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Introduction to the Special Issue of *Psychosomatic Medicine:* Mechanisms Linking Early-Life Adversity to Physical Health

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In the last two decades, a veritable explosion of research into the early-life determinants of physical health has demonstrated that social and environmental factors in early life play a critical role in predicting morbidity and mortality across the life-course. In particular, exposure to adverse experiences in childhood —including poverty, abuse, neglect, and violence—has been associated with elevated risk for the onset of a wide range of physical health problems in adulthood. Despite strong evidence for the links between early-life adversity and health outcomes, the mechanisms that underlie these associations remain poorly understood. Exploring these mechanisms is the goal of this special issue of *Psychosomatic Medicine*.

Compelling evidence for the influence of early-life adversity in shaping adult physical health was generated by the Adverse Childhood Experiences (ACEs) Study (1). This seminal study administered a brief survey assessing childhood maltreatment and other types of household dysfunction (e.g., parent criminal behavior, domestic violence) to a large sample of adults who also completed a standardized medical evaluation at a large HMO. Findings from the ACEs study provide compelling evidence for the association of early-life adversity with many leading causes of morbidity and mortality, including risky health behaviors (e.g., smoking), early markers of disease risk (e.g., obesity), and a wide range of physical health problems including cardiovascular disease, type 2 diabetes, cancer, respiratory diseases, chronic pain, gastrointestinal and metabolic disorders, and neurological and musculoskeletal problems (1, 2). These findings have been replicated in numerous retrospective studies of adults (3–6) as well as prospective studies of children and adolescents (7–10) and confirmed in meta-analysis (11). Strikingly, recent work suggests that early-life adversity is associated with premature mortality (12, 13).

Identifying the mechanisms underlying the associations of early-life adversity with poor physical health and chronic disease is critical for developing interventions to mitigate these risks. Although health behaviors are likely to play an important role, prospective studies that

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have directly examined smoking, alcohol use, physical activity, and body mass index as potential mediators demonstrate that early-life adversity continues to be associated with poor physical health even after adjustment for health behaviors (3, 6, 7, 14). This suggests that other mechanisms are involved in the pathway from early-life adversity to poor health. Numerous conceptual models developed by scholars from diverse backgrounds have proposed that these mechanisms are likely to reflect biological embedding, a process by which early experience alters neurodevelopment and the development of regulatory systems in the body, ultimately culminating in risk for a wide range of disease outcomes, in addition to mechanisms operating at multiple other levels of influence, including psychological and social processes (15–22). Yet, empirical research on mechanisms linking early adversity with physical health remains limited, particularly in relation to the wealth of knowledge that has accumulated regarding mechanisms explaining the association of adversity with psychopathology. One likely explanation for this pattern is that mental health problems following exposure to adversity typically emerge early in development, whereas many—though not all—chronic diseases and physical morbidities appear later in development, sometimes decades after adversity was experienced. As a result, much remains to be learned about these pathways. The empirical papers in this special issue strengthen the foundation for future research and catalyze innovation in this area.

The papers comprising this special issue draw upon a diverse set of samples to examine a wide range of potential mechanisms operating at multiple levels of influence, spanning physiological and psychosocial pathways that might underlie the associations of early adversity with health. Adverse environmental experiences, occurring in utero and across childhood and adolescence, are considered in relation to health outcomes and precursors of disease from infancy to adulthood. Studies presented here examine mechanisms involved in the association of early-life adversity with physical health outcomes that emerge early in development, such as asthma (23–25) and chronic pain (26), global measures of physical health in childhood and adolescence (27, 28) (Hagan, Whalen), as well as intermediate phenotypes that predate the onset of disease, including adiposity (29), body mass index (24), and biomarkers of cardiometabolic risk (30). Specific physiological mechanisms investigated encompass epigenetic modifications (29, 31), alterations in cellular aging (32) and inflammatory processes (23, 33), disruptions in stress response systems including the hypothalamic-pituitary-adrenal axis and autonomic nervous system (27, 31, 34), cardiovascular and metabolic changes (30), and altered pain signaling (35). At the psychosocial level, the role of mental health (24, 25, 28), social support (24), and family relationship quality (27) are also explored as mechanisms. Together, findings from these papers illuminate a complex array of mechanistic processes across a range of populations, exposures, and outcomes. In our final commentary, we integrate the findings of these articles and provide a framework on how to further advance the knowledge base for mechanisms linking early adversity with physical health (36).

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