From the associate editor's desk

By Edward Chow, MBBS, MSc, FRCPC

Time passes quickly. This is the last issue of the calendar year 2004. The invasion of the severe acute respiratory syndrome (SARS) in Toronto last spring is still vividly remembered by health care professionals and patients. Many essential medical and surgical services were cancelled due to SARS. Dr. Lee and his colleagues examined the effect of SARS on access to palliative radiotherapy in Rapid Response Radiotherapy Program. Also in this issue, Dr. Vachon features “Reflections on the life and death of Mary Pocock”, Ms. Faith discusses “Quality end-of-life care: Role of economics and the moral climate”, and Dr. Hayter highlights “The Canadian Society for the History of Medicine”.

In the research column, Dr. Wu informs NCIC CTG study update – Re-irradiation of painful bone metastases (SC 20 & SC 20U).

Our insert was written by Dr. Maida on cannabinoids in medical practice.

We hope this newsletter continues to provide useful information to our readers.

The effect of SARS on access to palliative radiotherapy in the RRRP

By Justin Lee, MD, Lori Holden, BSc, RTT, Kinwah Fung, MSc, Cyril Danjoux, MD, DMRT, FRCP, Edward Chow, MBBS, MSc, FRCPC, and Carol Gillies, RTT, MSc

In March of 2003, the first probable case of severe acute respiratory syndrome (SARS) was reported in the city of Toronto. By July 2003, after the World Health Organization removed Toronto from the list of areas with recent transmission, there were 246 probable cases, 130 suspected cases and 44 deaths reported in Ontario. During this period, extensive precautions were undertaken in an attempt to prevent the spread of this disease.

The objectives of the current study were to identify any significant change in the number of patients seen and/or treated by the Rapid Response Radiotherapy Program (RRRP) at the Toronto Sunnybrook Regional Cancer Centre, and to evaluate the impact of the SARS epidemic on patient demographics, tumour characteristics, treatment preferences and waiting times compared with historical norms.

Treatment records of all patients referred to the RRRP from January to May 2002 and 2003 were reviewed. Patient demographics were collected including age, gender and primary cancer site. Reason for referral was classified as either metastases to bone, brain, spinal cord compression or others. Date of referral, consultation date and treatment start dates were recorded for all patients and intervals between dates were calculated. The radiation dose and number of fractions prescribed were evaluated for all patients who underwent palliative radiotherapy. Patients were stratified into four groups based on the date of their RRRP clinic visit. The period of interest was defined from March 20 to May 31, 2003 based on the peak incidence of SARS cases and increased hospital precautions. Comparisons were made to the same time period in 2002 for differences in referral pattern, patient demographics, treatment waiting times and radiation treatment prescriptions. Patients seen from January 1 to March 19, 2002 were evaluated as a control group and compared with those seen during the same period in 2003 to identify variations between the two years.

From January to May 2002 and 2003, a total of 676 evaluable patients were scheduled to attend the RRRP clinic.

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In this issue: The effect of SARS on access to palliative radiotherapy in the RRRP; Reflections on the life and death of Mary Pocock; Quality end-of-life care: Role of economics and the moral climate; Historical vignette; Research Corner.
Reflections on the life and death of Mary Pocock

By Mary L.S. Vachon, RN, PhD

Mary Pocock was diagnosed with breast cancer in her early forties and died September 2004, shortly after turning 52. I first met Mary when she was diagnosed with breast cancer and we maintained contact throughout her journey. For many years, Mary lived with metastatic disease. She dealt with her disease through meditation practices, yoga, art, journaling, spending time with others with cancer and those without the disease, humour, filming her experience, and growing deeper into her oneness with the universe and her connection with others. She published her reflections in The Pocock Diaries at http://www.keylight.org/pocock.htm.

Some of Mary’s art and writings on living with cancer were used in the chapter on the Emotional Care of the Dying Person in the Oxford Textbook of Palliative Medicine, 3rd edition, Doyle, D., Hanks, G., Cherny, N., & Calman, K. (Eds.). Oxford: Oxford University Press.

Some days I am just too busy struggling to consider the possibility of relief from suffering, from pain, from hopelessness, from fear.

Other days, when crises are but a distant memory, my mind is flooded with plans and images of walks in the park, being able to travel, getting a dog and other similar normal daily agendas.

But I warn you, my friend, there is nothing normal about being palliative.

So I await eagerly my miracle.

– Mary Pocock

A couple of years ago, Mary and a friend came to speak with me about palliative care options. I suggested that, since Mary was a patient at Princess Margaret Hospital, she visit the new unit that was being planned at PMH. Instead of signing up on a palliative care waiting list, she signed up to do the art on the unit and produced large transparencies of nature scenes for each of the windows on the unit.

