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GUEST EDITORIAL

Multimodal cancer care research

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Research models must more closely take into account the interdependence of social, behavioral, psychological, organ system and cellular molecular mechanisms of disease.
— Norman Anderson[1]

Today, most oncologists would agree that Anderson's statement is common sense and subscribe to its expressed wisdom[2,3]. And yet most cancer centres are not set up to apply this wisdom to patients with advanced cancer, even the patients with serious multisystem problems. To do so requires access to interprofessional teams, ideally from first diagnosis. Palliative care is based on teams that address all dimensions of illness, but most still concentrate on end-of-life care; they provide comprehensive care only to a modest degree to patients and families early in the course of illness.

Oncologists commonly work in nurse–physician dyads; nurses are partners offering consistent ongoing patient follow-up. That approach, while laudable, cannot supply a full envelope of care. To do so requires adoption of the "multimodal team care" concept put forward by Fearon[4]. Following those principles, I use the term "multimodal" to mean care offered by a core team made up of nurses, physicians, physical and occupational therapists, social workers, and dietitians working as co-equals. They see patients and families at the same visit and formulate an articulated care plan. This core team may expand as needed to meet specific patient needs. Their care is continuous, not episodic; it is not characterized by isolated consults unto themselves.

An adage holds that "the beginning of wisdom lies in calling things by their right name." Without clarity, fine endeavours may fail in a morass of misunderstanding. "Multimodal care" meets the criteria for a rehabilitation team just as for a palliative care team[5,6]. Multimodal teamwork is also an exercise in prevention: "When sorrows come, they come not single spies, But in battalions"[7]. Indeed, symptoms feed on each other, and if not addressed early and well, may produce a crescendo of suffering and accelerate disease. An intertwining of approaches, perhaps regarded by many as separate entities, should therefore be seen as a common front.

It is unsurprising that many aspects of quality of life improve for patients working with multimodal teams, as documented by Gagnon *et al.*[8] and Chasen *et al.*[9] in this issue of *Current Oncology*. Improvement of this kind has consistently been demonstrated in palliative care programs, and the multimodal teams being spoken of are, in reality, based on palliative care principles. But is there a biologic rationale for their potential success in controlling symptoms and possibly improving the results of drug therapy and patient survival alike? I think that there is.

Tumour immune response is undoubtedly a two-edged sword. As advanced cancer progresses and metastasizes, the immune reaction engendered turns traitorous. The tapestry of cytokine and chemokine production stimulates tumour growth, angiogenesis, tissue invasion, and metastasis[10–12]. This aberrant chronic inflammatory state increases symptom frequency and severity, most notably the anorexia–cachexia syndrome[13,14], and clearly connotes a grim prognosis for survival[15].

Exercise, some dietary components, and psychosocial intervention have anti-inflammatory effects[16–21]. It can be hypothesized that adding sophisticated dietary counselling, follow-up exercise and self-help routines, and psychosocial interventions might not just increase appetite and help patients "feel good," but might also ameliorate the chronic inflammatory state and thus decrease cancer symptoms and inhibit tumour progress. Sound social *and* biologic rationales therefore underpin the idea of combining conventional anticancer therapies with multimodal team care from first diagnosis.

Only baby steps toward proving these hypotheses have been taken. The two papers in this issue—and the few other studies from teams dealing with cachectic cancer patients—have, in total, enlisted fewer

than 500 patients in nonrandomized trials. But if the Anderson concept is accepted as correct, as seems to be the case, and if a plausible biologic rationale supports comprehensive team activity, then surely we should advance research initiatives in this sphere—a task that, by long experience, is understood not to be easy for a range of reasons:

- Drug and radiotherapy orientation: Cancer centre research is heavily weighted toward drug and radiotherapy treatments. It sets out to prove clearly that drug A works in a highly selected subset of patients. Investigators may be fearful that combining specific team and symptom care research plans with drug studies will muddy the waters, thus disabling their primary outcome in respect of the efficacy of drug use.
- Support considerations: Related to the foregoing point, a large proportion of clinical research is supported by the pharmaceutical industry, which drives the research agenda and might not accept trial models of a pragmatic nature, although such trials might more accurately reflect study drug use in clinical practice. New cancer therapies are expensive and profit-generating. Teams are not profit-generating, and many drugs that those teams might wish to study (for example, omegas 3s, dietary supplements, nonsteroidal antiinflammatory drugs, and in future, beta-blockers) are off-patent and inexpensive.
- Mindset: Oncologists are trained in a heavily drug-oriented system. We might acknowledge the virtue of comprehensive care models, but right now we are preoccupied with "–mabs" and "–ibs" and gene-based therapies.
- Existing centre priorities: The big dog gets to feed first. Nutrition and physiotherapy programs are often underfunded and low on the resource chain.
- Platform research: A format linking multiple therapies is difficult to formulate within a research proposal. Such proposals might also be more likely to be discounted on methodologic grounds by grants panels more attuned to evaluating single-entity proposals.

I think that there may be ways to address those issues, including these:

- Helping public funding sources to recognize that they should prioritize multimodal care research. Before making that change, they can sponsor workshops to review the scientific rationale, the outcomes of existing programs, and the design scope of research protocols.
- Seeking willing pharmaceutical industry partners who, on a pro bono basis, might support a share of multimodal cancer care research. They might even have some new symptom-control drugs—notably antiinflammatory and anti-cachexia agents—that are best studied in concert with a multimodal care team.
- Leveraging community interest in diet, exercise, and therapies that allow people to be active participants in care. This theme is continually repeated in letters received by our programs, which convey patient or family satisfaction with truly being active team members and controlling their therapy with our advice. Many private foundations could also increase their interest in multimodal care, and hospital foundations could expand their reach and find a receptive audience by highlighting their involvement in these initiatives, which was certainly my experience in McGill hospitals and in the community. Our inaugural programs were funded by the Riddell family and the Webster Foundation and sustained to a large extent by the Jewish General Hospital Foundation and the Royal Victoria Foundation. Our participating hospitals, while financially strapped, generously maintained a degree of financial backing in difficult times. For example, Dr. Chasen's Ottawa program is backed by the highly supportive Élisabeth Bruyère palliative care program, and he has also received support from the Ottawa Regional Cancer Foundation.

Multimodal care is based on common sense; it will enjoy community support and understanding ("Why weren't you doing this all the time?"), it has a biologic rationale, and in one expression or another, is lauded by our cancer societies. Still, a wide gap exists between recognition and application. The hope is that the research published in this issue of *Current Oncology* will help in some small way to narrow the gap. I think that an informed public would expect us to do so.

CONFLICT OF INTEREST DISCLOSURES

The author has no financial conflicts of interest to declare.

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