The Mind-Body Health Relationship

Stress hormones exert many effects through the immune system, upsetting its balance and increasing susceptibility to disease

Bruce S. Rabin

The functions of the cellular components of the immune system are modified by the hormones, such as catecholamines and glucocorticoids, that bind to receptors on the cell membrane or in the cell cytoplasm. Thus, psychologic states, such as the perception of a stressor, that alter the plasma concentration of catecholamines and glucocorticoids modify the function of the immune system and alter its ability to resist infection or to exacerbate or ameliorate an autoimmune disease.

Many studies have focused on alterations of immune function induced by physiological and physical stress. For example, the antibody response to the hepatitis B vaccine is reduced when immunization occurs at a time of stress, and an enhanced antibody response occurs when individuals reduce their stress response by techniques such as meditation. Individuals who are happy and relaxed are less susceptible to upper respiratory infection.

Mediated via Hormones, Stress Affects Many Immune System Responses

Perception of a stressor causes an elevation of stress hormones, of which both catecholamines (epinephrine and norepinephrine) and cortisol are the major effectors. Stress hormones exert multiple effects, including changing the peripheral complete blood count, releasing neutrophils from the spleen, raising levels of CD8 and natural killer (NK) cells of the immune system, decreasing activity of lymphocytes based on their response to mitogens, and upsetting cytokine production and, with it, normal functions of the immune system. Those stress hormones also can alter the balance between Th1 and Th2 lymphocytes, in turn, changing one’s susceptibility to infectious disease as well as the course of other immune-mediated diseases.

The same hormones that have an effect on immune function also affect many other mental and physical aspects of health. Thus, if stress has altered the function of the immune system, it is likely that both mental and physical health are being altered. Stress hormones can affect mental function by impairing the ability to think clearly and focus, and may cause mild to moderate clinical depression. When stress hormones are elevated, the ability to remember things may decrease at a younger age than would occur if stress hormone were kept low.

The physical effects of elevated stress hormones include increased heart rate and blood pressure, accelerated accumulation of cholesterol into the blood vessels of the heart with narrowing of the blood vessels, and clumping of blood platelets that may clog blood vessels in the heart and elsewhere. Other effects include decreases in the body’s ability to resist infectious disease and to heal wounds, and aggravation of autoimmune diseases such as psoriasis, multiple sclerosis, rheumatoid arthritis, and inflammatory bowel disease. Other conditions such as diabetes, chronic fatigue syndrome, fibromyalgia, and irritable bowel syndrome may worsen or become more difficult to manage.

The interrelationship between stress hormones and health can be greatly influenced by early life events that may determine the quality

SUMMARY

➤ Stress hormones, including catecholamines and glucocorticoids, modify and may impair key functions of the cellular immune system.

➤ Chronically stressed individuals typically produce lower levels of antibodies than do those who are not stressed.

➤ Stress experienced by pregnant women may program the propensity of their children to develop various diseases.

➤ The mental and physical health of future generations depends on adults following healthy behaviors during their lives.
and duration of life. However, countermeasures are capable of reducing stress hormone elevations and enhancing the quality of mental and physical health.

**Damaging Effects of Stress in Utero and during Childhood**

Stress experienced by a pregnant woman has an effect on the mental and physical health of her child. Thus, the development of disease may be programmed in utero. High levels of stress during pregnancy may cause reductions in fetal birth weight and length of gestation, decreased brain volume in areas associated with learning and memory, increased risk of elevated body mass index and waist-hip ratio, hyperglycemia, hypertension, and elevated lipid profile. Stress during pregnancy also increases the risk of psychopathology, including anxiety and depression, disrupted emotional regulation, and impaired cognitive performance.

The risk for developmental delay or disability is higher among late-preterm infants compared with full-term infants. Late preterm is 34 0/7 (weeks and days of gestation) to 36 6/7, and full term is 37 0/7 to 41 6/7 weeks’ gestation at birth. Altered hypothalamic-pituitary-adrenal (HPA) axis function resulting from maternal stress, with either elevated or decreased glucocorticoid hormone concentrations, and altered function of the glucocorticoid receptor, may underpin these associations.

