

# Fatigue in Cancer Survivors

## Maintaining the Light at the End of the Tunnel

LAURA HUGHES  
DANIEL LANDER, ND, FABNO

With advances in early detection and treatment strategies, fewer people are dying from cancer. There are more than 13 million cancer survivors in the United States alone – a number which is expected to increase to 18 million by the year 2022.<sup>1</sup> The National Cancer Institute (NCI) Department of Cancer Survivorship uses the term “cancer survivor” to describe any individual diagnosed with cancer, from the moment of diagnosis through the rest of his or her life. This broad definition can be

further divided into 3 distinct phases: the time from diagnosis until the end of initial treatment, the transition from treatment to extended survival, and long-term survival.<sup>1</sup> The patient experience during each phase of survivorship is complex and challenging. However, it is well reported that those on the path to long-term survival, including those considered “cured” from disease, are often left to manage the physical and psychosocial consequences of their treatments without adequate support.

It is estimated that 30% of cancer survivors experience distressing fatigue

Cancer-related fatigue is at odds with what is meant by being a “survivor.”

that may persist for more than 10 years post-treatment.<sup>2</sup> This severely impacts quality of life and can lead to additional co-morbidities. Support for pharmacological interventions for cancer-related fatigue is limited.<sup>3</sup> The goal of this paper is to describe how naturopathic

medicine can play a role in alleviating the burden of fatigue in cancer survivors. This will be done by elucidating why fatigue has been an underdiagnosed and consequently undertreated symptom of cancer survival, and then briefly reviewing the latest evidence for available naturopathic interventions.

### Barriers to Treatment

Persistent fatigue in cancer survivors cannot be managed if it is not reported. One study has attempted to identify the barriers leading to a delay in treatment by asking for “additional comments” at the end of a fatigue severity questionnaire.<sup>4</sup> Upon analysis, it was found that cancer-related fatigue is at odds with what is meant by being a “survivor.” Study participants reported that there is such a societal emphasis on conquering and beating cancer, it is difficult to identify as a cancer survivor and to accept that their own story might be different than this one of hope. Furthermore, it is a struggle when support systems do not recognize the difference between looking well and feeling well. In the hierarchy of disease, cancer tops the list for many survivors, and since they are alive, they feel that they have no right to complain about anything that comes after treatment or cure. There was a general consensus among study participants that following the acute treatment phase, their functional status was no longer a concern to their medical team. They felt that follow-up appointments were to ensure that the cancer hadn't returned, not to deal with their new lives and challenges.<sup>4</sup>

It is important for naturopathic doctors to understand these schemas, because the nature of our medicine allows us the contact time to delve into such concerns. Educating patients with active cancer about the potentially enduring effects of their treatment may lead to greater awareness about what they can expect after treatment cessation,<sup>4</sup> and, consequently, to an increase in the number of patients who report lingering symptoms. One of the first studies aimed at understanding fatigue from the patient's perspective suggests that being able to name or assign cause to an experience allows one to give it a place in one's life.<sup>5</sup> Having their experience validated by a medical professional may decrease the distress associated with persistent cancer-related fatigue, and empower survivors to engage in available therapies.

### Naturopathic Interventions

To improve the management of cancer survivors suffering from fatigue after the completion of primary treatment, the American Society of Clinical Oncology (ASCO) very recently adapted the pan-Canadian guideline on screening,