On her first admission to the PMH PCU, Mary was frightened and thought she was going to die. She awakened that first night and was able to enter into her scene on the window of her room. She saw the angels there and felt she was being cared for and watched over. Realizing how much comfort this image gave her, she was able to realize how much comfort it would give to others – indeed she received feedback about the importance of her windows to other patients as well as to staff.

She wrote in The Pocock Diaries:

Since my hospital stay, my palliative status has been jimmied up a notch. My lungs have many tumours and I am on oxygen about five hours a day now. I call my oxygen generator O2/D2. It looks like a robot – too bad it can’t vacuum. My mind states fluctuate between worrying that I am dying to feeling fine and thinking I am on the mend. Then I come back to the present moment, accept what is and live my day. This is a difficult task; not getting caught up in mind states and emotion.

As Mary’s illness progressed, she dealt with the issues that she needed to address. Drawing on the Buddhist image of the lotus, we explored the fact that sometimes the issues we thought were resolved needed to be resolved in a deeper way, for the petals to open up. We spoke of Kathleen Dowling Singh’s book The Grace of Dying, which she really liked, and of how the process from surrender to transcendence was not an easy one. Mary reminded me of the fact that the lotus has its roots in the “muck” in order to develop in the presence of the sun. She listened to Ann Mortife’s songs, “This Is a Healing Journey” and spoke of the poignancy of Ann’s song “I Always Thought I’d Have Tomorrow”.

The day before she died, Mary spoke of a dream she had one or two nights before. She had received permission from the City of Toronto to put up a Cirque de Soleil tent in Trinity Bellwoods Park across the street from her apartment. She had permission to live there until she died. In the tent, people could come and go. There was a clown with a dog, there were Centring prayers for the Christians and prayers for the Buddhists. Mary was teaching dharma and had a spot to meditate in the corner. The film she had been doing with Michael Mitchell was playing in the background and she was being filmed by CBC on having fun while you are dying.

Mary was awakened by a Code Red in her hospital room the night of her death. This allowed her to have a conscious death with her husband Marcus. She was able to write to him that she felt loved and cared for. This had been her goal in dealing with her illness. Her friend Drolma, a Buddhist nun, was reading and chanting to her as she died and said that her rapid breathing became normal and she breathed her last just as the most sacred passage was being read.

Mary wrote this poem to be read at her funeral:

Live for me.
Laugh for me.
Do good and give to the world for me.
Grow for me.
Share for me.
Mourn for me.

But let your own spirit fill again
With friends, family and new laughter.
Or I’ll come down and kick your ass
As a gopher or horned owl - ha ha.

(some people at the funeral saw a baby skunk parade across the window outside the funeral home just as the gopher was mentioned).

Mary wrote this poem to be read at her funeral.

Mary Pocock (www.keylight.org)

Mary Vachon, RN, PhD, is a psychotherapist in private practice. She can be reached at maryvachon@sympatico.ca.
Quality end-of-life care: Role of economics and the moral climate

By Karen Faith, MEd, MSc, RSW

Health care professionals who provide care to dying patients will, at times, face the dilemma of how to respond to patient needs while upholding professional duties, facing financial constraints as well as complex work environments. According to the ethic of care, the most salient moral duty involves responding to the needs of patients within a context of sustained, caring relationships. Ideals inherent in the ethic of care are found in the values and mission statements of most, if not all, health care settings. We know that these same values have motivated good people to become doctors, nurses and allied health professionals. Is it getting harder for health care professionals to uphold these values when providing care at end of life?

One recent international consensus conference concluded that there is a problem in providing optimal end-of-life care in intensive care settings. The authors identified that optimal care at end of life must include effective pain management without hastening or postponing death, must affirm life and regard death as a normal process, should integrate the patient’s psychosocial and spiritual interests, and offer a system of support to both patients and families throughout the process of dying, loss and bereavement. All of these attributes are predicated on establishing effective means of communication, fostering mutual understanding in order to sustain meaningful therapeutic relationships.

I suggest that quality end-of-life care, consistent with the values of the ethic of care, requires continued attention to organizational ethics as well as the moral climate of health care settings. Organizational ethics involves the intentional use of values to guide the decisions of a system. The moral climate of a health care setting has much to do with how well organizational decisions, treatment of staff and patients, measure up to recognizable values or ideals.

