HOT SPOT

From the associate editor's desk

By Dr. Edward Chow, MBBS, MSc, FRCPC

We are pleased to inform you that the Rapid Response Radiotherapy Program has a new staff member joining us.

Dr. Toni Barnes is an Edmonton-trained radiation oncologist who has spent one year of fellowship in palliative medicine with Dr. E. Bruera at the M.D. Anderson Cancer Center. She will help bridge the connection between oncology and palliative care. She has written an article about palliative care at the University of Texas M.D. Anderson Cancer Center for this issue.

Our associate editor, Ms. Lou Andersson, has been awarded a prestigious award with her oncology nurse association. Dr. Danjoux has highlighted her significant contributions in cancer nursing in Canada.

In our insert, Dr. Richard Choo has updated us on the latest advances in neoadjuvant and adjuvant treatment of prostate cancer.

Other topics in this current issue include *"Palliative care is not euthanasia"* by Dr. Monica Branigan; Part II of Mary Vachon's *"Transformation from tragedy into grace in terminal illness"*, *"Charles Huggins: The Canadian who discovered hormone therapy for prostate cancer"* by Dr. Charles Hayter, and *"Evidence-based medicine: Are you practising it?"* by Dr. Rebecca Wong. We hope you continue to find **Hot Spot** a useful resource.

Dr. Toni Barnes

Palliative care is not euthanasia

By Monica Branigan, MD, MHSc

The recent release of *"Consensus Guidelines on Analgesia and Sedation in Dying Intensive Care Unit Patients"* has contributed to the distinction between palliative care and euthanasia. Laura Hawryluck, William Harvey, Louise Lemieux-Charles and Peter Singer from University of Toronto authored the study that sought the consensus of critical care specialists and coroners to help intensivists provide better end-of-life care. Although developed for the ICU, the guidelines may also provide some clarity for clinicians providing palliative care in other settings.

The guidelines state, "The intent of the physician administering narcotics and sedatives to the dying patient is the most crucial distinction between palliative care and assisted death (euthanasia/assisted suicide)." This statement is supported by the principle of double effect. Double effect recognizes that, although the intention of the physician is to relieve suffering, the use of narcotics and sedatives may foreseeably hasten death. The paper discusses that intent is not always completely discernable, but that certain documentation is likely to reflect the intent to relieve suffering in a dying patient. This includes:

1. the patient's medical condition and reasons for palliative care
2. the goal of care
3. how pain and suffering will be assessed
4. how drugs will be increased and why.

Intention is also shown in the selection of medication – medication without palliative intent is not selected, such as KCL or paralyzing agents.

The importance of individualized care of the patient to achieve palliative goals is emphasized. This is reflected in three guidelines. Factors to be considered in initial dosing are suggested: previous narcotic exposure, age, previous

continued on page 2...

HOT SPOT

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The transformation from tragedy into grace in terminal illness – part two

By Mary L.S. Vachon, RN, PhD

In the last issue of **Hot Spot,** we discussed the phase of *Chaos* from Kathleen Dowling Singh's book, **The Grace in Dying: How We Are Transformed Spiritually as We Die** (Harper San Francisco, 1998). *Surrender* and *Transcendence* will be discussed in this article.

"What happens from the time one hears a terminal diagnosis to the moment one surrenders to it, is suffering - the very essence of tragedy". In Singh's paradigm, the shift from chaos to surrender is the transformation from tragedy into grace. During this transformative process, there are profound changes in the quality of hope. "Hope in its previously known form (i.e. hope for the continuation of one's existence) is washed away like the dissolving letters of a prayer written on a beach. During the ups and downs of the ordeal of terminal illness, it is hard to say whether hope is taken away or hope is given up. Hope itself becomes difficult. The person is torn between the desire to live and the fear that allowing hope to emerge one more time would only create more misery if the treatment fails again".

