

# HOT SPOT

## From the guest editor's desk

By Dr. Charles Hayter,  
MA, MD, FRCPC,  
and Ms. Lou Andersson, RN, MA

This spring issue of **Hot Spot** contains an interesting and stimulating potpourri of articles on various aspects of care of patients with advanced cancer. In the feature article, Magdalene Winterhoff describes the important role of the social worker in palliative care, and provides a valuable list of resources. Mary Vachon draws attention to the significance of anxiety as a psychological problem in

cancer patients. The insert, written by Elizabeth Phillips, reviews a common oncological emergency, febrile neutropenia, and includes up-to-date knowledge about its management. Charles Hayter's historical vignette describes the evolution of the concept of fever. Finally, Rebecca Wong's research corner highlights the process and outcome of a recent very successful workshop sponsored by the NCIC on the research agenda in palliative oncology. We hope you find these articles enjoyable and thought-provoking.

## The role of the social worker in palliative oncology

By Magdalene Winterhoff, MSc

Patients referred to the regular clinics here at TSRCC frequently benefit from the involvement of social workers. Our role involves assessment of the patient's and family's ability to cope. A patient's age and stage in life, their socio-economic situation; their support system or lack thereof; their past experiences with the health care system, as well as the events leading up to the diagnosis, all impact on coping. While all patients are considered to be unique individuals, the reactions to a cancer diagnosis are similar regardless of patients' backgrounds. For most, there is shock, anger and, frequently, disbelief. Over time, the well-functioning patient and family can adjust to living with cancer. Chemotherapy and radiation treatments, and their attendant side effects, are seen as undesirable but necessary experiences. After all, they offer the hope of cure. During this time, patients frequently seek out social workers for

adjustment counselling, information on resources, as well as advocacy. One patient may need coaching on how to inform their young children about the diagnosis, another is concerned about their own role as caregiver to elderly parents, while another has suffered unemployment in the months prior to diagnosis or perhaps even lost a business. The stress of a cancer diagnosis will often render even a well-functioning individual temporarily incompetent. Social workers provide patients/families an opportunity to have their fears and concerns normalized; to learn how to navigate the complexities of the health care system; and to utilize community resources while struggling with the disease. Our assessments of patients and their support systems can provide other members of the health care team, both in hospital and the community, a better understanding of the complexities and uniqueness of each individual patient. This, in turn,

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## HOT SPOT

*The Newsletter of the  
Rapid Response Radiotherapy  
Program of Toronto Sunnybrook  
Regional Cancer Centre*

**Vol. 5, Issue 2, May 2003**

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**In this issue:** The role of the social worker in palliative oncology;  
Reflections on anxiety in confronting advanced cancer; Historical Vignette: Spring fever; Research Corner.

**Insert - Advances and challenges in the management of febrile neutropenia**

# Reflections on anxiety in confronting advanced cancer

By Mary L.S. Vachon, RN, PhD

In his recent fascinating first novel, Dr. Avery Weisman, Professor of Psychiatry Emeritus of Harvard Medical School and Former Principal Investigator of Project Omega, a research study of how cancer patients cope with illness and its ramifications, integrates his knowledge of years spent as a clinician and researcher with a rich fantasy life. As the principal character confronts the possibility of a diagnosis of cancer, Dr. Weisman notes:

“While Simeon might not have known, there is no standard or uniform response to cancer, no matter how fast or slow it grows, how pressing the sense of mortality, and how distressed the victim. Nevertheless, few people confront cancer with calm and equanimity, including presumably mature doctors and nurses who may blanch, tremble and attempt to deny when *they* become the unwilling patients. The future vacancy of time when they shall be dead cannot be imagined”.

Anxiety can be a problem at any point throughout the cancer continuum and may affect response to treatment. Patients with cancer are approximately twice as likely to have anxiety as matched controls. Initial data suggest that psychological distress on the day of the patient's first chemotherapy infusion is predictive of their subsequent risk of infection. Walker et al. found that the Hospital Anxiety and Depression Scale (HADS) anxiety score was a significant predictor of clinical response to chemotherapy – the higher the score, the poorer the response. Anxiety is common in terminally ill patients. Symptoms of anxiety in the latter stages of cancer may be part of a generalized

response to the disease or reflective of an adjustment disorder with anxious mood.

