

## The Role of Optimal Healing Environments in Patients Undergoing Cancer Treatment: Clinical Research Protocol Guidelines

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### ABSTRACT

Integrative cancer care (ICC) is the treatment of patients with cancer, under physician supervision, with appropriate conventional treatments in a healing context based on insights from research on nutrition, biochemistry, exercise, and psycho-oncology. It uses validated techniques and practitioners of complementary and alternative medicine (CAM), and strategies for enhancing treatment and side-effect management such as chronomodulated chemotherapy, therapies to reduce treatment resistance, and innovative assessments for individualizing treatment plans. The elements of ICC align well with the concepts of optimal healing environments (OHE). Expectations of well-being are fostered; transformative self-care practices are common therapeutic tools; development of healing presence among staff and therapeutic alliances with patients are emphasized; instruction in health-promoting behavior is standard; and collaborative integration of CAM in the practice is typical. Based on the authors' clinical experience, an OHE for patients with cancer is described and suggestions for meaningful research are identified.

### INTRODUCTION

**I**ntegrative cancer care (ICC) is a new, comprehensive approach to the patient that incorporates the use of complementary and alternative medicine (CAM) techniques, as well as insights from research in nutrition, biochemistry, exercise, and psycho-oncology into a full medical facility. The practices of centers emphasizing integrative care have, to some extent, been converging as research studies are published and discussed at conferences, so that a general outline of integrative practice can be sketched.<sup>1-3</sup>

For more than 20 years, the authors have been developing, assessing, and fine-tuning an integrative medical-cancer clinic, the Block Center for Integrative Cancer Care, and organizing a research facility, the Institute for Integrative Cancer Research and Education, in Evanston, IL. From our perspective that care which is fully integrative should parallel the model of the optimal healing environment (OHE) set out by Jonas and Chez in this supplement (pp. S-1-S-6).

The various components of this model are found, to a greater or lesser extent, in the various integrative centers, as outlined in the references above, but can and should be the defining characteristics of any integrative program.

The focus of this paper is on the role of the OHE in cancer patients undergoing active treatment (i.e., surgery, radiation and chemotherapy). Much research on CAM techniques in cancer explores their value in moderating the side effects and improving quality of life in patients engaged in these treatments.<sup>4</sup> For many patients, such as those with early-stage breast and colon cancer, adjuvant therapy shortly after cancer diagnosis is the end of their conventional cancer therapy, because in early stages of these cancers, surgery, radiation, and chemotherapy can be curative. A percentage of patients who complete initial treatment and survive their cancers are nonetheless physically and/or emotionally crippled from the assault of their therapies. Therefore, these patients may be cured but not healed. Equally important is that by concentrating on controlling the side-effects of cancer

treatment, and on the value of rehabilitation and health promotion after treatment, it should be possible to lower the percentage of patients who experience cure without healing.

As discussed below, the depth of concerns of patients with cancer extend far beyond the adjuvant treatment phase, because cancer is still, for too many patients, a terminal disease. Thus, for patients with cancer and those with other illnesses who have a greater perceived and actual risk of mortality, the ultimate goals of a true OHE assume added importance. These goals include a comprehensive focus on enhancing full quality of living for all patients, improved tolerance to disease and treatment-related factors, tangible increases in response and overall outcome, prolongation of survival and improvement in the chances for attaining an enduring remission. Thus, in every phase of an individual's disease trajectory, maintaining a focus on the potential for curing and healing can make these two seemingly separate goals—caregiving and curegiving—mutually enhancing.

Evidence is beginning to accumulate that long-term survival of patients with cancer can be influenced not only by conventional medical treatments, but also by health promotion education and modifications of diet, lifestyle, and psychosocial factors. A longitudinal study of consecutive patients with metastatic breast cancer receiving chemotherapy at our clinic found unexpectedly long survival times, and is supportive of further research on the impact of the integrative care model on survival and key quality of life factors.\* The importance of diet and lifestyle modification is also emphasized by equally impressive extended survival of advanced prostate cancer patients undergoing hormonal treatment at the Block clinic.† In both the breast and prostate cancer populations, survival times observed were twice those of apparently similar populations recorded in the literature.

Monitoring survival-related outcomes in the OHE will be important because other data, such as population-based studies, have indicated that patients who use alternative medicine may have survival times that are shorter than expected.<sup>5</sup> The alternative treatments used by patients in this study were separate alternative treatments, frequently used in various combinations by the patients studied. It also is not certain whether patients who seek CAM actually receive the recommended conventional medicine treatments, or whether in those who did receive conventional care, CAM treatments were associated with adverse interactions.<sup>6</sup>

Healing from cancer involves more than treatment tolerance, remission, survival, or relative freedom from recur-

rence. A sense of renewal that enhances resilience and wholeness can occur even in the absence of these. Thus, the higher dimensions of healing, such as benefit finding and vital reengagement in personally significant activities are appropriate goals of the OHE. Aspects of the OHE thus must take on some characteristics of a safe and sacred space in which patients with cancer feel free to probe and resolve the darkest aspects of their illnesses.<sup>7</sup> We outline below some of the existential issues that cancer patients face in the course of achieving such healing, and lend themselves to OHE research.

## CHARACTERIZING AN OHE FOR CANCER TREATMENT

Patients with cancer who are undergoing conventional treatment face a specific set of core issues in achieving healing, (physical) restoration and mind–spirit and emotional renewal.

### *The nature of the disease*

For most patients initially diagnosed with later-stage cancer, relapses and progressive metastases characterize the course of disease. However, the realistic concerns of a fatal outcome make the association of cancer and death prominent in the minds of both the newly diagnosed patient as well as those with progressive disease. We consider cancer to be a chronic disease. It is also true that cancer is not a single disease, but rather a broad collection of diseases and stages. The diverse and progressive nature of cancer dictates that treatment regimens in the OHE must be individualized to account for specific medical, as well as social, concerns.

