

# State of the Science: Stress, Inflammation, and Cancer

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2013 State-of-the-Science Lectureship

**D**iagnosis with a life-threatening illness such as cancer is almost universally experienced as stressful. The construct of stress has received substantial consideration as a correlate or predictor of psychological and health outcomes (Andersen et al., 2004) and has often been conceptualized within a stress and coping framework (Lazarus & Folkman, 1984). Biobehavioral factors have long been thought to affect many health processes. The relationship between inflammation of stress and cancer originated centuries ago and is now recognized as a facilitating characteristic of cancer (Mantovani, Allavena, Sica, & Balkwill, 2008). In addition, stress and the stress response are probable mediators of the effects of psychological factors on cancer, and specifically on progression of cancer (Powell, Tarr, & Sheridan, 2013). A substantial amount of new research activity has enlightened scientists and clinicians on the neuroendocrine regulatory function of physiologic pathways in cancer growth and progression (Lutgendorf & Sood, 2011). However, in spite of considerable research over the past several decades, inconsistent data remain a challenge in establishing evidence-based pathways between behavioral risk factors and cancer initiation.

The current state-of-the-science article focuses on stress and inflammation in the context of cancer and will address conceptual definitions, physiologic mechanisms linking stress and inflammation to cancer, and elusive measurement issues. In addition, this article describes approaches that may have value as preventive strategies for reducing risks of cancer progression.

## Conceptual Definitions and Connections

Although extensively studied, the definition of stress has varied widely. Stress has frequently been defined as the experience of a negative life event or the occurrence of an event without adequacy to effectively cope with it

(Lazarus & Folkman, 1984). Stress can further be characterized by psychological and physiologic responses to an event or circumstance that is perceived as threatening, harmful, or challenging, and typically includes an individual's appraisal of a stressor to indicate his or her perceived level of stress (Lazarus & Folkman, 1984; Kemeny & Schedlowski, 2007). As a result, cognitive appraisal is an important component of stress. Stress is normal; however, when the cellular repair mechanisms cannot catch up with damage, major inflammation can occur (Lutgendorf, Sood, & Antoni, 2010; Thaker & Sood, 2008). It has been well documented that stress increases inflammation at the cellular level, which can directly influence responses from the hypothalamic-pituitary-adrenal (HPA) axis and the sympathetic nervous system (SNS), as well as contribute to changes in health-related outcomes (Antoni, 2013). Although some stress can be beneficial, excessive stress throughout a long period of time can result in inflammation. Although stress has been described by many terms, "at the cellular level it has been called inflammation" (Xing, 2012, p. C7).

Inflammation is a physiologic reaction generated by the body in response to injury, infection, or irritation (Reuter, Gupta, Chaturvedi, & Aggarwal, 2010). The links between inflammation and cancer can be viewed as two pathways: "An extrinsic pathway, driven by inflammatory conditions that increase cancer risk, and an intrinsic pathway, driven by genetic alterations that cause inflammation and neoplasia" (Mantovani et al., 2008, p. 436). Inflammation can be either acute or chronic. Acute inflammation is an initial stage of inflammation, called innate immunity, which is mediated through activation of the immune system and can help ward off infections (Reuter et al., 2010). If acute inflammation persists for a short time, it can be beneficial. If inflammation lingers over time, chronic inflammation sets in and may predispose the individual to various illnesses, including cancer (Lin & Karin, 2007).