The clinical symptoms of anxiety, including anxious mood, increased attention, fearfulness, inability to concentrate, and restlessness, are easy to observe. Associated symptoms, such as dyspnea, tremor, palpitations, or sweat, can be due to cancer or its treatment, therefore these are less reliable for diagnosis.

Stiefel & Razavi, (1994) classify anxiety as follows:

## Situational anxiety

While some anxiety is normal in adjusting to cancer, a prolonged feeling of anxiety of an unusual intensity that interferes with the person's ability to cope with the disease or to engage in normal social activities is not normal. Imminent death is often not the most frequent source of anxiety which may be due more to concerns re: pain, isolation, anxiety, dependence, cachexia and shortness of breath.

## Psychiatric anxiety

In addition to adjustment disorders with symptoms of anxiety, anxiety may arise as phobias about some aspect of medical care, panic and generalized anxiety disorders. Anxiety is also a prominent symptom in up to 50% of delirious patients. Withdrawal from drugs or alcohol can also cause symptoms of anxiety.

## Organic anxiety

Organic anxiety may be caused by acute pain. Organic anxiety may also be associated with asthenia, nausea, shortness of breath, metabolic disturbances such as hypercalcemia and hypoglycemia, structural changes in the brain, and drugs such as corticosteroids and morphine.

## Existential anxiety

Existential anxiety may have a spiritual dimension. This anxiety may be associated with thoughts about a wasted life, fear of the current illness situation, and thoughts of the future, including the possibility of death.

## Intervention

Dr. Weisman suggested approaches to assessing what is causing the most concern in a terminally ill person.

In his novel, the oncologist asks:

“ ‘What has this been like for you?... Tell me how your morale has held up, principally?’ He implied that cancer was less a disease than a trial by ordeal. Being a captive of cancer was a credential that few untouched people could understand. ‘Almost everyone is frightened, then it gets less difficult, but it never goes away. Doctors try to be reassuring but mainly for their own sake. What makes it hard to deal with is that the disease, cancer, always must be understood against its broader effect on life and outlook. No one can be casually confident about cancer; everyone is awed by it, or should be. If they are not awed by cancer, the patient ought to see someone else who will understand how a person's life must change.’”

## Reference

Stiefel & Razavi. (1994) **Supportive Care in Cancer 1994**, Volume 2, pages 233-237.

*Mary Vachon, RN, PhD, is a psychotherapist in private practice. She can be reached at [maryvachon@sympatico.ca](mailto:maryvachon@sympatico.ca).*

### Research corner

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research group was felt to be an important initial step if we are to take this area forward. As well, the rich quality of life (QoL) database established through existing NCIC CTG studies, under the leadership of Dr. A. Bezjak, would provide a valuable starting point to get a better handle on the prevalence of radiation-

induced fatigue under different circumstances. This is being actively worked on by the group.

After a stimulating day of discussion, the workshop generated many concrete immediate and intermediate action plans that are now being implemented. More importantly, the workshop served as a unique team-building exercise, which no doubt will prove invaluable for future developments in this area for many years to come.

## Acknowledgement

*The workshop was generously sponsored by OrthoBiotech through an unrestricted educational grant.*

*Dr. Rebecca Wong is a radiation oncologist at Princess Margaret Hospital, Palliative Radiation Oncology Program, and Planning Committee Chair for Symptom Control in Radiation Oncology Workshop 2003.*

### *The role of the social worker...*

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can lead to more appropriate discharge or future care plans. In some situations, we may also recommend referral to psychology for counselling, or to psychiatry.

