



Figure 9-4. The stress response.

the body for intense physical activity (“fight or flight”). The increase in heart rate, blood pressure, breathing, circulating glucose, and mental alertness are meant to assist in winning the physical battle between you and your stressor. Unfortunately, most stress cannot be handled by hitting it or running away from it. People encounter daily stressors that are not physical threats but that create internal pressure, such as an argument or a deadline. Even a loud, hot, or crowded physical environment can spur on the stress response.

In the initial stage, the amygdala alerts the hypothalamus, and the hypothalamus activates the adrenal glands, which secrete epinephrine and norepinephrine. This step typically occurs before a person is even aware of the stressor. If this initial surge is not enough, the hypothalamus, pituitary gland, and adrenal glands, referred to as the HPA axis, keep the symptomatic nervous system turned up by releasing corticotrophin-releasing factor (CRF). CRF acts on the pituitary gland to secrete adrenocorticotropic hormone (ACTH), which then tells the adrenal gland to release cortisol into the blood stream (Figure 9-4). Cortisol is a steroid, specifically a glucocorticoid. It helps to increase glucose levels in the blood and is anti-inflammatory in the short term.

If the stressful situation is not resolved, the HPA axis continues to fuel the stress response at a lower intensity. This means that the body and brain are in a heightened physiologic state with higher-than-normal levels of circulating CRF, ACTH, and cortisol. Humans keep the HPA axis engaged by worrying or replaying stressful events in their minds.³ Prolonged activation of the HPA axis is believed to suppress immune function, damage hippocampal neurons, and lead to dysregulation of the HPA axis. Cortisol levels are monitored by the hippocampus, hypothalamus, and pituitary gland; once a high enough level has been reached, the flow of CRF and ACTH stops. Chronic stress makes the HPA less sensitive to cortisol and lengthens the time needed to return to homeostasis. Cortisol inhibits lymphocyte function and can slow wound healing. Chronically elevated levels wear out the glucocorticoid receptors on cytokines so that inflammation is no longer held in check.²⁰

Psychoneuroimmunology is the study of interconnections between the brain (neurology and neurochemistry), the mind (thoughts and emotions), and the processes of the immune and endocrine systems. Stress is so related to health that it is listed as a risk factor for cardiovascular diseases²¹ and type 2 diabetes mellitus²² and is a key component in the etiology of anxiety, depression, substance abuse, and eating disorders.^{22,23} Epidemiology studies have found a history of depression to increase the risk of Alzheimer’s disease.²⁴ The 2 are linked by neuron damage