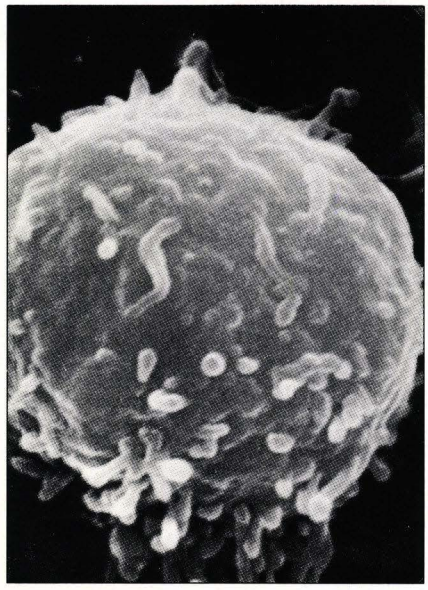
Stress and the immune system

Tracy B. Herbert

Many people have experienced the connection between stress and getting sick. Colds, influenza, herpes and allergies seem worse when we are severely stressed at work or in the home. Others are never sick until they go on vacation (that is, after the stress is over), and then they spend the whole time fighting the virus. Because of intrinsic connections like these, many researchers are today exploring whether (and how) stress and illness are actually linked. One specific focus of this research is to study the effects of stress on the immune systems; after all, if stress affects immunity, that would be one way in which stress could contribute to illness.

The function of the immune system is to protect us from organisms that cause disease, and from other materials that would be harmful to the body. Cells of the immune system (i.e., white blood cells) circulate throughout the body in the blood and are also located in various organs, including the bone marrow, thymus, lymph nodes and spleen. There are a number of different kinds of white blood cells, but the most important in this context are lymphocytes. Of the various tests that reflect the integrity of the immune system, some simply assess the number of white blood cells circulating in the blood; others quantify the amount of antibody in the circulation. Antibodies are proteins produced by certain lymphocytes when harmful substances invade the body. Once antibodies are produced, they attach to the harmful substance, mark it for destruction by other white blood cells, and prevent it from causing infections.

Other tests of the immune system determine how well specific lymphocytes are functioning. One test assesses "lymphocyte proliferation" – by incubating these cells for several days with substances that cause them to multiply (proliferate). More proliferation is thought to reflect better white blood cell functioning; proliferation is important because, when a harmful substance invades the body, immune cells must multiply to increase their numbers before they can successfully eliminate it. Another test assesses "natural killer cell cytotoxic activity". In this test, white blood cells are incubated for several hours with tumour cells to determine their effectiveness in killing the tumour cells. More killing is thought to reflect better natural killer functioning; the killing potential of natural killer cells is important because they are one of the fastest responders of the immune system in the fight against viruses and tumours.



A lymphocyte: stress may weaken the capacity of lymphocytes to combat infection.

Stressful factors

Studies aimed at determining the relationship between stress and the immune system have investigated the effects of factors as diverse as examinations, bereavement, divorce, unemployment, mental arithmetic, and looking after a relative with Alzheimer's disease. In general, these studies find that stress is related to changes in both the numbers of white blood cells in circulation and the quantity of antibody in the blood. Moreover, stress is associated with changes in the functioning of immune cells. That is, there is a relatively large decrease in both lymphocyte proliferation and natural killer cell activity in individuals who have experienced stress. There seems to be some connection between the duration of the stress and the amount of immune change. For example, the longer the stress, the greater the decrease in the number of specific types of white blood cells. It also appears that interpersonal stress (such as bereavement or divorce) produce different immune outcomes compared with the stress due to exams or unemployment.

Connections between negative psychological states (such as anxiety and depression) and immune system variables have also been explored. The results suggest that depressed and anxious mood states are associated with decreases in lymphocyte proliferation and natural killer cell activity, as well as changes in the numbers of white blood cells and the quantity of antibody circulating in the blood. It also appears that the body's ability to produce antibody to a specific substance is related to the level of anxiety that the individual is experiencing: with more anxiety the less antibody is produced after exposure to the potentially harmful susbtance.

How could stress or negative emotional states alter the immune system? Both physiological and behavioural mechanisms provide possible explanations. In the case of

physiological mechanisms, stress is associated with the activation of several systems, including the hypothalamic-pituitary-adrenal axis and the sympathetic nervous system. The activation of these two pathways results in elevated blood levels of specific hormones, namely cortisol and the catecholamines (epinephrine and norepinephrine). Blood levels of these hormones are related to immune functioning. For example, acute increases in cortisol and epinephrine are related to decreases in the number of white blood cells in circulation. Lymphocyte proliferation and natural killer cell activity are also decreased when there are acute increases in cortisol and epinephrine.

Other hormones released under stress – such as growth hormone, prolactin, and the natural opiates (beta endorphin and enkephalin) – have been implicated in influencing the immune system. At a cellular level, these hormones become attached to receptors on white blood cells and so affect them.

The way we behave

An alternative explanation involves the association of stress with specific behaviours that modulate the immune response. Stressed persons tend to sleep less, exercise less, have poorer diets, smoke more, and use alcohol and other drugs more often than non-stressed people. These behaviours have all been shown to affect the immune system.

The interpretation of these changes in the immune system due to stress is difficult. Even though decreased natural killer cell activity is evident in certain human diseases (such as cancer, chronic viral infection or autoimmune diseases), the direct health consequences of such a decrease have not been established.

A decreased lymphocyte proliferation response is associated with increased levels of mortality and an increased number of hospitalizations among the elderly, but there is no clear link with specific diseases that are mediated by the immune system. Nevertheless, it is clear that stress has an adverse effect on health, probably mediated – at least in part – by the body's immune system. It is hoped that future research will show how, by reducing stress, we can improve health. ■

Looking for a job. Uncertainty about employment is an important contributor to stress.

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Stress and cancer

For as long as 2000 years, doctors have recognized significant associations between stress and the development of malignancy. In the 19th century, British physicians believed that emotional distress was the most powerful cause of cancer, and increased rates of the disease were subsequently correlated with the psychosocial stresses that have progressively developed alongside "modern" lifestyles.

According to *Stress*, the newsletter of the American Institute of Stress, studies over the past five decades have convincingly demonstrated the profound effects that stress can exert in accelerating the development and growth of different malignancies, without actually causing them. Similarly, stress reduction strategies have been shown to retard tumours in laboratory animals and to prolong life in cancer patients. The disease has been called a "disease of adaptation."

As one goes down the wide range of animal forms, cancer becomes progressively rarer, and it is not seen in primitive forms of life. On the other hand, the ability to regenerate parts of the organism that have been injured or lost increases in a proportional fashion. In humans, it has been observed that tissue injury and loss of important emotional relationships are associated with a greater likelihood of developing cancer.

Some physicians propose that these trauma invoke atavistic responses – reverting back to our remote ancestry – that once had a purposeful *repair* function, but now result in new growth, or neoplasia, that is uncontrollable and therefore malignant. On the other hand, such positive emotions as a strong faith, social support and other stress reduction strategies seem able to retard or even reverse malignant growth, as occurs in cases of spontaneous remission of cancer.