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Integration of biomarkers to advance precision nursing interventions for family research across the life span

Elizabeth J. Corwin, PhD, RN, FAAN, Erin P. Ferranti, PhD, RN*
Nell Hodgson Woodruff School of Nursing, Emory University, Atlanta, GA

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ABSTRACT

Background: Integrating biomarker measurement into research protocols provides an opportunity for nursing scientists to identify underlying biological mechanisms that contribute to adverse health outcomes and to tailor and test precision nursing interventions.
Purpose: To describe how a better understanding of underlying mechanisms and a better ability to tailor and test interventions are particularly important for improving the health of family caregivers as this population frequently experiences prolonged stress that carries negative health consequences for both caregiver and care recipient.
Methods: This article provides an overview of family caregiving and the potential benefit of incorporating biomarkers into stress-related research studies, using a an exemplar the consequences of chronic stress experienced by humanity's first family caregivers; pregnant and postpartum women.
Discussion: Through this exemplar, details of how the integration of biomarkers supports precision nursing interventions to improve health across the life span are described.

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Caregiving

Providing care to a sick, dying, or vulnerable family member is not a recent phenomenon; it is not even restricted to humans. It is, however, very common. According to the latest survey of the National Alliance for Caregiving over 65 million individuals in the United States provide unpaid care annually for a chronically ill, disabled, or aged family member (National Alliance for Caregiving AAoRP–, n.d.). Of this group, most tend to be female (66%) and often provide care for a parent (35%) or child (14%). Many others care for infants and children or other family members who may not be ill but require continuing guardianship. As such, family caregiving is frequently longitudinal and although often rewarding (Beach, Schulz, Yee, & Jackson, 2000; Roth, Fredman, & Haley, 2015), can be stressful and physically demanding. It may also be sad, especially in situations of a worsening trajectory for the loved one and lonely in cases where the caregiver is unable to leave the family member unattended. As caregiving continues for an extended period, competing work and other family demands are common, as are financial worries. Caregivers of family members with dementia have been reported to devote an average of 16.6 hours

* *Corresponding author:* Dr. Elizabeth J. Corwin, Emory University, Nell Hodgson Woodruff School of Nursing, 1520 Clifton Road, NE, Atlanta, GA 30322-4027.
E-mail address: ejcorwi@emory.edu (E.J. Corwin).

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of unpaid work per week to the task of caregiving, a responsibility and challenge that may persist for years (Schulz & Martire, 2004).

Regardless of whether providing chronic care to a family member is a choice made freely or one made out of necessity, it is a decision that for some may carry health risks compared to noncaregivers of the same age (Gouin, Hantsoo, & Kiecolt-Glaser, 2008; Kiecolt-Glaser et al., 2003; Thomason et al., 2014). Although recent studies indicate that the association between caregiving and increased risks of morbidity and mortality are complex and do not hold true for many caregivers (Fredman, Cauley, Hochberg, Ensrud, & Doros, 2010; O'Reilly, Rosato, Maguire, & Wright, 2015), for some, especially those who report high-stress burden (Savundranayagam, Montgomery, & Kosloski, 2011), health risks have been identified, including in caregivers of patients after stroke (Haley, Roth, Hovater, & Clay, 2015), spouses of patients with cancer (Li & Loke, 2013), new mothers of even healthy children (Thomason et al., 2014), as well as parents of children with traumatic brain injury (Wharewera-Mika, Cooper, Kool, Pereira, & Kelly, 2015), mothers of children and adolescents with pediatric cancer (Klassen et al., 2012), and parents of children with autism (Lovell, Elliot, Liu, & Wetherell, 2014; Lovell, Moss, & Wetherell, 2012). When a caregiver's own health deteriorates, his or her ability to provide care may be compromised, impacting the health of the care recipient as well.

The purpose of this manuscript is to describe how, by integrating biomarkers into nursing research studies, nurse scientists and clinicians are better able to precisely tailor and test nursing interventions to improve the health and well-being of patients and families across the life span. An exemplar of chronic stress exposure during pregnancy is used to describe the process from theory-based hypothesis generation and testing, through the tailoring and testing of the intervention.

