

## ARTICLES

# Cancer Chemotherapy-Related Symptoms: Evidence to Suggest a Role for Proinflammatory Cytokines

Lisa J. Wood, PhD, BSN, Lillian M. Nail, PhD, RN, FAAN,  
April Gilster, RN, Kerri A. Winters, PhD, and Collin R. Elsea, BS

**Purpose/Objectives:** To provide an overview of the evidence that supports a role for the proinflammatory cytokines interleukin-1 $\beta$  (IL-1 $\beta$ ), tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), and interleukin-6 (IL-6) in the etiology of cancer chemotherapy-related symptoms.

**Data Sources:** Electronic nursing, psychology, and medicine databases; online meeting abstracts; and personal experimental observations.

**Data Synthesis:** Substantial evidence implicates the proinflammatory cytokines IL-1 $\beta$ , TNF- $\alpha$ , and IL-6 in the etiology of chemotherapy-related anorexia, cachexia, anemia, pain, sleep disturbance, fatigue, and depression.

**Conclusions:** Further investigation into the role of these cytokines in the genesis of chemotherapy-related symptoms is warranted. The development of appropriate animal models likely will be key to understanding the relationship among cancer chemotherapy, proinflammatory cytokines, and symptoms.

**Implications for Nursing:** Nurses traditionally have been leaders in symptom management. The symptoms experienced by patients undergoing chemotherapy have a profound negative impact on quality of life and patients' ability to receive prescribed treatments. An understanding of potential mechanisms underlying the physiologic and behavioral consequences of chemotherapy administration will aid nurses in the development of interventions to effectively manage chemotherapy-related symptoms.

### Key Points . . .

- Patients receiving chemotherapy experience a constellation of unpleasant symptoms such as fatigue, anorexia, anemia, cachexia, depression, pain, and sleep disturbance. All of the symptoms can have profoundly negative effects on quality of life and patients' ability to receive prescribed treatments.
- Clinical investigators have hypothesized that proinflammatory cytokines play a role in the genesis of chemotherapy-related symptoms.
- The idea of a common underlying mechanism for several chemotherapy-related symptoms contributed to current interest in understanding the structure of the relationships among concurrent symptoms, often referred to as symptom clusters, and also generated concern that the long-standing tradition of studying symptoms in isolation may have obscured the possibility that the symptoms might be produced by the same mechanism.

Poulter, & Hayley, 2005), which also occur in patients with cancer. Although sickness-behavior-like symptoms can exist in treatment-naïve patients, where they often are associated

Patients undergoing cancer chemotherapy with mechanistically distinct drugs display many of the classic symptoms of sickness behavior caused by the production of the proinflammatory cytokines interleukin-1 $\beta$  (IL-1 $\beta$ ), tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), and interleukin-6 (IL-6) by macrophages and other immune cells in response to an immune challenge (Bluthe, Laye, et al., 2000; Bluthe, Michaud, Poli, & Dantzer, 2000). For instance, similar to people with viral or bacterial infections, patients with cancer complain of fatigue, experience loss of appetite and pain, and suffer sleep disturbance (Lee, Dantzer, et al., 2004). Prolonged production of proinflammatory cytokines also can lead to a variety of symptoms, including anemia (Means, 2004), fat and muscle wasting (cachexia) (Argiles, Busquets, & Lopez-Soriano, 2005), and depression (Anisman, Merali,

*Lisa J. Wood, PhD, BSN, is an assistant professor in the School of Nursing at the Oregon Health and Science University (OHSU) Cancer Institute in Portland; and Lillian M. Nail, PhD, RN, FAAN, is the Dr. May E. Rawlinson Distinguished Professor and a senior scientist, April Gilster, RN, is a predoctoral student, Kerri A. Winters, PhD, is an assistant professor, and Collin R. Elsea, BS, is a senior research assistant, all in the School of Nursing at OHSU in Portland. This work was supported, in part, by pilot funding from the National Institute of Nursing Research Exploratory Nursing Research Center Grant 1P20NR07807-03. Wood is a recipient of an American Cancer Society Research Scholar Grant. Mention of specific products and opinions related to those products do not indicate or imply endorsement by the Oncology Nursing Forum or the Oncology Nursing Society. (Submitted April 2005. Accepted for publication October 6, 2005.)*

Digital Object Identifier: 10.1188/06.ONF.535-542