At the bedside, the moral significance of sustaining caring relationships with dying patients and their families is widely accepted. However, it is enormously important that multidisciplinary teams work within a moral climate conducive to patient-centred values. Key to maintaining a positive moral climate is having adequate resources including personnel while demonstrating interdependence and mutual respect within a well-functioning multidisciplinary team. Although identified organizational values are important, it is how decisions are made, how staff and patients are treated that set the moral tone of a caring environment.

At this time, health care institutions are facing enormous fiscal challenges and complex political, demographic and economic influences. From the bedside to the boardroom, care providers must be responsible stewards of limited resources. A likely ethical challenge that managers and administrators face involves how to ensure that economic concerns don’t obscure their moral compasses, steering decisions away from reflecting those values central to providing quality patient care. Maintaining an ethical framework for decision-making and reflecting back to institutional core values pertaining to patient care (thus end-of-life care) are essential to staying on course through choppy “fiscal” waters.

Karen Faith is a Clinical Ethicist at Sunnybrook and Women’s College Health Sciences Centre.

The Canadian Society for the History of Medicine

By Charles Hayter, MA, MD, FRCPC

The series of historical vignettes previously published in Hot Spot may have interested you in medical history, a fascinating scholarly discipline which draws together medical, biographical, cultural, and historical knowledge. How do you become involved in medical history? A good place to start is Professor Jackie Duffin’s lively and stimulating book, History of Medicine: A Scandalously Short Introduction (Toronto, University of Toronto Press: 1999). Duffin shows that history is not really about unravelling the historical threads of the present.

Another excellent resource is the Canadian Society for the History of Medicine which was founded in Quebec City in 1950 and currently has approximately 300 members. The purpose of the Society is to promote study, research, and communication concerning the history of medicine which embraces all of health care, and related disciplines. The Society seeks to serve all those interested in the general area of its concern.

Since 1976, annual conferences have been held in conjunction with the Congress of the Social Sciences and Humanities. The meeting is a unique opportunity for specialists and amateurs of medical history, including historians, physicians, nurses, librarians and archivists, to communicate the results of their research. The program is the result of a peer-review process. The next meeting will be held at the University of Western Ontario from June 3-5, 2005.

Since 1984, the official organ is the Canadian Bulletin of Medical History/Bulletin canadien d’histoire de la médecine, a bilingual, peer-reviewed journal, published twice yearly by Wilfrid Laurier University Press.

Further information about the Society can be found at its website: http://meds.queensu.ca/medicine/histm/cshmweb/cshmhome.html
NCIC CTG study update – Re-irradiation of painful bone metastases (SC 20 & SC 20U)

This is a study suitable for patients who had previously received palliative radiation for bone pain, and are now experiencing persistence or recurrence of bone pain in the same area.

We strongly advocate patient participation in this study. Patients should be made aware of the possibility and probable benefit of repeat irradiation for bone pain. We will need much support from our Canadian colleagues in oncology, palliative services, and family practice to continue the study for the next three years.

The target accrual rate is 150 to 200 patients per year. So far, over the last eight months, 40 patients have been accrued from several Canadian and Australian centres.

Although participation from the United Kingdom and the Netherlands is imminent (awaiting institutional ethics approval), accrual rate in Canada and abroad must increase dramatically over the next 12 months to keep the trial active.

A companion study, SC 20U (for urinary markers), is open to SC 20 patients. This substudy aims to explore potential relationship between urinary markers of bone turnover (osteoclast activity) and the rate of pain response to radiation. If such relationship exists, it may be possible in the future to better personalize treatment schedules during any of the four intervals analyzed.

Waiting times

Intervals between referral, consultation and treatment dates were calculated for all evaluable patients. There was a significant decrease in the total waiting times of patients seen during the SARS epidemic (median = six days) when compared with the previous year (median = 15 days). The total waiting time comprises the time from referral to consultation, and consultation to treatment. During the SARS epidemic, the median time from referral to consultation decreased from 12 to five days and the median time from consultation to treatment decreased from three to 0 days.

The impact of SARS on critical cancer services such as breast biopsies, chemotherapy and lumpectomy/mastectomy has been assessed in the Greater Toronto Area by the Institute for Clinical Evaluative Sciences. The number of patients accessing these services decreased in April and May of 2003 compared to the same time period in 2002. The decreases ranged from 6% in lumpectomy/mastectomy patients (May 2003) to 27% in the number of breast biopsies (April 2003). We observed a similar decrease in the number of patients seen at the RRRP (22%) and the number of patients receiving palliative RT (12%). There are multiple causes for decreased patient access to palliative radiotherapy during the SARS outbreak. The decrease in the number of patients seen is largely attributable to less follow-up patients attending clinic, with a 67% decrease during the period of interest compared with the previous year. Access to palliative radiotherapy may have been affected by patient and physician perception of the cancer centre, which is associated organizationally and geographically with Sunnybrook and Women’s College Health Sciences Centre, a tertiary centre that was associated with multiple probable cases of SARS. The reason for referral was most often bone metastases and treatment schedules employed multiple fractions; this did not change significantly during the period of peak SARS incidence. Given the increasing evidence demonstrating equivalent pain response for uncomplicated bone metastases, one strategy to decrease patient transfers and visits during future infectious disease outbreaks may be more frequent utilization of single fraction radiation treatments.