### *Fear and trauma*

Fear of the treatments, the implications of the diagnosis, and the omnipresent specter of recurrence progression, and traumatic life disruption are common accompaniments to a cancer diagnosis. Yet despite their frequency, distress disorders such as anxiety and depression in cancer patients are underrecognized and therefore underrelieved in most oncology settings.<sup>8</sup>

### *Loss of control*

The commonly expressed concerns of cancer patients about loss of control over their lives is in part a recognition that they have been unable to control their bodies, which have generated uncontrolled malignant growths.<sup>9</sup> Additionally, conventional treatments are commonly seen as unpleasant manipulations that are done to patients; that is, patients “undergo” chemotherapy and radiation rather than participate in “taking” relevant medications. The fact that conventional oncology typically represents to patients that

\*Block KI, Gyllenhaal C, Freels S, Tripathy D, Gustin D, Shoham J. Survival impact of integrative cancer care in advanced metastatic breast cancer. (in preparation).

†Block KI, Gyllenhaal C, Chodak G, Freels S, Shoham J. Survival impact of integrative cancer care in advanced metastatic prostate cancer. (in preparation).

once initial treatment is concluded, there is nothing they themselves can do to manage their disease except return for recommended follow-up visits, contributes to feelings of helplessness and lost control. In contrast, patients seeking integrative care are encouraged to engage by actively committing the time, emotional energy, and intellectual effort in their process of recovery, thereby adding an element of empowerment and a measure of control.

### *Information overload*

Upon diagnosis, patients must quickly assemble, evaluate, synthesize, and absorb a large amount of often inconsistent and technical information obtained too often from uncertain or disreputable sources, including many on the Internet. When confronted with crisis decisions, how people cope with a deluge of information can be characterized as “monitors” or “blunters.”<sup>10</sup> Monitors actively and sometimes anxiously seek out information, whereas blunters avoid accumulating more detailed information than is absolutely necessary. Overwhelming the blunter, or underwhelming the monitor, can trigger intense psychological and even physiologic distress.

### *“Rejection” by the medical establishment*

The image of the patient with cancer who is “sent home to die” is powerful in the culture, and with the associated feeling of loss of control frequently transforms into the patient who then in desperation seeks alternative medicine.<sup>11</sup> Because this feeling can be associated with a reluctance to ask questions or disagree with providers out of concern that offending a health professional may result in retribution or inadequate care, patients seeking CAM might be making critical decisions without a knowledgeable professional to coordinate and integrate their total care.

### *Issues of hope and hopelessness*

Patients who believed that treatments could prolong survival have reduced risk of death and longer time to relapse (patients who did not use avoidance as a strategy to cope with cancer, and who showed concern about their disease, also had better outcomes).<sup>12,13</sup> For patients with severe progressive disease, sustaining hopefulness may require configuring, collaboratively with the patient and family, a set of personally meaningful and appropriate goals.<sup>14</sup> Reframing hope can be instrumental in assisting patients to maintain a life-affirming attitude. The basic principle that underpins all communication should be to impart a strong measure of hopefulness sensitive to multiple personal and clinical circumstances and thus appropriate to the individual. This differs from providing unrealistic expectations of positive outcome which is not only inappropriate but destructive for both patients and families. This “false hopelessness” can result in excessive despair with

measurable consequences on a patient’s physiology, outcome, and life-spirit.

### *Healing and curing*

Both of these potentials, healing and seeking remission and cure, belong together. The exception is the palliative care center. Both palliative care and hospice are specifically oriented toward promoting healing, including spiritual healing, even in the absence of cure.<sup>15</sup>

These issues are among the parameters of healing faced in OHEs for those being treated for cancer, and dictate the types of services that should be in place in a truly comprehensive care setting. OHE is a place and a system comprising people, behaviors, treatments, and the psychological and physical parameters that pertain to them.<sup>16</sup> The goal of the OHE is healing, or a dynamic process of recovery, repair, restoration, renewal, and transformation that increases resilience and wholeness in the person treated. The following section discusses the components that should be in place in the cancer-directed OHE.

## **CONSCIOUS DEVELOPMENT OF INTENTION, AWARENESS, EXPECTATION, AND BELIEF IN IMPROVEMENT AND WELL-BEING**

### *Total communication framework*

From the patient’s first encounter with the OHE through the entire treatment sequence, communication with all staff members, clinical, administrative, and laboratory based, should be life-affirming and oriented toward promoting optimal wellness for the patient. OHE staff should be aware of the possibility of fear, anxiety, depression, anger, and resentment in patients, and should provide a healthy, supportive program for connecting with and adaptively expressing the full range of emotions, while offering continuous support for practical coping strategies. Because patients learn through different modalities, it is necessary that critical specifics be presented in several formats, oral and written, accompanied by an opportunity to question what has been presented. It is known that a large majority of adults who utilize CAM never divulge this information to their physicians.<sup>17</sup> The integrative care model remedies this by introducing both conventional and alternative therapies. A full communication network requires a system for patient feedback to evaluate and determine the correspondence between what patients actually experience and what the OHE staff believes they provide.

### *Lifestyle interventions that affect expectations*

The lifestyle recommendations typical of ICC, including diet change, exercise, detoxification regimens, and psycho-

logic support, can help counteract a lost sense of control and feelings of hopelessness that are common for cancer patients.<sup>11</sup> Simple lifestyle interventions such as exercise, hypnosis, individually suited imagery techniques, adjusted progressive muscle relaxation, or self-administered acupressure to control chemotherapy-related nausea<sup>18</sup> tell the patient that feared side-effects can be managed successfully, potentially raising hopes for better toleration of therapy.

### *Cognitive-behavioral interventions to effect expectations*

Individual or small-group cognitive-behavioral therapy is particularly useful with patients facing uncertainty or negative prognostic information. It can enhance patients' abilities to recognize the positive in their situation.<sup>19</sup> Themes that can be emphasized in this therapy include reframing chemotherapy or radiation from a noxious treatment to be undergone at the hands of impersonal doctors to what patients have expressed as "infusions for life" or healing beams of light. Individualized imagery can be a useful part of this therapy (standardized imagery tends to be ineffective in speaking to the individual patient's unique experience and values).

