STRESS AND THE IMMUNE SYSTEM

In a sense, the immune system is the body's surveillance system. It consists of a variety of structures, cells, and mechanisms that serve to protect the body from invading toxins and microorganisms that can harm or damage the body's tissues and organs. When the immune system is working as it should, it keeps us healthy and disease free by eliminating bacteria, viruses, and other foreign substances that have entered the body (Everly & Lating, 2002).

Immune System Errors

Sometimes, the immune system will function erroneously. For example, sometimes it can go awry by mistaking your body’s own healthy cells for invaders and repeatedly attacking them. When this happens, the person is said to have an autoimmune disease, which can affect almost any part of the body. How an autoimmune disease affects a person depends on what part of the body is targeted. For instance, rheumatoid arthritis, an autoimmune disease that affects the joints, results in joint pain, stiffness, and loss of function. Systemic lupus erythematosus, an autoimmune disease that affects the skin, can result in rashes and swelling of the skin. Grave’s disease, an autoimmune disease that affects the thyroid gland, can result in fatigue, weight gain, and muscle aches (National Institute of Arthritis and Musculoskeletal and Skin Diseases [NIAMS], 2012).

In addition, the immune system may sometimes break down and be unable to do its job. This situation is referred to as immunosuppression, the decreased effectiveness of the immune system. When people experience immunosuppression, they become susceptible to any number of infections, illness, and diseases. For example, acquired immune deficiency syndrome (AIDS) is a serious and lethal disease that is caused by human immunodeficiency virus (HIV), which greatly weakens the immune system by infecting and destroying antibody-producing cells, thus rendering a person vulnerable to any of a number of opportunistic infections (Powell, 1996).

Stressors and Immune Function

The question of whether stress and negative emotional states can influence immune function has captivated researchers for over three decades, and discoveries made over that time have dramatically changed the face of health psychology (Kiecolt-Glaser, 2009). Psychoneuroimmunology is the field that studies how psychological factors such as stress influence the immune system and immune functioning. The term psychoneuroimmunology was first coined in 1981, when it appeared as the title of a book that reviewed available evidence for associations between the brain, endocrine system, and immune system (Zacharie, 2009). To a large extent, this field evolved from the discovery that there is a connection between the central nervous system and the immune system.

Some of the most compelling evidence for a connection between the brain and the immune system comes from studies in which researchers demonstrated that immune responses in animals could be classically conditioned (Everly & Lating, 2002). For example, Ader and Cohen (1975) paired flavored water (the conditioned stimulus) with
the presentation of an immunosuppressive drug (the unconditioned stimulus), causing sickness (an unconditioned response). Not surprisingly, rats exposed to this pairing developed a conditioned aversion to the flavored water. However, the taste of the water itself later produced immunosuppression (a conditioned response), indicating that the immune system itself had been conditioned. Many subsequent studies over the years have further demonstrated that immune responses can be classically conditioned in both animals and humans (Ader & Cohen, 2001). Thus, if classical conditioning can alter immunity, other psychological factors should be capable of altering it as well.

Hundreds of studies involving tens of thousands of participants have tested many kinds of brief and chronic stressors and their effect on the immune system (e.g., public speaking, medical school examinations, unemployment, marital discord, divorce, death of spouse, burnout and job strain, caring for a relative with Alzheimer’s disease, and exposure to the harsh climate of Antarctica). It has been repeatedly demonstrated that many kinds of stressors are associated with poor or weakened immune functioning (Glaser & Kiecolt-Glaser, 2005; Kiecolt-Glaser, McGuire, Robles, & Glaser, 2002; Segerstrom & Miller, 2004).

When evaluating these findings, it is important to remember that there is a tangible physiological connection between the brain and the immune system. For example, the sympathetic nervous system innervates immune organs such as the thymus, bone marrow, spleen, and even lymph nodes (Maier, Watkins, & Fleshner, 1994). Also, we noted earlier that stress hormones released during hypothalamic-pituitary-adrenal (HPA) axis activation can adversely impact immune function. One way they do this is by inhibiting the production of lymphocytes, white blood cells that circulate in the body’s fluids that are important in the immune response (Everly & Lating, 2002).