The Stress Response

Exposure of an individual to a physical or mental stressor initiates rapid responses, the most significant of which includes activation of the two primary arms of the stress response; the sympathetic nervous system (SNS) and the hypothalamic-pituitary-adrenal (HPA) axis. The SNS response involves increased heart and respiratory rate and a shift in blood flow delivery toward the heart, brain, lungs, and skeletal muscles at the expense of other organs, thus preparing the host to fight or flee from the stressor (Dampney, 2015). Activation of the HPA axis involves the release of corticotropin-releasing hormone from the hypothalamus, leading to an increase in the release of adrenocorticotropin hormone from the anterior pituitary and, ultimately, increased cortisol from the adrenal gland (Sapolsky, Romero, & Munck, 2000). Activation of this pathway focuses the host's attention on the impending stressor and mobilizes the metabolic resources required to respond. Although both the SNS and HPA axis responses are necessary for the host to respond to an acute stressor, prolonged or chronic activation of either system carries an increased risk of cardiovascular disease, metabolic syndrome, anxiety, and depression (Anisman, 2009; Steptoe & Kivimaki, 2012).

A third, less well-known pathway of the stress response, also essential for the health and well-being of the host, is SNS activation of white blood cells (WBCs) to increase production of proinflammatory cytokines (Steptoe, Hamer, & Chida, 2007; Yang & Glaser, 2002). When faced with actual or perceived danger, the rapid production of proinflammatory cytokines prepares the host to respond to potential injury or infection. However, proinflammatory cytokines also directly and significantly stimulate all levels of the HPA axis, the hypothalamus, anterior pituitary, and adrenal gland, ultimately leading to an increase in circulating cortisol levels (Figure 1). Through this mechanism, and via direct and indirect effects of proinflammatory cytokines on the brain and throughout the body, prolonged elevation of proinflammatory cytokines has the potential to increase disease risk, including cardiovascular disease, cancer, depression, and Alzheimer's disease (Kim, Na, Myint, & Leonard, 2016; Kolb, Liu, Janowski, Sutterwala, & Zhang, 2014; Li, Deroide, & Mallat, 2014; Verdile et al., 2015; Wang, Tan, Yu, & Tan, 2015).

The Cytokine–Glucocorticoid Feedback Cycle

With any disturbance in homeostasis, the body responds in ways aimed at returning the system toward the previous set point. A key pathway by which homeostasis of the proinflammatory immune response is achieved is via the cytokine–glucocorticoid feedback cycle, which when activated, limits further inflammation (Besedovsky & del Rey, 2006).

As levels of proinflammatory cytokines rise in response to a mental or physical stressor, circulating

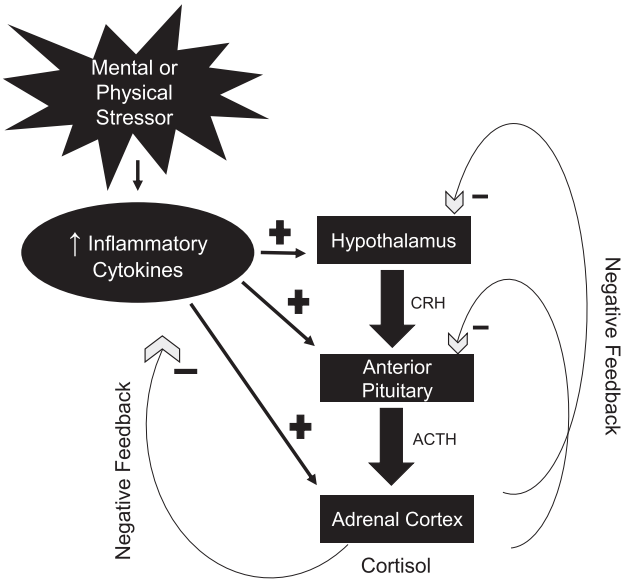

Figure 1 – The cytokine–glucocorticoid negative feedback circuit. ACTH, adrenocorticotropic hormone; CRH, corticotropic releasing hormone.