Effect of SARS - continued from page 1...

Five hundred patients were treated with palliative radiotherapy (RT). Multiple comparisons between all four groups showed no significant difference in the number of patients receiving RT, the number of missed appointments or the age of patients. There was a significant decrease in the proportion of follow-up visits during the period of SARS incidence when compared with the previous year (p<0.0001), but there was also a significant inter-annual difference between January 1 to March 19, 2003 compared with the same period in 2002.

Tumour characteristics

Bony metastases were the most common reason for referral, representing 42% of all visits for palliative RT. During the period of interest, 56 of 138 patients (41%) were referred for bone metastases comparable to 72 of 176 patients (41%) in the previous year. Our study found no significant difference in the number of patients with regards to primary site of disease nor in the proportion of patients treated for spinal cord compression between the four groups.

Treatment characteristics

Fractionation schedules were grouped into short (one to three fractions), intermediate (four to nine fractions) and long courses (10 fractions or more). Intermediate courses of radiotherapy (usually 2000cGy in five fractions) were the most common fractionation schedule, prescribed to 280 of 500 (56%) of all treated patients. During the SARS epidemic, short fractionation schedules (usually 800cGy in one fraction) were employed in 37 of 110 patients (34%) treated. During the same period in the previous year, 42 of 125 patients (34%) underwent short courses of radiotherapy.

There was no significant difference in treatment schedules during any of the four intervals analyzed.

The newsletter of the Rapid Response Radiotherapy Program of Toronto Sunnybrook Regional Cancer Centre is published through the support of:

Abbott Laboratories, Ltd
AstraZeneca
Amgen
Aventis
Boehringer Ingelheim
GlaxoSmithKline
Ortho Biotech
Purdue Pharma
Solvay
Valeant Canada
VitalAire
Cannabinoids in medical practice

The cannabinoids

- The term “cannabinoid” is a collective expression that refers to a class of chemical compounds that are classified as tricyclic dibenzopyrans. The most prevalent and most potent cannabinoid is Delta 9-THC.

- There are three main types of cannabinoids:
  - Phytocannabinoids derived from botanical sources: cannabis (marijuana, hashish) = “medical marijuana”
  - Pharmaceutical cannabinoids: Dronabinol and Nabilone
  - Endogenous cannabinoids: Anandamide, 2AG, and PEA

- The overall clinical efficacy of cannabinoids increases with upward dose titration. However, this remains challenging as a result of side effects.

- Tolerance to side effects develops rapidly, usually within seven to 10 days. Younger patients and those with prior exposure to cannabinoids tend to have more tolerance to side effects.

Medical marijuana

- Medical marijuana refers to the use of smoked marijuana for medical indications. It can be obtained through Canadian government-sanctioned “Marijuana Medical Access Regulations (MMARs)” under three categories.

- The MMARs are currently undergoing reform. However, the CMPA, CMA, and CPSO are generally not supportive of the use of medical marijuana.

- Smoked marijuana has been demonstrated to reduce local broncho-alveolar immunity. It is also associated with all the risks associated with tobacco smoking, and perhaps more so, since it generates fivefold more tar than tobacco.

- Therapeutically, medical marijuana may have advantages in its more rapid onset of action, ease of dose titration, and broader spectrum of cannabinoid activity as it delivers more than 60 different cannabinoids.

- Smoked marijuana has definite dependency and addictive potential. This has not been definitively demonstrated with pharmaceutical cannabinoids.

The science of cannabinoids

- Cannabinoid receptors are ubiquitous in the human body. In fact, there are tenfold more cannabinoid receptors than opioid receptors in the human body. To date, two types of receptors have been identified and cloned: CB1 and CB2.

- Cannabinoid CB1 agonism is thought to be involved in neuromodulation and to alter neurotransmission through the following processes:
  - inhibition of P/Q type calcium channels
  - activation of potassium channels
  - inhibition of adenylyl cyclase
  - activation of mitogen activated protein kinase (MAP).

