learn educational sessions, held in the workplace; developing a template for the organization of support groups across Canada; and linking women with ovarian cancer to support groups. A newsletter will also be launched this year.

Even those who did not know Corinne Boyer believe she would be pleased with the efforts of the organization that bears her name. "Corinne said, 'Go where there is no path, and leave a trail,'" quotes Elisabeth Ross. "I hope she would find that's what we're doing."

For further information, call (416) 971-9800, ext. 1321, or check the Web site at www.corinneboyerfund.org.

advances in radiation therapy

The first in a new generation of radiation treatment machines to be installed in Canada will be ready for use with patients this fall at the Toronto-Sunnybrook Regional Cancer Centre (T-SRCC). The PRIMUS linear accelerator is the first machine to integrate and automate the delivery of conformal therapy — a type of cancer treatment that targets radiation more precisely to the size and shape of a patient's tumour.

"As never before, we will be able to tailor the radiation dose and beam to where we want it to go, while protecting the surrounding healthy tissue that we don't want to treat," explains Dr. Gillian Thomas, head of Radiation Oncology at T-SRCC.

The machine is one of four PRIMUS linear accelerators by Siemens Oncology Systems to be installed at the Centre over the next 18 months at a total project cost of about $10-million. The PRIMUS is faster, quieter, runs cooler, and is smaller — "and should be less intimidating for patients" — than earlier-model linear accelerators, according to Sheila Robson, manager and head of Radiation Planning and Treatment Delivery.

A number of major equipment accessories to linear accelerators are used in the radiation treatment process and each normally has its own computer. "On the PRIMUS, these computers are integrated and only one computer controls the major accessories and the treatment machine itself," explains Peter O'Brien, chief physicist and head of the Department of Medical Physics.

The PRIMUS provides "the safest and most elegant way" to deliver intensity-modulated radiation therapy (IMRT), a sophisticated method used to create irregularly shaped treatment fields to match the three-dimensional tumour target, he adds.

To change the shape of the radiation beam when using conventional technology, a radiation therapist must lift and install heavy blocks of lead into the overhead part of the machine during the patient's treatment. With the PRIMUS, built-in, movable "fingers" automatically adjust the beam shape according to the patient's treatment plan.

A new data management system will link all linear accelerators in the Centre and will allow desktop access to patient treatment information.

The four new PRIMUS machines will replace four of the Centre's original treatment machines from the early 1980s, three of which are now out of service. Another three PRIMUS linear accelerators are on order for the new Windsor Regional Cancer Centre, which is scheduled to open in 2000. It is expected that all Ontario cancer centres will obtain the technology for conformal therapy from various suppliers as they replace equipment in the next few years.

Peter O'Brien (left), Sheila Robson (centre), and Dr. Gillian Thomas check installation progress on Canada's first PRIMUS linear accelerator.

Dr. Ken Shumak

Sharing knowledge about cancer

In March, Dr. Ken Shumak became president and chief executive officer of Cancer Care Ontario (CCO). He succeeds Dr. Charles Hollenberg, who retired from the position and remains as senior consultant. The former CEO of the Toronto-Sunnybrook Regional Cancer Centre and Cancer Care Ontario Central East Region, Dr. Shumak has had a distinguished academic career with the University of Toronto and its teaching hospitals. He has served as president of the Medical Council of Canada and the Canadian Hematology Society. Dr. Shumak chairs the National Blood Safety Council, which is responsible to the federal Minister of Health for the safety of the Canadian blood supply.

As I begin my term as president, I would like to pay tribute to the vision and leadership of Dr. Charles Hollenberg in establishing Cancer Care Ontario and directing the agency in its early years. Dr. Hollenberg ensured that the best interest of patients was always at the heart of decisions about cancer care. This commitment to meeting the needs of people with cancer and their families will remain our touchstone as we continue to build a coordinated cancer care system in Ontario.

Earlier this year, Dr. Hollenberg and I travelled across the province to meet with the eight Cancer Care Ontario Regional (CCOR) councils. They include people from organizations that provide cancer care, and community representatives who have had personal experience with the disease. I was very impressed with the progress CCORs have made in identifying regional needs and priorities, which varied greatly around the province. It was exciting to see such a high level of energy, enthusiasm, and commitment all focused to ensure that people with cancer receive high-quality care no matter where they live. I look forward to working closely with the CCORs in the coming years.

Cancer Care Ontario is made up of talented people with tremendous expertise in cancer prevention and early detection, treatment, research, and the supportive care services required by people with cancer. I believe that CCO should embrace as part of our central mission all opportunities to better share knowledge about cancer with patients and their families, members of the public, government, and health care colleagues. Using creative approaches, we can make significant progress in this area.

We are on the threshold of exciting developments in cancer research, which will result in major advances in the prevention, diagnosis, and treatment of cancer. CCO must be ready to adapt quickly to changes in the field of cancer care. By the fall, our Board and management team — in consultation with a range of stakeholders — will have completed work to refine Cancer Care Ontario's strategic plan. This plan will guide us into the new millennium as we strive to achieve our primary goal of reducing the growing burden of cancer for the people of Ontario.

"CCO must be ready to adapt quickly to changes in the field of cancer care."

On the Cover

Christine Ayoub: Look out, world!

If I had my way, my bag would be packed at all times — ready to see the world on a moment's notice. My experience with Hodgkin's disease, a cancer of the lymphatic system, brought out the wanderlust in me. It opened my eyes to what's really important: family, friends, and the amazing world we live in. I've been to the Middle East, New York City, and Acapulco, and I've just come back from Puerto Vallarta in Mexico. Next year, I hope to visit my aunt in Sydney and go to the first Olympic Games of the new millennium.

In 1996, when I was 22 and in university, I developed a swelling in the side of my neck, a dry cough that wouldn't go away, and night sweats. It was Hodgkin's and I was treated with chemotherapy at the Ottawa Regional Cancer Centre. My hair fell out in clumps and the chemo made me ill, but I didn't want to miss my cousin's wedding. So I bought a good synthetic wig and walked up the aisle with the rest of her wedding party. I got more compliments on my hair that day than I'd ever had before!

My cousin had already experienced Hodgkin's, and today we're both doing very well. Another close relative is now undergoing treatment. In the future, it will be interesting to see if researchers discover an inherited form of Hodgkin's disease.

"…Hodgkin's disease…opened my eyes to what's really important: family, friends, and the amazing world we live in."

Cancer Care Ontario

Cancer Care Ontario (CCO) is a government agency with a mandate to coordinate the province's cancer system. Eight Cancer Care Ontario Regional (CCOR) councils plan and coordinate regional cancer services. CCO is a leader in cancer prevention, screening, treatment, supportive care, research, and the development of treatment guidelines. The agency is the Ministry of Health's principal adviser on cancer issues, and also manages Ontario's eight regional cancer centres, the Ontario Breast Screening Program, the Ontario Cancer Genetics Network, and the Ontario Cancer Registry.

Cancer Care Spring/Summer 1999 Volume 3, Number 2

Cancer Care is a publication of Cancer Care Ontario.
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Ce magazine *Action Cancer* est disponible en français.

Printed on recycled and recyclable paper.