### *Issues of meaning*

Patients with cancer often are preoccupied with the question, "Why me?" Patients who are diagnosed at a young age may have a particular struggle with this question, especially if a potentially terminal cancer threatens to take them away from young children. Patients who are following an integrative medicine or CAM program may struggle with guilt for not having adhered perfectly to widely publicized dietary recommendations for cancer prevention, or for continuing habits such as smoking or consuming alcoholic beverages. Thus, patients will benefit from individual or group counseling on a variety of scientific and philosophical subjects related to cancer risk factors, genetics, multifactorial causation, the roles of life stress in dietary habits and addictions, and the difficulty of making lifestyle changes without professional support.

The patient's religion or spiritual beliefs may have a substantial influence on the way he or she handles issues of meaning, as well as many other existential questions. It is necessary to inquire whether the patient would like to discuss spiritual or religious implications of their health care, and, if so, what aspects of their religion or spirituality they feel it is important the medical practitioner keep in mind while caring for them. Supporting and understanding individual religious beliefs and respectful attitudes toward all religious affiliations, while avoiding the inadvertent imposition of the health provider's own belief system, are fundamental to the full consideration of individual needs in the OHE. Pastoral counseling referrals can be helpful if patients appear to have religious or spiritual struggles with their can-

cers (e.g., cancer as punishment, divine providence and cancer).

The approach to issues of meaning in an OHE, or any medical environment, depends at a deeper level on the philosophy of healing. Healing, in our view, allows patients to reconnect with purpose and meaning in their lives by freeing them, as much as possible, from pain; by reducing fears and fostering biological wellness to enable deeper engagement with living; and by encouraging the examination, repair and resolution of relationship issues that come to light in the course of grappling with disease. Passion, humor, celebrations, and playfulness also hold a place in the healing process, as constant immersion in emotional heaviness and clinical detail is unhealthy and unproductive for both healers and patients.

### *Presence of an integrated OHE team*

For the patient and his or her closest support persons, seeing a team of physicians, nurses, dietitians, psychological and physical therapists, yoga, *qigong*, and other integrative practitioners develop a coherent plan of action helps to stimulate hope and positive expectation. To develop such coordinated and individualized programs it is necessary that the clinical team have regular meetings to discuss cases, and provide ongoing staff training in the most current research, applied methodologies and interventions. The OHE team should work with the patient's "team" of family and friends in supporting patients as they go through multidisciplinary regimens.

## **TRANSFORMATIVE SELF-CARE PRACTICES THAT FACILITATE PERSONAL INTEGRATION AND THE EXPERIENCE OF WHOLENESS AND WELL-BEING**

### *Knowledge of the whole person*

Effective practices that promote transformation and wholeness demand individualization responsive to the wide variety of challenges with different cancers, stages, and phases during the recovery trajectory and each patient's unique backgrounds and spiritual values. Exploration of the patient's biochemical and clinical differences, their life priorities, lifestyle habits, special stresses, physical abilities and restrictions, and existing social support network must be taken into account in the planning of an individually effective regimen of self-care practices.

### *Component practices*

For individualization, a range of transformative self-care approaches must be available. The mind-spirit practices effectively used by patients with cancer include cognitive-be-

havioral coping strategies, guided imagery, meditation, biofeedback, autonomic training, Logo therapy, yoga, *qigong/ta'i chi*, and related practices. In addition to mitigating side-effects of treatment, relaxation training and focused imagery have been found to have positive effects on a variety of emotional variables in patients undergoing cancer treatments, including tension, confusion, vigor, fatigue, overall mood, and emotional adjustment.<sup>20</sup> The traditional health care systems from which some of these interventions spring may also have specific medical and psychosocial contributions, and practitioners of some of these systems (e.g., Traditional Chinese Medicine, Ayurveda, homeopathy, naturopathy) may be integrated into the OHE. To ensure the cohesiveness of each patient's program, it can be helpful to work with traditional practitioners whom the patient is seeing outside of the OHE.<sup>21</sup>

### **TECHNIQUES THAT FOSTER A PALPABLE HEALING PRESENCE BASED ON COMPASSION, LOVE, AND AWARENESS OF INTERCONNECTIVITY**

#### *Staff selection and training issues*

An OHE will only be as effective as the personnel who provide patient care. Important characteristics of staff include being comfortable talking about crisis issues, possessing a warm presence and truly empathic listening skills, communicating with professional assurance, and using humor as well as gravity in communication. Staff members, including CAM practitioners, should be professionally trained and certified where appropriate. But even the most selective hiring should not obviate a trial period to determine the true appropriateness of new personnel to an OHE. Once hired, to acclimate new staff better, systematic orientation and training with frequent cross-training among providers is essential to creating a cohesive team of integrative caregivers. Special emphasis should be given during staff training sessions on strengthening attitudes of hope and connection with and between patients. Staff members also need specific training in dealing with their own grief that ensues when caring for and about people with advanced cancers who do not survive. High levels of emotional stress are encountered among health care workers in the cancer setting, resulting in a need for self-care in order to prevent burnout. Therefore, staff members are encouraged and trained to engage in the same self-care practices that are recommended to patients.

#### *Communication of realistic hope*

While appropriate prognostic information should not be withheld from patients, a life-affirming attitude that emphasizes hope, reframing essential data to present real potentials is an imperative. Hope, in this context, can be

thought of as belief in the possible in the face of uncertainty. Because most hopes are actual possibilities, regardless of the odds, a focus on supporting and valuing the belief in hope in no way need undermine the integrity of the caregiver's communications.

#### *Support groups*

Psychologic support groups should be available to patients for whom these would prove helpful. Support groups should be led by specially trained professionals and be time-limited but of sufficient length to accomplish desired goals. They should be structured and focused on the development of new coping strategies for living with and beyond cancer, and on the promotion of well-being rather than chiefly on expression of emotions. Evidence suggests that support groups best serve those people who do not have a close network of family or friends and emotional confidantes. Although support groups can help foster a sense of interconnectivity to counteract any possible feelings of isolation, some patients do not comfortably participate in groups and others may not see them as beneficial. Another option is "twinning," in which one patient is referred to another with the same disease and treatment regimen who has successfully negotiated its challenges. This can be especially powerful in fostering both interconnection and hope.

