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Guest Editorial

Stress, Inflammation, and Autoimmunity: The 3 Modern Erinyes

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There is no more relevant time to be addressing the effect of stress as the health, economic, and emotional stressors associated with coronavirus disease 2019 have engulfed the entire planet.[1] Stress has been particularly apparent among health care workers, who are more exposed and susceptible to infection as well as to the emotional strain of caring for patients with severe acute respiratory syndrome coronavirus 2.[2]

Stress, inflammation, and autoimmunity may stand for the Erinyes of modern times. In ancient Greek mythology, the Erinyes, also known as the Furies, were female chthonic deities of vengeance, especially for crimes committed against the natural world order.[3] The first mention of stress possibly contributing to disease pathology was by Hippocrates, who advised a patient with asthma to contain his anger because Hippocrates believed it contributed to the patient's condition.[4]

Mounting evidence has shown that stress[5,6] adversely affects many different diseases, especially autoimmune,[7,8] and inflammatory[9,10] disorders, such as aging,[11] allergies,[12,13] Alzheimer disease,[14] asthma,[15,16] autism spectrum disorder,[17,18] cancer,[19,20] coronary artery disease,[21,22] multiple sclerosis,[23] and myalgic encephalomyelitis/chronic fatigue syndrome.[24]

Stress typically activates the hypothalamic–pituitary–adrenal axis, the "fight or flight" system developed to ensure the survival of the organism, via release of catecholamines and corticosteroids from the adrenal glands. Acute stress increases the readiness of the organism and typically decreases the function of the immune system. In contrast, prolonged stress has the opposite effect, contributing to chronic inflammation[25] via blunting the cortisol effect and/or activation of the tissue immune cells—the mast cells.[26]

Mast cells contribute to both health and disease.[27,28] Mast cells are located around blood vessels and nerves in all tissues, including the brain, acting as sensors of environmental and pathogenic "danger" signals[29] by secreting multiple proinflammatory mediators.[30,31] Mast cells may mediate the proinflammatory effect of stress in response to stimulation by neurohormonal triggers,[32] especially the key stress mediator corticotropin-releasing hormone.[33] In fact, corticotropin-releasing hormone stimulates mast cells and is synthesized by mast cells.[34]

In this May issue of the *Clinical Therapeutics*, part 1 of the Stress and Immunity Update emphasizes the effect of stress on skin immune processes.[35–38] Scientists address the effect of stress on itch and chronic urticaria, as well as the effect of stress on levels of immune molecules and neurotransmitters. The June issue will focus on the effects of acute and chronic stress on neuroimmune processes and the reprogramming of the immune system.

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