"The movement into the present brings changes in identity, changes in levels of consciousness known and experienced. Arising at the same time come changes in meaning. Meaning is a powerful psychodynamic in the transformation from tragedy to grace. Meaning is the attribution of a purposeful construct to the suffering experienced. It is an important aspect of personhood... *Our ability to intuit meaning that has value, depth, and reality is related to the ease of our transformation".*

Acceptance is a cognitive stance, spiritually the transformation in consciousness begins in earnest only after the stage of acceptance begins. "*Acceptance is, in some senses, an ingathering of the attention that is the key to all transformative processes, in preparation for the arduous passage that follows"*. Acceptance involves a last look backward, as well as a last look forward, in preparation for the present-centred groundedness of *Surrender*. Acceptance is a moment of calm in the psychospiritual process of dying. "There is, however, much hidden and interior movement, subterranean upheaval, and inner conversion about to take place behind this facade. This is the movement towards Surrender… It proceeds in feeling states that weave in and out of each other kaleidoscopically, chaotically, uniquely for each of us".

As the pretence about prognosis ends, acceptance arises and opens the way to the naked experience of our alienation. "We have cut ourselves off from our self, from others, and from Spirit. With mortality breathing down our necks, we begin to become aware of our myopic focus. Our attention shifts. This state of alienation becomes, in the dying process, painfully uncovered and revealed". This is an essential component of the experience of suffering in terminal illness.

In the terminal phase of illness, the self becomes increasingly conscious of its own disconnection from Spirit which it is beginning to intuit and encounter. Whether or not people have been religious or spiritual at other points in their lives, an experience with life-threatening illness will often lead to their exploring these issues.

Mary Pocock, an artist in her 40s, wrote of her experience which can be conceptualized as going from Chaos, to Surrender and into Transcendence. She wrote this in 2001 and is still actively living today:

When I heard my diagnosis several years ago, my logical mind could not bend around my inevitable demise - in three to five years - treatment options - that will make you very ill - and the ravages and statistics of my two kinds of invasive cancer.

I sit here eight years later, wondering how and why I have survived. The cancer has spread to my bones, lungs and possibly heart sac. I have a low grade pain in my spine and my present treatment gives constant fatigue and nausea. I am happy to be alive and in the same breath contemplate how to bring contentment into an unknown future, bringing with it the probability of worsening pain and organ breakdown.

My quality of life has worsened the past few years. I am often short of breath and dog-tired, as they say. I eat not from hunger, but to quell nausea. And yet, ironically, I am much happier these days. I feel it is my meditation on this forced pilgrimage which has allowed joy to rise in the midst of difficult circumstances.

Singh speaks of the period of *Surrender* into *Transcendence* as being a stage in which the individual can rest in the "natural great peace". In this phase, people frequently report seeing visions of spiritual figures, family members, or friends who have died. These visions may or may not be congruent with their previous belief systems. On the day before he died, a Jewish atheist with no belief in an afterlife found himself going back and forth between his hospital room and an incredibly beautiful garden. He said, "I don't believe in anything beyond this life, but it looks like I am going there".

Mary Vachon, RN, PhD, is a psychotherapist in private practice. She can be reached at maryvachon@sympatico.ca.

Palliative care, continued from page 1...

drug/alcohol use/abuse, underlying illness, underlying organ dysfunction, current level of consciousness, level of availability of psychological/spiritual support and patient's wishes regarding sedation. Reasons for titration up include: patient request, signs of respiratory distress, physiological signs, facial grimacing/tearing/vocalization and restlessness. Finally, no maximum dose of narcotics or sedatives exists. Thus, a clinician needs to find the dose of drug that will relieve suffering in each patient. An arbitrary limit may cause clinicians to undertreat patients, for fear of litigation.