### **DEVELOPMENT OF LISTENING AND COMMUNICATION SKILLS THAT FOSTER TRUST AND A BOND, SOMETIMES CALLED THE "THERAPEUTIC ALLIANCE," BETWEEN PRACTITIONER AND PATIENT**

#### *Sensitivity to patient information needs*

Staff members should receive training in how to identify with a quick assessment and then meet the needs of both monitors and blunders. In providing information, respect and understanding of each patient's personal health beliefs and cultural background are basic to the therapeutic alliance that is core to healing and enhances patient satisfaction as well as greater adherence to full medical care.

#### *Assessing quality of life and emotional issues*

Staff training in applying questionnaires for the assessment for quality of life and emotional well-being should be routine. The information can be applied clinically to screen patients who could benefit from mind-spirit strategies, but who may be reluctant to communicate their emotional concerns, or who may be unaware that their emerging problems could be usefully discussed in therapeutic sessions. Item-by-item evaluation of these instruments, or use of multiple quality-of-life scales that focus on particular symptoms of interest, rather than simple analysis of overall quality-of-life

scores,<sup>22</sup> may be necessary to identify specific difficulties for patients that should be discussed in counseling.

### **INSTRUCTION AND PRACTICE IN HEALTH PROMOTION BEHAVIORS THAT CHANGE LIFESTYLE TO SUPPORT SELF-HEALING AND THE DEVELOPMENT OF SOCIAL SUPPORT AND SERVICE**

#### *Diet, supplements, exercise, and other physical therapies*

Evidence is accumulating that all of these areas of health promotion can contribute to the survival and survivorship of patients with cancer. The goal is to create an optimal internal environment for healing cancer in the biochemistry of the patient, as well as an optimal external environment. A set of dietary guidelines that is relevant to cancer control as well as cancer prevention is emerging. These guidelines include high intake of vegetables and fruit,<sup>23</sup> low inflammatory potential,<sup>24</sup> and modulation of insulin resistance.<sup>25</sup> Obesity and weight gain are emerging as risk factors for mortality in specific cancers (e.g., breast cancer), and must be addressed where appropriate.<sup>26</sup>

Thorough diagnostic testing is needed to appropriately individualize not only medical interventions, but also the use of diet, lifestyle and supplements to move the patient toward the optimal internal environment. Such testing includes laboratory assessments, questionnaires, and clinical evaluations such as validated questionnaires for assessment of quality of life, anxiety and depression; assessment of muscle strength, aerobic capacity and daily living activities; and a comprehensive nutritional/biochemical/immunological laboratory fingerprint. When possible, tumor tissue testing is implemented in order to determine which specific molecular-target therapies should be implemented. The information from these measurements allows a comprehensive diet and supplement program that promotes healing and avoids potential interaction with conventional treatments.<sup>8,22</sup>

Exercise and physical therapies also are showing evidence of substantial and specific benefit to patients with cancer.<sup>27</sup> Routine physical assessment and individualized prescription of exercise regimens are critical to ensure safety and efficacy of exercise programs.

#### *Group and individual training in behavioral health*

Group sessions in cooking demonstrations, relaxation training, and exercise classes offer both efficient teaching and opportunities for mutual support and modeling among patients. Weekend classes that last more than 1 day have been used successfully for such training. Individual coun-

seling, however, is also necessary to customize regimens to meet specific medical needs of patients.

### **RESPONSIBLE APPLICATION OF INTEGRATIVE MEDICINE VIA THE COLLABORATIVE APPLICATION OF CONVENTIONAL AND COMPLEMENTARY PRACTICES IN A MANNER SUPPORTIVE OF HEALING PROCESSES**

#### *Conventional medicine*

Both standard and experimental protocols should be available in the OHE setting. With chemotherapy, the OHE should feature both up-to-date application of drug therapies that reduce side effects, and use of modifications of chemotherapy administration procedures aimed at reducing side effects and improving efficacy, such as chronotherapeutic<sup>28</sup> or fractionated dosage schedules.

#### *Complementary practices*

There are specific areas to which complementary practices can contribute. To the extent that diet (sometimes based on traditional or alternative eating patterns), exercise, and supplementation are considered alternative or complementary, these would be included under complementary practices. Other practices, such as cancer-appropriate massage treatments, as well as other body therapies, such as orthobionomy, acupuncture, acupressure, acuscope, relaxation strategies, self-suggestion/hypnosis and imagery,<sup>29</sup> can contribute to pain management. Practices, such as aerobic and strength exercises; or promotion of flexibility, stretching and meridian, balancing through yoga, *qigong* and *t'ai chi*, can enhance ability to perform activities of daily living, and thus enhance overall well-being.<sup>30</sup> Aerobic exercise, acupuncture, hypnosis, biofeedback, and other cognitive-behavioral strategies as well as supplementation can contribute to side-effect management. Hypnosis, imagery and progressive muscle relaxation have been found to diminish chemotherapy-induced and anticipatory nausea and vomiting.<sup>31,32</sup> Supplements should support chemotherapy or other conventional treatment through such pharmacologic activities as increasing sensitivity of cancer cells to chemotherapy.<sup>33</sup>

#### *Coordination of complementary and conventional practices*

Complementary practices need to be coordinated with medical needs that arise during the treatment-recovery cycle. Diet and lifestyle practices need to be adjusted depending on whether the patient is undergoing a physiologic crisis (e.g., caused by cachexia or metastasis); going through chemotherapy, radiation or surgery; recovering

from conventional treatment; or attempting to sustain remission.

### THE PHYSICAL SPACE IN WHICH HEALING IS PRACTICED, INCLUDING CHARACTERISTICS OF LIGHT, MUSIC, ARCHITECTURE, AND COLOR AMONG OTHER ELEMENTS THAT CAN INFLUENCE THE IMPACT OF AN OHE

Little or no research is available in this area. Our recommendations are based on clinical observation and experiences with patients with cancer in the integrative medicine setting.

#### *Individual and group space*

Private spaces are demanded in the OHE for patients undergoing chemotherapy. Group spaces are essential for support sessions, exercise classes, and even informal, unstructured opportunities for mutual sharing and reinforcement among patients and their loved ones. The group space should be a comfortable “living-room-like” setting conducive to conversations during support or spontaneous group meetings. Both individual and group spaces should avoid as much as possible the sterile chrome-and-tile presentation often found in medical facilities.