Some of the more dramatic examples demonstrating the link between stress and impaired immune function involve studies in which volunteers were exposed to viruses. The rationale behind this research is that because stress weakens the immune system, people with high stress levels should be more likely to develop an illness compared to those under little stress. In one memorable experiment using this method, researchers interviewed 276 healthy volunteers about recent stressful experiences (Cohen et al., 1998). Following the interview, these participants were given nasal drops containing the cold virus (in case you are wondering why anybody would ever want to participate in a study in which they are subjected to such treatment, the participants were paid $800 for their trouble). When examined later, participants who reported experiencing chronic stressors for more than one month—especially enduring difficulties involving work or relationships—were considerably more likely to have developed colds than were participants who reported no chronic stressors (Figure).
In another study, older volunteers were given an influenza virus vaccination. Compared to controls, those who were caring for a spouse with Alzheimer's disease (and thus were under chronic stress) showed poorer antibody response following the vaccination (Kiecolt-Glaser, Glaser, Gravenstein, Malarkey, & Sheridan, 1996). Other studies have demonstrated that stress slows down wound healing by impairing immune responses important to wound repair (Glaser & Kiecolt-Glaser, 2005). In one study, for example, skin blisters were induced on the forearm. Subjects who reported higher levels of stress produced lower levels of immune proteins necessary for wound healing (Glaser et al., 1999). Stress, then, is not so much the sword that kills the knight, so to speak; rather, it's the sword that breaks the knight's shield, and your immune system is that shield.

**STRESS AND AGING: A TALE OF TELOMERES**

Have you ever wondered why people who are stressed often seem to have a haggard look about them? A pioneering study from 2004 suggests that the reason is because stress can actually accelerate the cell biology of aging.

Stress, it seems, can shorten telomeres, which are segments of DNA that protect the ends of chromosomes. Shortened telomeres can inhibit or block cell division, which includes growth and proliferation of new cells, thereby leading to more rapid aging (Sapolsky, 2004). In the study, researchers compared telomere lengths in the white blood cells in mothers of chronically ill children to those of mothers of healthy children (Epel et al., 2004). Mothers of chronically ill children would be expected to experience more stress than would mothers of healthy children. The longer a mother had spent caring for her ill child, the shorter her telomeres (the correlation between years of caregiving and telomere length was $r = -.40$). In addition, higher levels of perceived stress were negatively
correlated with telomere size ($r = -.31$). These researchers also found that the average telomere length of the most stressed mothers, compared to the least stressed, was similar to what you would find in people who were 9–17 years older than they were on average.

Numerous other studies since have continued to find associations between stress and eroded telomeres (Blackburn & Epel, 2012). Some studies have even demonstrated that stress can begin to erode telomeres in childhood and perhaps even before children are born. For example, childhood exposure to violence (e.g., maternal domestic violence, bullying victimization, and physical maltreatment) was found in one study to accelerate telomere erosion from ages 5 to 10 (Shalev et al., 2013). Another study reported that young adults whose mothers had experienced severe stress during their pregnancy had shorter telomeres than did those whose mothers had stress-free and uneventful pregnancies (Entringer et al., 2011). Further, the corrosive effects of childhood stress on telomeres can extend into young adulthood. In an investigation of over 4,000 U.K. women ages 41–80, adverse experiences during childhood (e.g., physical abuse, being sent away from home, and parent divorce) were associated with shortened telomere length (Surtees et al., 2010), and telomere size decreased as the amount of experienced adversity increased.

(Figure 2). Telomeres are shorter in adults who experienced more trauma as children (adapted from Blackburn & Epel, 2012).

Efforts to dissect the precise cellular and physiological mechanisms linking short telomeres to stress and disease are currently underway. For the time being, telomeres provide us with yet another reminder that stress, especially during early life, can be just as harmful to our health as smoking or fast food (Blackburn & Epel, 2012).