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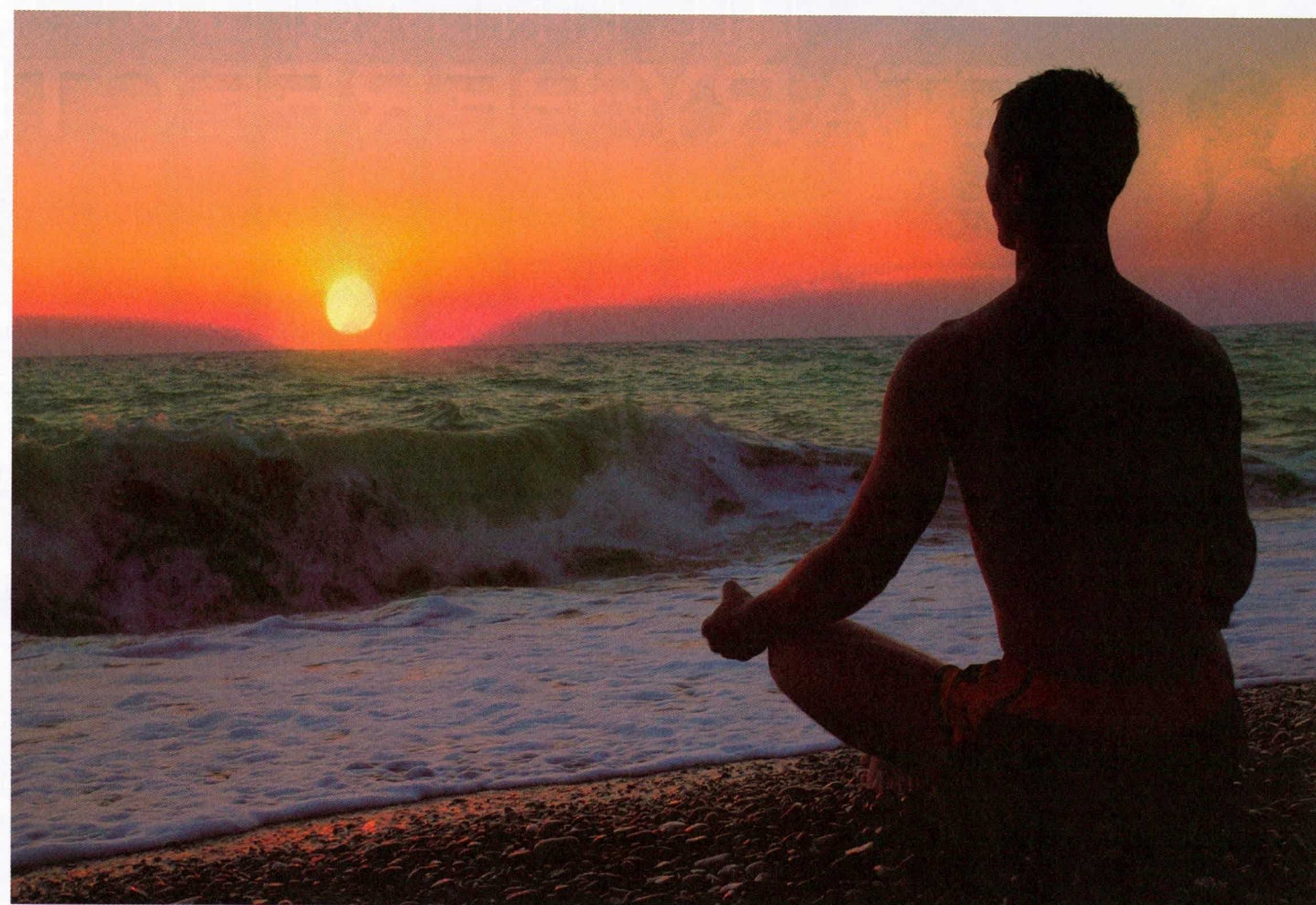
assessment, and care of cancer-related fatigue in adults with cancer, the National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines) for Cancer-Related Fatigue, and the NCCN Guidelines for Survivorship into 1 set of recommendations.<sup>6</sup> Based upon review of the literature until early 2013, exercise and psychosocial interventions (ie, cognitive behavioral therapy) were identified as being clearly beneficial for management of fatigue.<sup>6</sup> Here, we summarize the remaining treatment guidelines in the context of the latest research.

### Mindfulness

The ASCO considers mindfulness potentially beneficial. Results from a recent randomized controlled trial (RCT) by Johns et al<sup>7</sup> strengthens this recommendation by showing that a mindfulness-based stress reduction program not only improved the fatigue of cancer survivors randomized to the intervention, but that the improvement was maintained at 6 months of follow-up (Table 1, online). From this study, it appears that mindfulness is well accepted by cancer survivors, and it is a therapy that they can continue on their own after the conclusion of a formal program.<sup>7</sup>

### Acupuncture

ASCO considers acupuncture potentially beneficial. The most up-to-date meta-analysis of RCTs set out to focus on cancer survivors who completed post-primary treatment.<sup>8</sup> However, due to the limited number of studies of such individuals, the inclusion criteria were expanded



to include cancer patients undergoing treatment. In the analysis of 7 RCTs, no statistically significant difference between acupuncture and sham acupuncture was found. However, heterogeneity between studies was an issue. Since the release of ASCO guidelines, 2 additional RCTs have been published on acupuncture for fatigue in post-treatment cancer survivors (Table 1, online). In a group of 30 breast cancer survivors, Smith et al showed a statistically

significant reduction in fatigue for acupuncture vs wait-listed controls after 2 weeks.<sup>9</sup> In contrast, Deng et al observed no statistically significant difference between acupuncture and sham acupuncture in 74 cancer patients, although both groups experienced a reduction in fatigue.<sup>10</sup> Smith et al identified that the treatment effect was greatest when acupuncture was administered twice a week, and that less frequent treatment may explain outcome differences.<sup>9</sup> There are also power limitations to published acupuncture studies. A larger RCT has been planned to address this.<sup>9</sup>