These guidelines are consistent with the recommendations of the Chief Coroner of Ontario, which were not specifically formulated for use in the ICU. They are also consistent with 1998 CMA policy on euthanasia and assisted suicide: "Euthanasia and assisted suicide must…. be distinguished from withholding or withdrawal of inappropriate, futile or unwanted medical treatment or the provision of compassionate palliative care, even when these practices shorten life." The main way to distinguish, according to the consensus guidelines, is through the specific documentation of intent. The authors acknowledge, however, that the line between euthanasia and palliative care "may never be crystal clear." As clinicians, we can strive to have our intention to provide the best palliative care be crystal clear to our patients and families through our actions, our words, and our caring.

For complete report, see www.collinsassoc.ca/jcb.htm.

Palliative care at the University of Texas M.D. Anderson Cancer Center

By Toni Barnes, MD, FRCPC

I have recently joined the radiation oncology department at Toronto Sunnybrook Regional Cancer Centre, having completed a one-year clinical fellowship in palliative care at the University of Texas M.D. Anderson Cancer Center in Houston, Texas, following my radiation oncology residency in Edmonton.

The development of formal palliative care programs has been slower in the United States than in Canada or Europe. Traditionally in the United States, when patients have exhausted active curative or palliative treatment options, they are referred to hospice. Medicare hospice benefit provides 100% coverage for elderly terminally ill patients, and provides care mainly in the home setting. Radiation therapy or blood transfusions are rarely offered due to the financial constraints of the hospice (per diem allowance of $100/patient). Care is mainly delivered by nurse specialists with little physician involvement. Now, with the establishment of palliative care programs in comprehensive cancer centres, the goal is to integrate symptom management earlier into the course of the patients' disease, and to bridge the gap between active cancer therapy and community hospice programs.

M.D. Anderson is one of the 37 comprehensive cancer centres in the United States, and is considered one of the largest cancer centres in the world. In July 1999 the palliative care department was founded, providing inpatient and outpatient consultations. An acute inpatient palliative care unit opened in February 2002, allowing intensive symptom management for patients with advanced disease.

When I started work at M.D. Anderson, I found the size of the hospital overwhelming, with over 500 inpatient beds and 3,200 outpatient visits daily. I had received all my training up to this point in Canada, where we traditionally are more conservative in our therapeutic management. Therefore, I was amazed at what I perceived as quite aggressive cancer treatment, with patients receiving multiple lines of chemotherapy for metastatic disease, and many patients operated on for certain locally advanced and metastatic conditions. This must be qualified by saying that I am trained in radiation as opposed to medical or surgical oncology, and the patients I saw as inpatient consultations were under the care of these specialists, as radiation oncologists in the United States generally do not admit patients.

With respect to palliative radiotherapy, I felt this may be underutilized, as physician preference seemed to be with the administration of systemic therapy. When patients received radiotherapy, protracted fractionation regimes were generally used. For example, bone metastases were treated over a two-week period rather than in a single day (as is commonly done in Canada and Europe). This discrepancy has been previously reported in the medical literature.

People seeking treatment at one of the best cancer hospitals in the world, where the motto is "Making Cancer History" do not readily accept the news that they have incurable disease. It was therefore very challenging to help patients accept their prognosis, and to replace their hope for cure with that of optimizing quality of life. It was a great opportunity and learning experience to study with one of the leaders of palliative care, in one of the most prestigious cancer centres in the world, and to work in the American health care system. I look forward to applying the knowledge I have gained during this year to my radiation oncology practice in Canada.

Historical Vignette:

Charles Huggins: The Canadian who discovered hormone therapy for prostate cancer

By Charles Hayter, MA, MD, FRCPC,

The insert in this edition of **Hot Spot** describes the hormonal treatment of advanced prostate cancer. It is often forgotten that the discovery that led to this treatment was made by a Canadian, Charles Brenton Huggins, born in Halifax, Nova Scotia, in 1901. Huggins was educated at Acadia University and at the Harvard Medical School, where he graduated with an MD in 1924. After graduate training, he went to the University of Chicago where he had a prolific career as a surgeon and cancer researcher.