- CB1 receptors are present within the CNS (especially in the basal ganglia, hippocampus, cerebral cortex, and cerebellum), peripheral nerves, and nociceptors.

- CB2 receptors are present within lymphoid tissue such as spleen, tonsils, lymph nodes, as well as mast cells, lymphocytes, and macrophages.

Emerging medical indications

- Antineoplastic-animal models demonstrate inhibition of primary tumour growth and increased survival

- Anti-inflammatory/immunosuppressive

- Anti-glaucoma

- Neuroprotective
  - Parkinson’s disease
  - Alzheimer’s disease
  - CNS trauma

- Anti-dystonic
  - Huntington’s disease
  - Benign essential blepharospasm
  - Tourette’s disease

- Antispasmodic
  - Multiple sclerosis
  - Bladder hyper-reflexia

- Bronchodilator

Potential roles in oncology and palliative care

- Nausea and vomiting
- Analgesia
- Anorexia-cachexia
- Antispasmodic
- Sedative
- Antipyretic
- Antipruritus
- Anti-hiccough
Cannabinoids in medical practice

Cannabinoids in nausea/vomiting management

Nausea and vomiting occurs in 40 to 70% of patients with advanced cancer. Despite the advent of novel agents that include the 5-HT3 antagonists, the incidence and severity has not improved over the past two decades.

There are numerous etiologies that include:
- Iatrogenic
- Chemotherapy
- XRT
- Opioids
- Toxic
- Liver + renal failure
- Tumour products
- Hypercalcemia
- Visceral
- Gastric stasis
- Bowel obstruction
- Mesenteric metastases
- Autonomic failure
- Raised ICP

Opioids remain a leading cause of nausea/vomiting as they are a major cause of gastroparesis and constipation.

The best available literature considers the known antiemetics only in the context of chemotherapy. In this setting, cannabinoids have been found to be superior to Prochlorperazine, Metoclopramide, Haloperidol and Domperidone. Furthermore, cannabinoids were favoured by patients over other agents for future chemo sessions.

Although the mechanisms through which cannabinoids exert their antiemetic effect remain unclear, it is thought that they do so through pathways other than those mediated via serotonin, dopamine, and histamine. As such, they may be regarded as useful adjuvants.

Cannabinoids in chronic pain

- 30% of Canadians suffer from chronic pain and up to 50% of cancer patients have poorly controlled pain.
- Cannabinoids exert analgesia through the following mechanisms:
  - VR1 agonism
  - Decreased peripheral kinin release (via CB2)
  - Retrograde afferent blockade (via CB1)
  - Potentiation/synergy with opioids
  - Potentiation/synergy with alpha-2 adrenergic agonists
  - Antagonism of nerve growth factor (NGF)
  - Indirect effects via sedation/distraction/affective mechanisms
  - Enhanced descending inhibition via PAG of midbrain
  - COX-2 > COX-1 inhibition
  - Reduction of hyperalgesia
- Cannabinoids are demonstrating particular efficacy in the management of neuropathic pain syndromes, especially:
  - Painful peripheral neuropathies
  - Sympathetically maintained neuropathic pains
    - Phantom pain syndrome
    - CRPS I & CRPS II
  - Central neuropathic pain states
- Cannabinoids appear to be less effective in nociceptive pain. Cannabinoids are not effective in the management of post-operative pain.

Exercise caution when using cannabinoids in the following:

- History of psychosis
- Hepatic insufficiency
- Hypotension and CAD (may cause hypotension and reflex tachycardia)
- Concomitant use with:
  - Benzodiazepines (potentiated sedation)
  - Barbiturates
  - Alcohol
  - Fluvoxamine (2C9, 2C19, 3A4 inhibition)
  - Paroxetine (2C9, 2C19 inhibition)
  - Amiodarone (2C9, 3A4 inhibition)

Conclusions

- Cannabinoids are an exciting, albeit controversial, class of chemical compounds.
- The “evidence base” supporting cannabinoid clinical efficacy is rapidly accumulating for a number of clinical indications.
- Cannabinoids have a broad spectrum of activity that may benefit oncology patients, especially those suffering from multiple troublesome symptoms.
- Current drugs of choice for pain, nausea, anorexia, and seizures remain ineffective in 20 to 30% of cases. It therefore indicates the need to provide our patients with empiric trials of emerging drugs such as cannabinoids.
- Although it is unlikely that they will emerge as first-line agents, they may serve as useful and effective adjuvants, operating through novel mechanisms, in such clinical contexts.

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Supported by an educational grant from Solvay Pharma