In an editorial<sup>11</sup> that accompanied the publication of the RCT by Smith et al, Molassiotis suggests that future studies should also include objective primary (physiological) outcomes in order to show how acupuncture works for cancer-related fatigue, consensus around use of traditional Chinese medicine acupuncture concepts vs Western medical concepts, and which specific points to use.<sup>11</sup>

### Yoga

The ASCO considers yoga potentially beneficial. Two recent RCTs strengthen a role for this intervention (Table 1, online). In a study of 200 breast cancer survivors, a 12-week hatha yoga intervention was not only

associated with a statistically significant improvement in fatigue scores compared to wait-listed controls, but also significantly lower blood concentration of tumor necrosis factor-alpha (TNF- $\alpha$ ) and interleukin (IL)-6 after 3 months of practice.<sup>12</sup> Similarly, another study of 31 breast cancer survivors showed that compared to controls, a 12-week intervention of Iyengar yoga was associated with a statistically significant reduction in gene expression of a number of inflammatory markers, in addition to an improvement in fatigue scores after 3 months.<sup>13</sup> A critique of many interventions for cancer-related fatigue is that it is impossible to tell how the therapy works when objective, physiological outcomes are not measured. It has been suggested that this lack of measurable biomarkers has led to the failure of cancer-related fatigue being classified as either an acute or chronic model of illness, which in turn has led to patients' concerns being dismissed by some medical practitioners.<sup>4</sup> Therefore, these trials are an important contribution to the literature.

### Additional Naturopathic Modalities

The ASCO did not include any dietary or botanical interventions in their guidelines; however, from a naturopathic standpoint, it would be remiss to not consider these important factors in healing. Observational

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evidence suggests that there are dietary differences between fatigued and non-fatigued survivors (Table 1, online). Studies by Alfano et al<sup>14</sup> and Zick et al<sup>15</sup> support the hypothesis of an inflammatory basis for fatigue in cancer survivors, and a potential role for diet in mitigating this inflammation. Intriguingly, due to their use of a multidimensional fatigue scale, Alfano et al showed that markers of inflammation appeared more associated with physical fatigue than psychological fatigue. Hopefully, the first RCT of omega-3 fatty acids in cancer survivors designed with fatigue as outcome measure<sup>16</sup> will shed light on the potential of dietary interventions in this population.

From a botanical perspective, *Panax quinquefolius* (Wisconsin ginseng) shows promise as an intervention to improve post-cancer fatigue (Table 1, online). In a double-blind RCT, 2000 mg of *Panax quinquefolius* per day improved fatigue in cancer survivors compared to placebo over an 8-week period.<sup>17</sup> Furthermore, there was no difference in toxicity and reported side effects between treatment arms. This intervention included both patients who were undergoing active treatment and who

had finished treatment; those in the former group reported slightly greater benefit from the intervention. Further studies are needed, but given the limited evidence supporting pharmaceuticals as a treatment for fatigue in cancer survivors,<sup>3</sup> prescribing *Panax quinquefolius* is worth considering as a safe and effective alternative.

**Conclusion**

Fatigue contributes greatly to the morbidity of cancer survivors. In 2006, the Institute of Medicine (IOM) identified that cancer survivors are at risk of being lost to follow-up by scientific research and the healthcare system, and recommended that oncology teams implement survival-care plans (SCP) for each patient. The goal of the SCP is to promote care coordination, improve communication between physicians, increase primary-

care practitioner knowledge regarding survivorship care, and deliver education to survivors about their future healthcare needs.<sup>18</sup> Although patients report a high degree of satisfaction with SCPs, there have been significant barriers to wide-scale implementation.<sup>18,19</sup> Naturopathic doctors are in a position to help identify and treat cancer survivors burdened with persistent fatigue. While it is imperative that practitioners familiarize themselves with up-to-date screening, assessment, and management guidelines, it is important to remember that individualized medicine is especially important for cancer survivors as they struggle to identify with their own unique journeys. ▀

Table 1 available online at [ndnr.com](http://ndnr.com)



**Laura Hughes** is a 3rd-year naturopathic student at the Canadian College of Naturopathic Medicine in Toronto. She obtained her BSc and MSc in nutritional science from the University of Guelph, and her PhD in cancer epidemiology from Maastricht University. A keen explorer of the world, she participated in the 2014 CCNM brigade to Nicaragua with Natural Doctors International (NDI), and is co-leading an upcoming CCNM global health trip to India. In addition to oncology, she has a special interest in palliative care, and hopes to incorporate both into her future practice.