Physical, mental, or sexual abuse affects the physical and mental health of children when young and throughout life. Whether the effects are more profound in children born to mothers who have experienced high levels of stress during pregnancy has not been evaluated. Childhood physical abuse is associated with depression, posttraumatic stress disorder symptoms, number of lifetime sexual partners, legal troubles, and incarceration. For women, a history of sexual abuse is associated with an increased risk of arthritis and breast cancer. Multiple episodes of sexual assault carry a two- to threefold increased risk of these diseases compared with a single episode. Women with a history of both physical and sexual child abuse have poorer overall health compared to women without these histories.

Adults who experienced six or more Adverse Childhood Experiences (recurrent physical abuse; recurrent severe emotional abuse; contact sexual abuse; growing up in a household where someone was in prison or where the mother was treated violently; where someone was an alcoholic or a drug user, where someone was chronically depressed, mentally ill, or suicidal; where at least one biological parent was lost during childhood, regardless of cause) die nearly 20 years earlier on average than those without Adverse Childhood Experiences (60.6 years vs 79.1 years). When abused and nonabused populations are compared, those in the abused population show more telomere shortening and nonspecific markers of inflammation.

Being bullied also has an effect on long term health. Nearly one-fifth of adults reported having experienced bullying when they were at school. Those reporting that they had been bullied had poorer mental and physical health compared to those who had not been bullied and were at a significantly increased risk of having been diagnosed with depression between the ages 31–51 years.

**Workplace Stress Affects Health**

Considerable evidence suggests that the work environment is an important factor in influencing health. Stress increases burnout, emotional exhaustion, depression, and anxiety. Variables such as work interference with family life, the amount of influence employees have over their jobs, the hours worked, and an increase in psychological demand, are predictors of health alterations.

A study of male British civil servants aged 20 – 64 found an inverse association between grade (level) of employment and mortality from cardiovascular heart disease (CHD). Men in the lowest grade (mes- sengers, doorkeepers, etc.) had a threefold higher mortality rate than men in the highest grade (administrators). A critical factor in the increased risk was the amount of control over their work environment perceived by the employee.

**Association between Personality and Health**

Although the answers to what shapes personality are not fully defined, there are known associations between personality characteristics and health that suggest that the quality of health does not operate outside the reach of psychosocial influences. Individuals who are well-adjusted, socially stable, and well integrated into their communities are at significantly lower risk for disease
than those who are more unstable, impulsive, isolated, and alienated.

Optimistic people are at a reduced risk of developing heart disease and having a stroke. Optimism may also function as a buffer of immune alterations when individuals experience moderate but not high levels of stress.

Baseline cortisol concentrations differ in individuals with different personalities. Those who experience more anxiety and distress have higher baseline cortisol levels than do those who do not have these traits. Individuals who respond to stress with high levels of cortisol have lower self-esteem, negative self-concept, depressed mood, and more physical health problems compared with those who respond to stress with lower levels of cortisol.

Angry or hostile people are at an increased risk of developing heart disease. Subjects with more social support have more rapid recovery from stroke and better post-stroke function. Having interactions with family members, friends, religious organizations, and community activities reduces the extent of functional impairment after a stroke, possibly because those with social support find aversive events less burdensome, less painful, and less frightening when they have someone to share it with and have less of an elevation of stress hormones.

Individuals who are high in intrinsic religiosity where their faith is internalized—rather than being used for external reasons, such as social acceptability—have a better quality of health than individuals who are low in religiosity. Affiliation and participation with a religious community is associated with lower use of hospital services by medically ill individuals age 60 or greater. Mental and physical health related benefits found to be associated with religious factors include reduced depression; less hostility, anxiety, and blood pressure; and greater life satisfaction.

It is possible that different central nervous molecular and hormonal systems define personality. If so, it is possible that the same hormonal systems affecting personality also have an effect on the function of the immune system, and mental and physical health.