Patients coming for treatment at the Rapid Response Radiotherapy Program are likely to have metastatic or terminal cancer. They may come from another hospital or from the community. RRRP patients are frequently unique because of their medical situation. In many cases, their disease is diagnosed at a stage when it

is widespread, advanced, and well beyond curative treatment. Patients and families must adjust, not just to the diagnosis, but also to the poor prognosis and patient's palliative condition. Their information and level of understanding may be poor. They can be expected to react with shock and anger, and to be operating in a crisis mode. All of the reactions experienced by other cancer patients are exhibited by the RRRP patients, however, they do not have the luxury of time to learn to adjust to the various stages. As a social worker, I may provide them with information both about the diagnosis and prognosis. I

can, based on experience, anticipate their needs as well as those of their caregivers. Patients are likely unaware of services they may need and to which they are entitled, such as those available through Community Care Access. Or they may have financial concerns and not realize the possible entitlement to Canada Pension Plan Disability. And lastly, there may be a need to 'tell their story' to someone other than a doctor or RN, who can understand their experience, tolerate their emotions, and offer nonjudgmental advice and guidance. Table One lists some resources that may be helpful.

#### **Table One: Some helpful resources**

##### **Nursing Services**

- ❖ for private agencies, see Yellow Pages
- ❖ Community Care Access Centres – community care, placement, information & referral services. Services include: nursing, physiotherapy, occupational therapy, speech therapy, social work, nutrition counselling, personal care, respite care, placement into long-term care facilities such as nursing homes or homes for the aged.  
East York: (416) 423-3559; Etobicoke: (416) 626-2222; North York: (416) 222-2241; Scarborough: (416) 750-2444; Toronto: (416) 506-9888; City of York: (416) 780-1919; Peel Region: (905) 796-0040; York Region: (416) 221-3212; Durham: (800) 263-3877; Halton Region: (866) 442-5866; Simcoe: (888) 721-2222; Kitchener: (519) 748-2222; Hamilton-Wentworth: (905) 526-3600

##### **Financial Assistance**

- ❖ Ontario Works (Welfare) including assistance with funeral costs. Toronto: (416) 392-5100; Vaughan: (905) 850-3490; Newmarket: (905) 895-5166; Georgina: (905) 989-1883; Markham: (905) 513-0880; Peterborough: (705) 740-2274; Brampton: (905) 793-9200; Hamilton: (905) 354-3561
- ❖ Ontario Disability Support Program - General Enquiry, Metro Toronto: (416) 326-5079, outside Toronto: (888) 256-6758
- ❖ Canada Pension Plan Disability: (800) 277-9914

##### **Information Services**

- ❖ Cancer Connection: (800) 263-6750

**Supportive Care for Cancer** 3rd Edition published by Toronto Sunnybrook Regional Cancer Centre.

**Community Resource Guide:** Lists resources available in Toronto, Halton-Peel, Durham, York and Simcoe. Available for \$20. Call Dianne Dilnot at (416) 480-5891.

### *Historical Vignette:*

## Spring fever

**By Charles Hayter, MA, MD, FRCPC**

The insert in this issue of **Hot Spot** focuses on the management of febrile neutropenia.

Fever is one of the oldest conditions to be studied and classified by doctors. As historian Edward Shorter points out, up until about a hundred years ago, fever was the most common condition seen by doctors. The introduction of the thermometer as a diagnostic instrument, around 1850, allowed the precise measurement of variations in body temperature. Fever patterns and co-existing symptoms allowed fever to be classified into many types, such as

scarlet, typhoid, hemorrhagic, rheumatic, miliary, puerperal and so on. Various types of fever still occupy almost four pages in **Stedman's Medical Dictionary**.

For many centuries, the practice of medicine was governed by the idea that illnesses were caused by imbalances in the four humours: black bile, yellow bile, phlegm, and blood. Fever and its accompanying sweating were seen as natural processes by which the body attempted to rid itself of toxins. In other words, fever was seen as beneficial, and doctors sometimes encouraged it by warming the fevered patients with blankets and giving hot spicy drinks.

Fever has sometimes been deliberately induced to treat disease. After he noticed that symptoms from syphilis improved with fever, Austrian psychiatrist Julius Wagner-Jauregg treated syphilis patients with malarial fever. He won the 1927 Nobel Prize for this discovery.

Following the discovery of bacteria and viruses in the late nineteenth century, it became clear that most fevers were due to infection by one of these agents and were easily treated with antibiotics. Nonetheless, fever remains one of the most common conditions encountered by physicians.