In 1939, Huggins made a very simple observation that altered the therapy of advanced prostate cancer forever. Following experiments with dogs, he noted that the prostate gland was under the control of androgens (male sex hormones) and concluded that preventing the production of androgens might control prostate cancer. This could be accomplished either through removal of the testicles (surgical castration) or by the administration of female sex hormones to neutralize the effect of androgens produced by the testicles. In 1941, he began to inject his prostate cancer patients with the hormones stilbestrol and hexestrol, and, in a landmark article co-authored with C.V. Hodges, he was able to report that of the first 20 patients treated, four were still alive after 12 years. Later workers, inspired by Huggins's work, treated women suffering from cancer of the breast with the male hormone testosterone and claimed improvement in some 20% of the cases.

As the insert describes, nowadays men with prostate cancer are treated with newer, safer agents that do not have the side effects of female sex hormones, but the principles of androgen deprivation as outlined by Huggins are the same. In recognition of his pioneering work, Huggins received the 1966 Nobel Prize for Physiology or Medicine.

Left, Dr. C. Huggins

Research Corner

By Rebecca Wong, MB, ChB, MSc, FRCPC

Evidence-based medicine: Are you practising it?

Although the term 'evidence-based medicine' (EBM) is relatively new, being first coined in 1992 by a group led by Gordon Guyatt at McMaster University, the fundamental principles can be traced back to the nineteenth century. For the most part, we all practise EBM, perhaps to a variable extent, depending on clinical context, individual expertise and commitment to this process. The term EBM, for the uninitiated, may imply many new rules and skills that are threatening the art of medicine, when, in fact, EBM is enunciated in order to complement and facilitate it.

Definition

EBM can be defined as the integration of our clinical expertise and our patients' values with the best available research evidence.

In order to decide whether you are practising EBM, think of a clinical question you have asked yourself today, and answer the following checklist:
Did I:

- ❑ 1. Define an answerable question
- ❑ 2. Search the best evidence
- ❑ 3. Critically appraise the literature
- ❑ 4. Integrate the evidence with the unique circumstances of the patient
- ❑ 5. Evaluate our effectiveness in conducting 1-4

So what do we mean by an answerable question?

This is one that 'specifies' in terms of patient population, intervention, outcomes, and clinical setting narrowly enough to allow the question to be answered without making inappropriate generalizations, but not so narrowed that it ignores reasonable generalizations. An example could be: "What is the effectiveness of *pamidronate* in the *relief of pain* from *bony metastases* in *patients* with *multiple painful sites?"* versus "What is the effectiveness of *bisphosphonates* in *cancer?"*.

Searching the literature

The point to be made here is we can now search for 'secondary publications', evidence sources that have been critically appraised by others, as well as the searching of 'primary evidence'. The value of systematic reviews is rapidly gaining importance. The reading of systematic reviews requires critical appraisal too, but this is a really good place, and arguably the best place, to start.

Examples of good sources of secondary publications include:

- Cochrane library (http://www.cochranelibrary.com) (Require University of Toronto proxy server or individual/institution subscription)
- ACP journal club (http://www.acpjc.org/)
- Treatment Guidelines (e.g. http://www.ccopebc.ca/ guidelines.html)
- NHS centre for review and dissemination (http://www.york.ac.uk/inst/crd/welcome.htm)

Critical appraisal

The fundamental question here is whether the evidence is valid and clinically important. Try the websites above for examples and working guides.

Integrating the evidence with the unique circumstances of the patient

Clinical experience, knowledge of prognostic factors, appreciation of our patients' preferences, joint treatment decision-making… these are all the elements that can be referred to as the art of medicine that we practise daily.

Evaluation of our effectiveness of all of the above

This could range from an evaluation of our effectiveness in doing a literature search to evaluation of patient outcomes. The point here is that we provide feedback to ourselves that we are practising this effectively.

From the less-initiated to the experts in EBM, there is always more to learn and discover. Check out the University of Toronto website http://www.cebm.utoronto.ca on EBM. Live, learn and teach!