**Stress Buffers and Countermeasures**

The most obvious way to reduce the influence of stress on health is to reduce the amount of stress one encounters. This may be possibly for some, but they would be the exceptions. A pharmacological approach may work if side effects, such as lethargy, could be eliminated. The most feasible approach is to reduce the influence of stress on activating the stress reactive areas of the brain, resulting in less elevation of the stress hormones.

Social support has been shown to have physiological effects in experimental situations. Subjects given a stressful task to perform have less heart rate elevation and blood pressure elevation when a friend is present in comparison to subjects who perform the task without a friend being present. This is not surprising. We generally do not become friends with someone who we find annoying. This suggests that those elements within the brain that are activated and motivate the desire for friendship are capable of buffering stress effects on physiological reactivity.

Coping with stress involves behaviors associated with lower the perception of stress by the brain. Behaviors including being socially interactive, high in optimism, physically active, having a sense of humor, and enjoying participation in religious or spiritual activities have been associated with an increased ability to cope with stress. Ideally, these behaviors would be incorporated into daily life routines so that they would be utilized as routine behaviors.

I recommend using the word RELAX to help remember stress-buffering behaviors.

**Reflection:** enjoying participation in spiritual or religious activities, or simply taking time to reflect on the things that add meaning, purpose, and joy to your life helps to reduce the negative influence of stress on health.

**Expectations:** Being high in optimism, seeing the glass as half full rather than half empty.

**Laughter:** Having a sense of humor and being able to laugh at some of the things you do.

**Acquaintances:** Being socially active and spending time with people you enjoy being with.

**Exercise:** Being physically active (walking as often as you can) and not just sitting around watching television or playing games on a computer. Stress buffering techniques are provided on our website at www.healthy lifestyle.upmc.com.
The mental and physical health of future generations depends on healthy adults utilizing healthy lifestyle behaviors over their life span, not only for their benefit but also to serve as meaningful role models for those that look to them for guidance. The health of our future population and the costs of our illness management systems depend on healthy adults in whom healthy behaviors are ingrained and who do not have to be asked to change behavior. One strategy for providing this is to provide a culture in which children grow up using healthy behaviors throughout their lives. This can be accomplished through a system of healthy lifestyle education and teaching and modeling healthy behaviors to improve nutrition and physical activity. The result can be the reduction of the incidence and prevalence of preventable diseases and a significant improvement in the quality of life. Finally, it is important to be aware that the longer one stays healthy as one ages, the shorter one’s demise. Indeed, increasing one’s ability to cope with stress will promote a high quality of health as one ages.

Rabin focuses on stresses that arise “when people are abusive to others,” he says. “How many times have you seen a child being abused by an adult at the supermarket? Have you intervened? Yet, I see that child 30 years down the road. It causes me stress to see individuals being abused because of the long-term effects abuse has on health, longevity, and the quality of life.” To cope, he uses many of the same skills that he urges others to practice, including deep breathing, chanting, meditation, thinking of funny things, having a strong social network, exercise, and participating in religious or spiritual activities. “When stressors occur, I am able to stay calm, think clearly, and remain focused,” he says.

Today Rabin, 71, directs the University of Pittsburgh Medical Center Healthy Lifestyle Program, which focuses on stress-reduction practices that support the immune system as people age in an effort to avoid prolonged and incapacitating conditions. “Stress will not go away, [so] we must change the way our brain perceives stress,” he says. “Who wants to be debilitated, suffering, being a burden to themselves and their family? Our goal is to help people remain healthy and functional as they age, and then to check out quickly.”

Rabin moved to Pittsburgh in 1972 to establish the clinical immunopathology laboratory at the University of Pittsburgh Medical Center, and has held that position for 40 years. When he was 40, however, he shifted his research focus from studying immune-mediated disease mechanisms to disease prevention and the role of stress on the immune system. “As an immunologist, I decided to focus on how function of the immune system influences healthy aging,” he says. “I initially studied nutrition and stress in mice, and how each affected immune function. Both were important in our initial studies, but I decided to restrict my studies to the effect of stress on immune function.”

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