# Research Corner

By Rebecca Wong, MB, ChB, MSc,  
FRCPC, Princess Margaret Hospital

## Defining the research agenda in symptom control in radiation oncology

Symptom control research in radiation oncology encompasses a wide spectrum of research ranging from the use of radiation to relieve symptoms related to cancer, to the management of symptoms caused by radiation therapy. They share three important challenges. First, research in this area requires specific methodological expertise because many subjective outcomes need to be measured and compared. Secondly, we need to interact with many conventional disease site groups to find the clinical expertise and the relevant patients. Finally, this is traditionally an under-studied area - but not for much longer!

Recently, the National Cancer Institute of Canada Clinical Trials Group (NCIC CTG), in collaboration with the Canadian Association of Radiation Oncologists (CARO), jointly sponsored a one-day workshop to define the research agenda for the NCIC CTG symptom control group, with a specific focus around radiation oncology. This was a timely initiative, capitalizing on the palliative groups that have emerged in recent years across Canada, in part modelled after the work being done at both Princess Margaret Hospital (Palliative Radiation Oncology Program) and Toronto Sunnybrook Regional Cancer Centre (Rapid Response Radiotherapy Program) right here in Toronto.

The workshop took place in Toronto, at the Sutton Place Hotel in October 2002. It was organized as a pre-conference workshop to the annual CARO meeting. The workshop was attended by over 40 experts, representing radiation and medical oncologists, palliative care physicians, oncology nurses, radiation therapists, methodologists and translational researchers. The agenda focused on four preselected areas, identified through needs assessment and surveys conducted across Canada. These were bone and brain metastases, radiation-induced mucositis and fatigue.

The workshop commenced with systematic reviews of the state of the

knowledge in these areas, followed by possible research opportunities, presented by Drs. J. Wu (Calgary), M. Tsao (Toronto Sunnybrook Regional Cancer Centre), J. Wright (Hamilton Regional Cancer Centre), and G. Duncan (Vancouver Cancer Centre). The participants then divided into smaller discussion groups facilitated by Drs. A. Bezjak (PMH), K. Sultanem (McGill), M. MacKenzie (Vancouver Cancer Centre), and M. Brundage (Kingston Regional Cancer Centre). The facilitators served the key role of focusing the discussion, with the mandate of establishing one to two potential research questions and an action plan. The day concluded with a final discussion of the recommendations. After much stimulating discussion, the group emerged with the following specific recommendations.

- In the area of *bone metastases*, the group identified and prioritized three research topics:
  1. How useful is re-irradiation for patients who did not achieve complete response (or are experiencing progressive pain) following previous radiotherapy?
  2. Can novel hypofractionation schedules (e.g. 17Gy in 2 fraction) be more convenient and equally or more effective?
  3. Can the early use of radiotherapy reduce skeletal complications in early bone metastases?The first question is currently being developed as an NCIC CTG-led trial under the leadership of Drs. E. Chow and J. Wu. You may soon be helping to answer this question as this study opens at a centre near you!
- In the area of *brain metastases*, an important but humbling question was again being asked:

For patients with poor or intermediate prognosis, is whole brain radiotherapy better than best supportive care? While not a new question, it remains unanswered due to the methodological challenges. Other ideas included: What is the optimal timing for the use of whole brain radiotherapy in asymptomatic brain metastases?; and What agents are practical and effective to minimize late neurocognitive sequelae in

patients with better prognosis undergoing whole brain radiotherapy?. The group recommended a survey on the feasibility of the first question, which is currently being developed under the leadership of Dr. M. Tsao.