#### *Integration of exercise space and access to out-of-doors area*

Exercise facilities should be accessible to patients undergoing chemotherapy, because chemotherapy-induced nausea can sometimes be relieved with mild exercise before chemotherapy treatment. With portable chemotherapy pumps, patients may be able to walk outside and exercise through the chemotherapy infusion, so access to safe out-of-doors areas and/or walking paths is beneficial.

#### *Integration of low-light spaces and well-lit spaces*

Low-light, intimate spaces are typical of rooms where massage and some other physical care therapies are given; they are also useful in some counseling situations for encouraging self-disclosure and intimacy. Most areas in the OHE should be well-lit with as much natural light and outdoor views as possible to avoid drabness and to allow sufficient light for medical procedures.

#### *Color*

While specific research on the impact of color on the moods of patients with cancer is lacking, the importance of maintaining a psychologically warm and accepting atmosphere would dictate use of “warm” rather than “cool” (i.e.,

blue) tones in many areas. However, the warm tones should not be bright or dominant (e.g., red), which appear to be anxiety-provoking.<sup>34</sup> Drab or gray colors, associated with depression, should be avoided.<sup>35</sup> Avocado and yellow-green tones are associated with nausea and typically banned from aircraft interiors and boats,<sup>36</sup> and thus should be avoided in chemotherapy, surgery, or radiation units.

#### *Aromatherapy*

Massage incorporating essential oils has been noted as being beneficial for patients with cancer.<sup>37</sup> However, inhalation aromatherapy was not found to diminish anxiety in patients undergoing radiation therapy.<sup>38</sup> As a practical matter, on the chemotherapy unit, aromatherapy in public spaces may be problematic as some patients find they cannot tolerate significant aromas. Encouragement of home use of aromatherapy for patients who desire it, and availability of aromatherapy massage in restricted areas, are options that could be explored.

#### *Music*

Use of music to reduce anxiety prior to or during troubling medical procedures such as diagnostic procedures, surgery and radiation therapy has been found to have some value.<sup>39–42</sup> Evidence of the effectiveness of group music therapy sessions and soothing sounds in lowering stress parameters in patients with cancer also exists.<sup>43</sup>

## DESIGN AND ANALYSIS ISSUES

#### *Setting*

Two settings for the study of OHEs in cancer can be distinguished. The university setting favors recruiting patients and assigning them randomly to treatment groups. Many universities have developed units to study the application of CAM practices in cancer. However, not all of these will constitute potential OHEs. Instead, a number of them are research units in which specialists in various aspects of CAM have been recruited to staff particular research studies. Thus, the degree of actual collaboration and integration between the conventional oncology staff and the integrative care programs may not be clear. Large hospitals that have research staffs and cancer CAM units that work with patients in active treatment may be considered to be functionally equivalent to universities.

The other setting in which possible cancer-directed OHEs may be operating is within the independent ICC clinic. Such private centers are more likely than universities to have established programs and staffs. Importantly, they demonstrate the economic viability of the OHE model in the current health care system, because they typically function without support from grants or institutional funds. One of the chal-

lenges in designing trials in the independent OHEs is that they are unlikely to randomize part of their current patient populations to control groups, because their patients have specifically sought out the clinics because of their integrative medicine approaches. Potential sources of patient referrals may engage in "gate-keeping," a practice that also impacts university-based trials.<sup>44</sup> The types of trials that are most likely to be carried out successfully at the independent clinics are smaller phase I and phase II type trials, including small randomized trials. Conducting clinical trials at community clinics will certainly entail some broadening of the responsibilities of clinic staff, who will need to adopt the role of clinician-researchers.

Collaboration of independent clinics and universities will also be necessary to accomplish studies in the independent clinic setting. While the clinics have the functioning OHE staff and programmatic setting, universities have necessary expertise in experimental design, data analysis, statistics, analyses of nutrition, physical assessments and chemical analysis of supplements that will be important in the execution of studies of the OHE. Collaboration could be accomplished in two ways. First, universities could give scientific support to trials carried out in the independent clinics themselves. Second, independent clinics could set up satellite locations at universities, which could then function as OHEs in the university environment. The second strategy would entail substantial investment of funds and staff time from both the university and the clinic, and would probably be more profitably pursued after positive outcomes of the independent clinic OHE have been established in preliminary studies.

There are potential problems in working with the university–OHE collaborative situation. Universities located near the independent clinics may not have staff members interested in starting research on OHEs or CAM-related topics, or they may be frankly hostile to CAM-related research. There may be a reductionistic bias in the university, and studies of whole systems, which most studies of OHEs should be, may be regarded as inappropriate. Moreover, universities may lack expertise in analysis of phytochemicals and other nutritional variables. However, there are several university centers that have substantial grant funding to explore CAM in cancer, and collaborative relationships could be established with one of these centers.

### *Nonrandomized studies*

A preliminary type of nonrandomized study in the OHE would be the qualitative or ethnographic study of the experiences of patients undergoing treatment for cancer in OHEs, perhaps conducted alongside similar studies in purely conventional treatment centers. Such exploratory studies have been conducted with patients undergoing treatment for cancer in traditional systems (e.g., Native American<sup>21</sup>) with resulting emergence of themes revealing emotional aspects of

the diagnostic and healing processes. The qualitative study of the OHE would be an important first step in the analysis of the process of healing, as contrasted with curing, and may reveal aspects of such factors as the role of healing presence that will allow more specific research questions to be developed on these important topics.

Retrospective or prospective studies of patient outcomes in a variety of independent and university OHEs may be a helpful first step in assessing the viability of current OHE models.<sup>4,\*</sup> Preliminary studies in OHEs can include phase I-type studies in which patients who have self-selected the OHE are followed prospectively for a variety of outcome variables. These populations could be compared to the literature on outcomes for patients with similar disease and stage. Studies with control groups could follow or be run concurrently with phase I studies.