Award of Excellence

By Cyril Danjoux, MD, DMRT, FRCPC

Lou Andersson, Primary Nurse in the Rapid Response Radiotherapy Program (RRRP), received the Award of Excellence in Clinical Practice at the recent Canadian Association of Nurses in Oncology (CANO) annual conference in Winnipeg. The award is one of the highest forms of recognition for oncology nurses in Canada. It is given on the basis of nominations by peers and selection by a national awards panel. Lou has been with the RRRP since its very beginning in 1996. Apart from her busy clinical practice, she has been involved with teaching and research. Lou is working on her PhD in psychology. Congratulations Lou.

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HOT SPOT

Expanded role of hormone therapy as neoadjuvant or adjuvant therapy in prostate cancer patients undergoing definitive treatment

By Richard Choo, MD, FRCPC, Radiation Oncologist, TSRCC

Funded by an educational grant from Aventis

Background

- Estimated 18,200 new prostate cancer cases in 2002
- Recent widespread use of PSA results in increasing proportion of younger patients and earlier stage at diagnosis

Stage classification of prostate cancer: TNM staging

T:	Primary tumour
T1:	Tumour not palpable or visible by imaging
T2:	Tumours confined within the prostate
T3:	Tumour extending beyond the prostate capsule (including seminal vesicles)
T4:	Tumour invading adjacent structures other than seminal vesicles (e.g. bladder neck)
N:	Regional lymph nodes
N0:	No regional lymph node metastasis
N1:	Regional lymph node metastasis
M:	Distant metastasis
M0:	No distant metastasis
M1:	Distant metastasis

Curative treatment modalities for clinically localized cancer (T1-4 N0M0)

Surgery
(radical prostatectomy; usually limited to T1-2 N0M0), *or*
Radiation treatment (RT)
(external beam radiotherapy or brachytherapy)

Hormone therapy

1. Traditionally utilized for palliation of metastatic prostate cancer

2. Recent role expansion as neoadjuvant and/or adjuvant therapy in conjunction with surgery or radiotherapy for clinically localized prostate cancer

3. Two types

i. Androgen ablation
- suppress testosterone production
- orchiectomy, LHRH analogues (Suprefact, Lupron, Zoladex), estrogens, and progestational agents

ii. Anti-androgen
- prevent testosterone from binding to the androgen receptor in prostate cancer cells
- Casodex, Nilutamide, and Flutamide
- Usually used in combination with LHRH analogues

4. LHRH analogues are usually used in the clinical setting of neoadjuvant and adjuvant hormone therapy, as they are reversible.

Definitions

- **Neoadjuvant therapy**: additional therapy applied before and/or during primary definitive treatment to improve the efficacy of definitive therapy
- **Adjuvant therapy**: additional therapy applied after and/or during primary definitive treatment to improve the efficacy of definitive therapy

Neoadjuvant hormone therapy

• Radiotherapy (RT) setting

1. Rationales:

i. Androgen ablation induces programmed cell death (called apoptosis) of androgen-dependent cancer cells. This means a reduction of tumour clonogens that need to be eradicated by irradiation.

ii. Androgen ablation leads to a reduction of tumour volume, which in turn can improve oxygenation and tumour environment making irradiation more effective.

2. Randomized studies demonstrate that the addition of neoadjuvant hormone therapy to RT resulted in improvement of local control, disease-free survival and a reduction in distant metastasis compared to RT alone. However, there has been no survival benefit. Neoadjuvant hormone therapy is often considered for clinically localized, but bulky cancer (T2-4 N0M0) treated by radiotherapy.

3. The use of neoadjuvant hormone therapy in RT setting can be summarized as shown in Table One (based on phase III studies).

Table One: Neoadjuvant Hormone Therapy in RT

Indication	Duration	Timing in relation to RT	Effects (in comparison with radiotherapy alone)
Bulky T2-T4 N0M0	Usually three to four months	Start two to three months before RT ± continue for two months during RT	Improved local control and disease-free survival. Decreased distant failure rate. No survival benefit yet.