- The term *radiation-induced mucositis* perhaps immediately leads one to think of head and neck cancer treatments. However, other symptoms such as esophagitis, enteritis and proctitis are all badly in need of more intensive study. The group developed two potential study questions in the area of oral mucositis including: 1. testing the effectiveness of combination of sucralfate and magic mouthwash (with steroid); and 2. testing the effectiveness of amifostine, a radioprotectant, against the current standard practice. The third question addressed the prevention of radiation esophagitis as experienced by patients undergoing mediastinal irradiation. The study of sulcrate and magic mouthwash in this capacity received the greatest interest. Dr. F. Wong has taken the lead to conduct a pilot study at Fraser Valley, BC, which could pave the way to more definitive studies.
- *Cancer-related fatigue* is perhaps much more prevalent than radiation oncologists care to admit, in part due to the lack of effective interventions. The many methodological challenges in studying this area were discussed. The formation of a multidisciplinary

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## Advances and challenges in the management of febrile neutropenia

### What is febrile neutropenia (FN)?

- Common complication of cancer chemotherapy affecting 12 to 50%, or more, of patients
- An oncologic emergency and the most common reason cancer patients are admitted to hospital
- Sustained fever greater than 38°C in combination with an absolute neutrophil count less than  $0.5 \times 10^9 /L$  ( $< 500/\mu l$ )

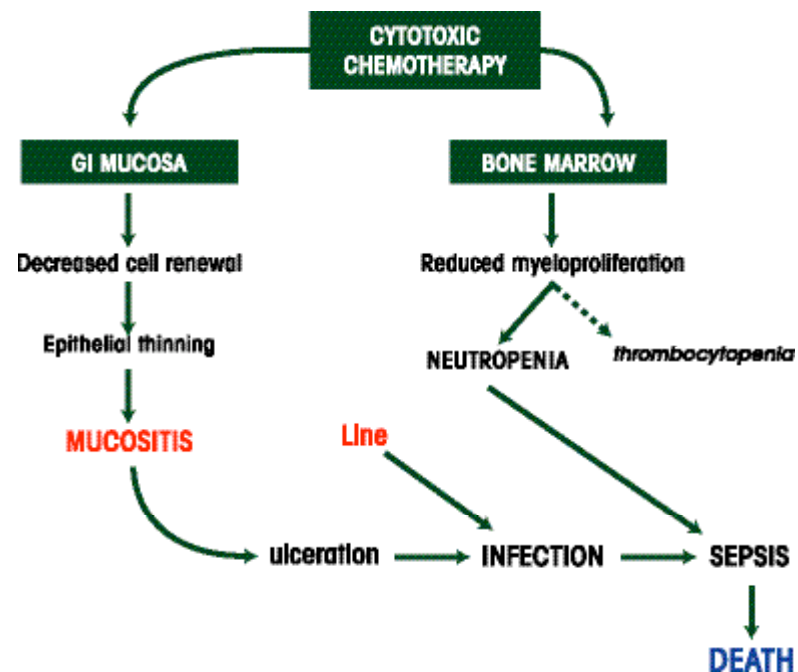
### What are the consequences of FN?

- Risk and severity of infection is proportionate to degree and duration of neutropenia.
- When neutropenia is severe ( $< 0.5 \times 10^9/L$ ) or prolonged, significant infection-related morbidity and mortality result.
- Generally leads to patient hospitalization which has a negative impact on quality of life and is costly.
- May necessitate dose reduction and/or delays of future chemotherapy which can impact on treatment success.

### How to evaluate FN?

- Diagnosis is made when the patient presents with a sustained fever greater than 38°C, and an ANC that is either less than  $0.5 \times 10^9/L$  or expected to be less than  $0.5 \times 10^9/L$  over the next 24 hours.
- Assumed to be infectious in etiology although  $< 40\%$  of patients will have a clinical or microbiologic source of infection uncovered
- Evaluation of the patient should include full:
  - **History** (to elucidate specific symptoms, time from previous chemotherapy, history of antibiotic allergies and other medical co-morbidities).
  - **Physical examination** paying particular attention to patient vital signs and potential foci of infection (the mouth, perianal area and line sites are common sites where infection can originate).
  - **Investigations:** Should include, at a minimum, complete blood count and differential, electrolytes, creatinine, liver function tests, chest x-ray, and cultures from central and peripheral venous catheters. Other investigations may be necessary and targeted to patient symptoms or signs (eg. lumbar puncture, abdominal imaging, stool for *Clostridium difficile* toxin, etc.).

Figure One: Pathogenesis of FN



### What is the typical clinical presentation of FN?

- The most common presentation of FN (at least 40% of the time) is actually fever alone in the absence of other clinically overt signs or symptoms.
- Fever commonly first appears around the nadir of the neutrophil count.