Control groups for nonrandomized studies could include comparable patients in the same community or hospital who did not choose to use the OHE. However, in outcomes such as survival, these designs could be problematic, because it has been reported in one study that patients with cancer who use alternative medicine have initially worse prognoses and ultimately poorer outcomes than patients who do not seek out alternative medicine.<sup>†</sup> One reason for this may be that patients who use alternative medicine may not take advantage of efficacious conventional treatments; thus, the use of such treatments both before and after participation in studies at an OHE should be determined in assessing outcomes in this group of patients. Because of our lack of understanding of the factors that differentiate patients who use only conventional options from patients seeking alternative or integrative care, a design such as a "matched" case-control study is likely to be influenced by numerous unmeasurable factors, and thus difficult to interpret. A potential design to account for the poor prognosis of patients using alternative medicine would be to recruit a comparison group from cancer patients who are using alternative medicine in addition to conventional medicine on their own, without accessing an OHE-type clinic. A group of patients using only conventional medicine would also be added as a comparison to the community standard.

Within the context of both nonrandomized and randomized studies there is also the possibility of conducting correlational studies that may shed light on factors that are important in healing. In such studies, patients could be recruited from the community, independent or university clinics, or other trials, and given questionnaires that explore various aspects of healing. The data could then be evaluated for associations with identified outcomes and further subjected to multivariate analyses. Valuable studies of this type have already contributed to our knowledge of the dynamics of healing at a spiritual and psychological level in cancer patients, and a possible relationship to improved medical outcomes.<sup>45</sup>

*Randomized studies*

Small phase II-type randomized studies for patients undergoing chemotherapy may be able to be carried out in independent clinics as well as at university-based OHEs, as long as the independent clinics can develop adequate recruitment plans. Trials with larger patient populations may have to be restricted to the university/large hospital setting in order to take advantage of the greater ease in recruitment and randomization. It might be possible to accomplish moderate-sized studies by setting up integrative cooperative oncology groups. Larger-scale multicenter randomized studies of OHEs are not yet appropriate, since the efficacy of OHEs in cancer has not yet been established in smaller scale trials.

Special consideration needs to be given to the type of control conditions when designing a randomized study of an OHE for patients with cancer. Many patients with cancer are interested in the use of CAM techniques, and especially those who attend integrative medicine clinics evaluate closely the services offered by different clinics and trials in deciding where to go and what trials to join. Patients may be unwilling to join trials that have unacceptable control conditions as found in a randomized trial sponsored by the Office of Cancer Complementary and Alternative Medicine of the National Cancer Institute (NCI). They proposed comparing an alternative cancer treatment based on enzymes and detoxification techniques with a standard chemotherapy treatment for pancreatic cancer, widely acknowledged to be resistant to conventional treatment and associated with a short survival time. Patients who joined the trial refused to participate in the control arm; the trial was thus changed to a single-arm observational study of the alternative therapy. In the SELECT trial, a large-scale trial of the efficacy of selenium and vitamin E in prostate cancer prevention, some patients refused to participate in the placebo arm and thus were unable to enter the study.<sup>46</sup>

To attract patients to a randomized trial of an OHE, ethical considerations make it necessary to have a control condition that offers a CAM or diet and lifestyle intervention that is of some potential benefit and interest to patients. The control condition should include substantial exposure to the therapist(s) involved with the patient to balance the extensive presence of therapists inherent in an OHE. Offering a single CAM intervention such as dietary supplements or regular massages may not involve sufficient perceived personal provider interaction to be a credible sham intervention. Consideration should be given to creating a positive identity for the control intervention and being certain the control team members function as a cohesive and appropriately enthusiastic group to prevent detection by patients randomized to this group of their control status. The following are examples of CAM interventions that could be part of a control diet and lifestyle program:

- A dietary program based on American Cancer Society or American Heart Association recommendations and administered chiefly through pamphlets, without dietary individualization
- Low-dose supplementation or supplements that improve general health (possibly combined with placebo supplements)
- Simple exercise programs based on a single exercise modality such as walking
- Simplified individual and/or group psychologic counseling with models that have not been demonstrated to have benefits in cancer and do not emphasize cancer coping skills, but may have general benefits (e.g., reminiscence therapy)<sup>47</sup>
- Occasional massage therapy sessions aimed at relaxation rather than treatment of specific clinical problems arising with cancer treatment or symptoms
- Self-administered acupressure using points not directly relating to cancer treatment or symptoms, or sham acupuncture points.<sup>48</sup>

*Outcomes*

*Quality of life and related variables.* Several instruments exist for measurement of this variable, including the EORTC quality of life questionnaire, the FACT (Functional Assessment of Cancer Therapy), and FACIT (Functional Assessment of Chronic Illness Therapy) systems. Effect on activities of daily living is also an important variable for patients during treatment and has been assessed in many studies. Pain assessments are especially relevant for patients with advanced disease. Fatigue, a widespread symptom among cancer patients, can be measured with several scales. A standard system (the NCI Common Toxicity Criteria) exists for grading of cancer treatment toxicities, and this should be used in studies of chemotherapy and radiation. Patient satisfaction measurements can be conducted using a program evaluation type of model.<sup>49</sup>

A related set of outcome variables pertains to the assessment of physical fitness in the patient with cancer, a critical role in the patient's ability to cope with activities of daily life. Relevant measures on these variables include body composition analysis on percentage of lean tissue or muscle mass of total body weight and body mass index. Standard physical therapy measurements of strength, aerobic capacity, and flexibility should also be part of any exercise assessment program. Adherence to exercise recommendations should be measured, typically using structured journals.

Measurements of nutritional status can include standard dietetic evaluations, especially in the case of malnourished patients experiencing cachexia or anorexia. Repeated 24-hour food recall questionnaires administered by telephone are a standard practice in nutritional research; a multimodal approach that uses both recall and food frequency ques-

tionnaires gives even more information.<sup>50</sup> Computer programs allow characterization of data from these questionnaires as to calories, percentages of macronutrients and content of micronutrients. Assessment of adherence to supplement recommendations can be tracked using conventional methods such as pill counts. The greater problem lies in the use by patients of agents outside the recommended set of supplements.<sup>51</sup> This should periodically be assessed by specific questionnaires.