**Daniel Lander, ND, FABNO**, is a fellow of the American Board of Naturopathic Oncology (FABNO). He holds a BSc degree in nutritional sciences from the University of Guelph, and graduated from CCNM in 2006. His clinical training included a residency at the Cancer Treatment Centers of America. He is currently an associate professor at CCNM, teaching oncology and clinical nutrition, and supervises 4th-year interns in adjunctive cancer care at the Robert Schad Naturopathic Clinic at CCNM. He also maintains a small private practice in Toronto, in which he focuses in integrative oncology, supporting people with cancer during and after their conventional care.

**REFERENCES**

1. Siegel R, DeSantis C, Virgo K, et al. Cancer treatment and survivorship statistics, 2012. *CA Cancer J Clin*. 2012;62(4):220-241.
2. Bower JE. Treating cancer-related fatigue: the search for interventions that target those most in need. *J Clin Oncol*. 2012;30(36):4449-4450.
3. Minton O, Richardson A, Sharpe M, et al. Drug therapy for the management of cancer-related fatigue. *Cochrane Database Syst Rev*. 2010;(7):CD006704.
4. Pertl MM, Quigley J, Hevey D. 'I'm not complaining because I'm alive': barriers to the emergence of a discourse of cancer-related fatigue. *Psychol Health*. 2014;29(2):141-161.
5. Holley S. Cancer-related fatigue. Suffering a different fatigue. *Cancer Pract*. 2000;8(2):87-95.
6. Bower JE, Bak K, Berger A, et al. Screening, assessment, and management of fatigue in adult survivors of cancer: an American Society of Clinical Oncology clinical practice guideline adaptation. *J Clin Oncol*. 2014;32(17):1840-1850.
7. Johns SA, Brown LF, Beck-Coon K, et al. Randomized controlled pilot study of mindfulness-based stress reduction for persistently fatigued cancer survivors. *Psychooncology*. 2014;24(8):885-893.
8. Zeng Y, Luo T, Finnegan-John J, Cheng AS. Meta-Analysis of Randomized Controlled Trials of Acupuncture for Cancer-Related Fatigue. *Integr Cancer Ther*. 2013;13(3):193-200.
9. Smith C, Carmady B, Thornton C, et al. The effect of acupuncture on post-cancer fatigue and well-being for women recovering from breast cancer: a pilot randomised controlled trial. *Acupunct Med*. 2013;31(1):9-15.
10. Deng G, Chan Y, Sjoberg D, et al. Acupuncture for the treatment of post-chemotherapy chronic fatigue: a randomized, blinded, sham-controlled trial. *Support Care Cancer*. 2013;21(6):1735-1741.
11. Molassiotis A. Managing cancer-related fatigue with acupuncture: is it all good news for patients? *Acupunct Med*. 2013;31(1):3-4.
12. Kiecolt-Glaser JK, Bennett JM, Andridge R, et al. Yoga's impact on inflammation, mood, and fatigue in breast cancer survivors: a randomized controlled trial. *J Clin Oncol*. 2014;32(10):1040-1049.
13. Bower JE, Greendale G, Crosswell AD, et al. Yoga reduces inflammatory signaling in fatigued breast cancer survivors: a randomized controlled trial. *Psychoneuroendocrinology*. 2014;43:20-29.
14. Alfano CM, Imai Y, Neuhouser ML, et al. Fatigue, inflammation, and omega-3 and omega-6 fatty acid intake among breast cancer survivors. *J Clin Oncol*. 2012;30(12):1260-1267.
15. Zick SM, Sen A, Han-Markey TL, Harris RE. Examination of the association of diet and persistent cancer-related fatigue: a pilot study. *Oncol Nurs Forum*. 2013;40(1):E41-E49.
16. McDonald C, Capra S, Coll J. The muscle mass, omega-3, diet, exercise and lifestyle (MODEL) study - a randomised controlled trial for women who have completed breast cancer treatment. *BMC Cancer*. 2014;14:264.
17. Barton DL, Liu H, Dakhil SR, et al. Wisconsin Ginseng (*Panax quinquefolius*) to improve cancer-related fatigue: a randomized, double-blind trial, N07C2. *J Natl Cancer Inst*. 2013;105(16):1230-1238.
18. Forsythe LP, Parry C, Alfano CM, et al. Use of survivorship care plans in the United States: associations with survivorship care. *J Natl Cancer Inst*. 2013;105(20):1579-1587.
19. Mayer DK, Nekhlyudov L, Snyder CF, et al. American Society of Clinical Oncology clinical expert statement on cancer survivorship care planning. *J Oncol Pract*. 2014;10(6):345-351.

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