

## The Effects of Depression on Body Immunity

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From: *Theosophical Digest* – y1993 v5 i3 p78

Recently a diverse group of researchers began combining expertise and resources to study the interrelationship between psychological trauma and alterations in brain function and their combined effect on the activity of the immune system. This relatively new field of medical research, which is bringing together psychiatrists, psychologists, neurochemists, and immunologists, is called psycho-neuroimmunology.

Dr. Michael Irwin, Assistant Professor of Psychiatry at the University of California-San Diego School of Medicine (UCSD) has concentrated on measuring the activity of a special type of immune cell called the natural killer (NK) cell and how it is affected by psychological stress, studying NK cell activity is important because its primary function is to guard against virally infected and cancerous cells. Because of this immunologic surveillance function, many consider to be the body's first line of defense. NK cell activity measures the ability of a particular type of immune cell to destroy tumor cells.

Prolonged mourning after the death of a spouse can lead to many extreme psychological reactions, particularly depression and anxiety. A number of clinical studies have shown that many older people who become severely depressed soon after the death of a spouse tend to develop declining health, increased susceptibility to cancer, and higher mortality than other people of the same age and economic background in the general population. A growing number of researchers and clinicians believe the stress brought on by bereavement triggers chemical changes in the brain that can suppress the immune system.

The women who had the most symptoms of depression had significantly lower NK cell activity than did the women with the fewest depressive symptoms.

Although the clinical studies indicated an association between severe depression and decreased NK cell activity, the next step of inquiry required finding a link between the two. Previous research had suggested that the adrenal glands and the sympathetic nervous system might be involved. The sympathetic nervous system has nerve endings in both the spleen, which contains a high concentration of lymphocytes, and the adrenal glands, which secrete epinephrine and norepinephrine. Lymphocytes have receptors for both of these compounds, and higher than normal levels of each have been found in the urine of severely depressed people. In addition, both substances inhibit NK cell activity.

In an experiment to determine if a simulated stress reaction could trigger the sympathetic, or autonomic, nervous system and thereby affect NK cell activity, Dr. Irwin and Dr. Marvin Brown, Associate Professor of Neurosciences at UCSD, studied corticotropin-releasing factor (CRF) in the brains of rats. CRF initiates biological reactions in the brain that are similar to those observed under stressful conditions. Dr. Irwin's own research had demonstrated that CRF administration affects NK cell activity. The CRF effect was mediated by the sympathetic nervous system.

Whether norepinephrine is the prime inhibitor of NK cell activity is still open to question, according to Dr. Brown. “There are very few instances in regulatory biology when a single substance controls an important function. However, I think it would be safe to conclude that CRF-controlled NK cell activity is regulated by the sympathetic nervous system,” he explains.

With good evidence that a stress-related chemical imbalance of the nervous system affects NK cell activity, Dr. Irwin and his colleagues are turning their attention to other psychological disorders to see if the same relationships exist.

“Right now, we’re looking at people who care for Alzheimer’s disease patients in a long-term study to assess their life-styles, severity of depressive symptoms, norepinephrine levels, and immune functions,” Dr. Irwin explains.

The long-range goal of this type of research is to develop treatments to protect those undergoing severe emotional stress from increased susceptibility to disease, Dr. Irwin says. However, until there is enough evidence showing a cause and effect relationship between stress and immune suppression, development of treatments will be delayed.

“All we have now are associations. I think the long-term studies will clarify whether those associations that we find are indeed causally related, but those studies will take at least 5 years,” Dr. Irwin cautions.

Dr. Weiner agrees that such treatments may be years away. “It’s a relatively new field and the problems are enormously complex,” he notes.