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## What are the general principles of FN treatment?

- Antimicrobial therapy should be initiated empirically in all patients with FN.
- The spectrum of antibiotic coverage should be broad and include:
  - *Staphylococcus aureus* and *Streptococci*, now the most common causes of infection, as well as
  - *Gram negative bacilli*, which are associated with a high mortality rate with delayed treatment.
- Choice of empiric treatment should be based on institutional epidemiology and local antibiotic resistance patterns.
- Examples of commonly-used regimens in Canadian centres that have appropriately broad coverage include cefazolin plus tobramycin or piperacillin-tazobactam.
- Regular re-assessment and close monitoring is key:
  - Treatment should be re-assessed, generally at three-day intervals, for febrile response, and therapy is optimized accordingly.
  - In patients who become afebrile, broad spectrum treatment should continue for three to five days in the absence of a defined clinical or microbiological source.
  - If patients are still febrile and neutropenic at days five to seven, despite optimization of antibacterial therapy, consideration should be given to initiating antifungals such as amphotericin B. Newer drugs, such as caspofungin (clinical trials in FN ongoing) and voriconazole (yet to be approved in Canada) are less toxic than amphotericin B and, unlike fluconazole, have activity against *Aspergillus spp.*

## What is the evidence and feasibility of outpatient therapy for FN?

- Published reports by Talcott et al. (1988, 1992) first lent credence to the risk-based approach to management of patients with FN.
- More recently, validated risk indices such as Multinational Association of Supportive Care in Cancer (MASCC) may have a higher predictive value than the Talcott score for identifying lower-risk patients potentially eligible for outpatient therapy.

- Two large randomized trials (Freifeld et al., and Kern et al., 1999) compared inpatient intravenous therapy with inpatient oral therapy (ciprofloxacin/amoxicillin-clavulanate) and encouragingly showed equivalent responses.
- Close monitoring is required, regardless of where they are managed.
- A suggested approach to risk-based treatment of FN is outlined in Figure Two.

## What is the role of prophylactic and adjuvant treatment in FN?

### Antibiotic prophylaxis

- Not routinely recommended
  - No evidence to support that prophylaxis reduces infectious morbidity and mortality.
  - Increases antibiotic resistance, which may make fluoroquinolones less useful for the outpatient treatment of lower-risk FN.

### Hematopoietic growth factors

- Based on current published guidelines from the American Society of Clinical Oncology\* and Cancer Care Ontario†, **primary prophylaxis** with growth factors should be considered and may have particular economic benefit if there is a significant ( $\geq 40\%$ ) risk of FN based on the host and chemotherapeutic regimen. In addition, more recent evidence suggests that G-CSF can improve survival in patients over age 60 years with aggressive

histology lymphoma receiving CHOP if it is used to decrease the cycle interval of CHOP from three to two weeks.

- **Secondary prophylaxis** in patients who have experienced FN is recommended in the setting of:
  - Patients on curative treatment who have already experienced a dose reduction or delay due to FN are candidates for prophylaxis for subsequent chemotherapy cycles.
  - Use may also be warranted for specific tumour types such as advanced breast or small cell lung cancer where secondary prophylaxis has been associated with improved survival.
- Growth factors should also be considered in the **active treatment** of patients with FN who have serious bacterial and/or fungal infections that are not responding to current antimicrobial therapy, or when it is anticipated that neutropenia will be prolonged.

\*ASCO Health Services Research Committee. (1996, June). Update of recommendations for the use of hematopoietic colony-stimulating factors: evidence-based clinical practice guidelines. American Society of Clinical Oncology. *J Clin Oncol.*, 14(6), 1957-60.

†Rusthoven, J., Bramwell, V., Stephenson, B., and the Provincial Systemic Treatment Disease Site Group. (1998). Use of Granulocyte Colony-Stimulating Factor (G-CSF) in Patients receiving Myelosuppressive Chemotherapy for the Treatment of Cancer. *Cancer Prev Control*, 2(4), 179-190.

**Figure Two: Risk-based strategies for managing febrile neutropenia**