Certain biologic markers can be assessed to give more insight into the nutritional impact of dietary/supplement programs. These include variables such as blood levels of phytonutrients or essential fatty acids, C-reactive protein (a measurement of inflammation), C-peptide, blood sugar, insulin, insulin-like growth factor-1 (IGF-1), a variety of oxidative stress measurements, cholesterol, and triglycerides.

Emotional and spiritual issues also need to be measured in assessing the overall effect of the OHE.<sup>52</sup> Measuring distress levels, particularly anxiety and depression, using standardized questionnaires such as the Hospital Anxiety and Depression Scale (HADS) provides clinicians with an indicator for patient intervention and investigators a valid assessment of the effectiveness of programs designed to relieve identified emotional difficulty surrounding the disease and its treatment. The Mental Adjustment to Cancer scale measures coping styles related to fighting spirit, helplessness/hopelessness, anxiety, fatalism and avoidance. Some instruments have been developed specifically to assess spiritual well-being in patients with cancer. The FACIT Spiritual Scale measures meaning and purpose, harmony and peace, and strength in faith and spiritual beliefs. A scale not specifically related to cancer, the Principles of Living Survey, measures spiritual practices, spiritual growth and embracing life's fullness. Direct inquiries or journals can be used in assessing participation in yoga, meditation and other practices. To measure the patient's perception of positive personal change after experiencing a traumatic, life altering event, the 1996 Post-Traumatic Growth Inventory by Tedeschi and Calhoun, a 21-question, self-report inventory, can be used.

There are also other variables linked to and embedded in the clinical relationship in medicine, such as the nature and variety of healing relationships, issues of timing and attunement of healers and patients, and distinction of different types of healing encounters. This topic has previously been discussed by Miller and colleagues.<sup>53</sup> These issues lend themselves to systematic qualitative inquiry, since quantitative assessments to fully capture this information are currently lacking. We endorse the potential value of the "double-helix" research design proposed by Miller et al.<sup>53</sup> in adding studies of healing relationships and other qualitative questions to the research design of a randomized trial, cohort study or matched case-control design.

### *Survival-related variables*

The classic outcome in trials of chemotherapy and radiotherapy is response to treatment expressed as shrinkage of solid tumors that can be visualized on successive computed tomography (CT) scans. While response is not always correlated with longer survival, the variable most highly valued by patients with cancer, it is necessary to include tumor response to treatment as a variable in studies of OHE, if only for comparison with studies of conventional regimens. There are a variety of survival and other time-linked variables that should also be assessed. These include overall survival from diagnosis or from metastasis, disease-free interval after treatment and time to recurrence. Intermediate endpoints relating to survival that may be of relevance in particular cancers include tumor markers, surrogate markers of response such as immune system impacts, and innovative application of newly recognized molecular targets.

For situations in which survival is a relevant variable, studies designed and powered to detect the magnitude of survival differences should be conducted because of their existential importance to cancer patients. Observational studies of patients at our clinic indicated that patients with metastatic breast and prostate cancer attending the clinic had median survival times about twice those reported in the literature for patients with similar conditions.\*†

## SELECTION OF SUBJECTS

Selection of subjects is based on accessibility of subjects (including the problems of gate-keeping mentioned above), ability to recruit the large numbers of subjects needed for phase II and III trials, survival variables, and inclusion/exclusion criteria that ensure that patients will be able to comply with the various interventions that make up the OHE. Studies that demand large numbers of patients will necessarily have to be done among common cancers such as breast, prostate, lung, colon and bladder cancers and melanoma.

Patients with advanced disease are more likely to seek out CAM and integrative medical techniques, and survival-oriented studies in later-stage disease may be implemented in these settings. Advanced cancers in which expected survival is typically longer include advanced breast, prostate, melanoma, ovarian, glioblastoma multiforme, cervical cancers, and colorectal cancer with regional metastases. However, some diseases with particularly short survival times might be poor selections for survival-oriented studies because the short expected survival would not allow time for the OHE interventions to take effect, and because disease burden may be too great for even combined conventional and CAM interventions to modify outcomes. Studies of quality of life-related variables, however, would be feasible and advisable with these populations.

While inclusion/exclusion criteria for trials in the OHE should be dictated by many of the standard and predictable

measures for cancer clinical trials, there is an additional consideration for trials of cancer-directed OHEs or cancer CAM. Often patients with advanced cancer present at CAM clinics for treatment after several conventional therapies have failed to produce desired results. While extending the survival time of these patients is a substantial clinical challenge that integrative clinics may be successful in meeting, the very fact that the patient survived through several conventional therapies might mean that they represent an unusual subpopulation. In the typical cancer survival curve, many patients die early in the disease, while other patients, who are perhaps healthier to begin with or who have less aggressive disease, live for longer or even extended periods. Patients who present at alternative clinics after surviving several treatments may belong to the latter group, and thus may not be representative of patients with cancer in general.

The time between initial diagnosis or diagnosis of metastatic disease and presentation at a clinic is called lag time. Some authors have discussed the lag time issue in the context of CAM in cancer, and point out that it may contribute to unusually long survival statistics in cancer patients who use CAM.<sup>54</sup> Thus, in determining inclusion/exclusion criteria for OHE trials in cancer, lag time should be taken into account either by stratified randomization dependent on lag time, or by cutoff periods (i.e., only patients within 6 months of diagnosis admitted to trials). Lag time should be approached with some consideration of the disease and treatments being studied: patients with metastatic breast cancer, especially those with bone metastases, are frequently treated hormonally before being recommended for chemotherapy.<sup>55</sup> In studies of patients receiving chemotherapy for metastatic breast cancer, a longer lag time would thus be acceptable. Other considerations for inclusion/exclusion criteria are similar to those used in conventional cancer trials. Exclusions based on short expected survival times might be inappropriate for observational trials in which comparability with the community cancer treatment setting would be of value. For randomized studies, exclusions based on short expected survival would be tolerable because the comparison groups would also be subject to the same exclusion criterion.

Descriptors for the patient populations should include all those normally cited in studies of cancer treatment: age, gender, disease stage, prognostic factors (selected according to the particular cancer), previous conventional and alternative treatments, socioeconomic status or education and performance status. Other variables that may be of interest include religious/spiritual affiliations, family constellation, occupation, distance from home to treatment center, and presence of anxiety and depression.