HOT SPOT

Expanded role of hormone therapy as neoadjuvant or adjuvant therapy in prostate cancer patients undergoing definitive treatment, *continued...*

By Richard Choo, MD, FRCPC, Radiation Oncologist, TSRCC

Funded by an educational grant from Aventis

4. Unresolved issues
i. The role of neoadjuvant hormone therapy for brachytherapy or dose-escalation external beam RT.
ii. The optimal sequence and/or combination of neoadjuvant and adjuvant hormone therapy.
iii. The optimal duration of neoadjuvant hormone therapy is being investigated (e.g. three months versus eight months)

• Surgery setting
1. Rationales:
i. Androgen ablation induces programmed cell death of androgen-dependent cancer cells, leading to tumour volume reduction. This may, in turn, reduce the rate of positive surgical margins and recurrence risk.
ii. Tumour volume reduction achieved prior to surgery may reduce operative difficulty.
2. The conclusions from several randomized studies which evaluated the efficacy of a short-term (three months) neoadjuvant hormone therapy prior to surgery are:
i. Neoadjuvant hormone therapy reduces the rate of positive surgical margins. This has not translated to improved disease-free survival. Thus, the use of neoadjuvant hormone therapy before surgery is not supported and is limited to clinical studies.
ii. Neoadjuvant hormone therapy has no significant advantage with respect to the technical aspects of surgery, blood loss or surgical complications.
3. Unresolved issue:
An ongoing study examines whether a longer duration of neoadjuvant hormone therapy (e.g. eight months) is beneficial.

Adjuvant hormone therapy

• Radiotherapy (RT) setting
1. Rationales:
i. In locally advanced or poorly differentiated tumour, the therapeutic gain achievable by strategies to improve local control (such as radiation dose escalation) is limited by the prevalence of occult distant metastasis.
ii. Additional systemic treatment such as adjuvant hormone therapy needs to be explored to reduce the risk of distant relapse.
2. Recent randomized studies comparing RT alone with RT plus adjuvant hormone therapy for locally advanced or poorly differentiated cancer reported that the addition of adjuvant hormone therapy to RT decreased local failure and distant metastasis, and increased disease-free survival. A European study demonstrated statistically significant survival gain with adjuvant hormone therapy.
3. Based on phase III studies, the use of adjuvant hormone therapy in RT setting can be summarized as shown in Table Two.
4. Unresolved issues:
i. The optimal duration and timing of adjuvant hormone therapy.
ii. The optimal sequence and/or combination of neoadjuvant and adjuvant hormone therapy. There is one study comparing the efficacy of adjuvant hormone therapy with that of neoadjuvant hormone therapy. Preliminary analysis suggested that adjuvant hormone therapy was better than neoadjuvant hormone therapy with respect to local control, distant metastasis rate, and disease-free survival, but no difference in overall survival between the two strategies was observed.

• Surgery setting
1. Rationales:
Same as in RT setting
2. The role of adjuvant hormone therapy following radical prostatectomy is not well-defined. The only exception is for patients diagnosed with lymph node metastasis following radical prostatectomy, where adjuvant hormone therapy is recommended on the basis of a phase III study demonstrating improvement in survival with adjuvant hormone therapy. The benefit of adjuvant hormone therapy for positive surgical margins and/or pathological T3 disease is currently under investigation.

* A future **Hot Spot** issue will address hormone therapy for metastatic prostate cancer and its potential side effects.

Table Two: Adjuvant Hormone Therapy in RT

Indication	Duration	Timing in relation to RT	Effects (in comparison with radiotherapy alone)
T3-T4 N0M0 or poorly differentiated (i.e. Gleason Score ≥ 8)	Usually two to three years	Start usually at the beginning of RT and last for the total duration of two to three years	Decreased distant failure rate, improved local control, disease-free survival and overall survival