### **FAMILY AND OTHER SUPPORTIVE ELEMENTS**

The presence of a supportive network of family, friends, religious affiliates, and other sources of social support can

assist cancer patients in coping with disease and treatment. At the same time, the stresses of disease and treatment can affect all members of the support network.<sup>56</sup> Some results of these impacts can include role reversals in the family structure, employment cutbacks, financial instability, and severely diminished social interaction. Family stresses and tensions can also intensify patient unease; for example, family conflicts over treatment decisions involving CAM and cancer have been discussed in the literature.<sup>57</sup> While supporting the patient with a full complement of care, the cancer-directed OHE should also offer services to family members and others acting as primary caregivers to patients with cancer.

Family members may support or negate decisions to change diet, which can promote or undermine adherence to diet recommendations. Development of assessment models to determine real experienced support, lack thereof, or troubling interrelationships among family and friends of patients with cancer undergoing integrative treatment may help in evaluating the ability of the OHE to impact lifestyle change. Such measurements could also help to identify who would most benefit from specific supportive interventions. Qualitative research in this area will be a necessary initial step in the development of such models<sup>58</sup> and in the design of effective measurements.

### **INVESTIGATOR TEAM**

There are two groups of investigator teams necessary for research on cancer-directed OHEs, the OHE clinical team potentially at an independent OHE clinic, and the research specialist team. The OHE team will consist of physicians, nurses, allied health professionals such as physical therapists, and CAM professionals (certified in their disciplines). In addition, if the OHE is an independent clinic, an additional research staff will be necessary onsite: research coordinator, clinical research associate, and grant manager. If the research program represents a large addition to the clinic population, additional clinical staff may need to be hired. Staff with ability to write grant proposals and papers may be located in the OHE as well. The clinical team will need to meet frequently to discuss clinical progress of patients and track research project needs. The clinical staff may also need training in research and research ethics. An analogous team will need to be in place for a CAM control intervention.

The research specialist team will typically be located at a university, hospital, or research institute. Suggested specialties are clinical trial design, statistical analysis and data management, nutrition and dietary assessment, psycho-oncology, exercise physiology/rehabilitation, pharmacognosy (chemistry and pharmacology of natural dietary supplements), and grant administration. If the OHE clinic is located at the university, a dynamic program head will be

needed to represent the clinic's interests in the university administration. The principal investigator for the overall project may be located at the university, where facilities for grant submission and management are easily available. Depending on expertise and other affiliations, however, the principal investigator could also be located at an independent OHE with specialized research activities subcontracted to the university. The model of the clinician-researcher is common in the academic setting, and there is no reason that a similar model could not be operative in the integrative care OHE. The project will need to be managed with regular meetings of all project staff, in addition to subgroup meetings for the OHE and control group programs, and meetings with the university or OHE staff involved in data collection and analysis aspects of the program.

### SUGGESTED HYPOTHESES FOR TESTING

For the study of OHEs *per se*, we recommend studying whole systems and entire interventional environments, rather than individual CAM interventions such as massage or a single type of supplement. The following are a set of hypotheses to be tested that we believe should be emphasized early in the work on the role of OHEs in cancer.

#### *Nonrandomized studies*

1. Qualitative or ethnographic studies of patients treated for cancer in OHEs should be conducted to develop more specific hypotheses about the factors that differentiate OHEs, and the experiences of their patients, from non-OHE treatment centers. Such studies may allow development of hypotheses and methods of study of such important questions as the role of healing presence in the OHE.
2. Quality of life in patients undergoing adjuvant or neoadjuvant chemotherapy or radiation in OHEs, or therapy for metastatic disease, as measured by a variety of quality of life measurements, physical fitness, and symptom control, is better than that in a control group receiving treatment in conventional community clinics or university hospitals, matched for disease, stage, age, prognostic factors, and socioeconomic status. Simple prospective studies of quality of life in these populations could also be conducted, with comparisons to data in the literature of quality of life of patients undergoing chemotherapy. In this case, the type of chemotherapy would be the main variable to be matched.
3. Survival or tumor response/duration of remission in patients receiving conventional treatment and long-term follow-up in OHEs is as good as or better than that recorded in the literature for patients with similar disease, stage, age, prognostic factors, and socioeconomic status. Comparisons could also be made with concurrent control groups receiving treatment in conventional settings.
4. Basic data are needed comparing the demographic, social and medical status of patients who present at OHEs for cancer treatment versus those who present at conventional clinics.
5. Studies are needed to test the hypothesis that patients undergoing nutritional, fitness, stress management, and supplementation programs at OHEs actually adhere to the recommendations of the programs.

#### *Randomized studies*

1. Preliminary questions for randomized studies are whether patients can actually be recruited to randomized studies of OHEs; what sort of control conditions can be offered that will attract patients to the studies and that will represent ethically sound commitments of their time, energy and survival potential; and whether patients in these groups can detect their control status. Small-scale randomized studies can be used to examine these questions about recruitment and appropriate control conditions.
2. Randomized trials comparing quality of life, fitness and nutritional status in patients undergoing cancer treatment at OHEs and in control environments are a priority once the ability to recruit appropriate control populations has been documented. The most common cancers should be targeted first, because the burden of patient morbidity and familial/societal disruption is great for these cancers.
3. Randomized studies of nutritional variables that impact survival as well as well-being should be conducted, especially for the issue of weight gain and loss in patients with breast cancer. The frequent utilization of fitness and nutritional interventions in integrative medicine clinics may have a positive impact on chemotherapy-related weight gain, and this hypothesis needs to be tested in the OHE setting. The impact of OHE nutritional programs on insulin, blood sugar, and IGF-1 for cancers in which these play a role should be studied.
4. Randomized studies of survival-related outcomes should be conducted, especially for those cancers in which non-randomized outcome studies indicate possible effectiveness of OHEs or CAM interventions in increasing survival. Overall survival, tumor response to chemotherapy/radiotherapy, disease-free intervals and intermediate outcomes such as tumor markers in certain cancers (e.g., prostate-specific antigen [PSA] in prostate cancer) are potential outcome variables.

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