

## Medicine by John Grauerholz, M.D.

### Mind and immunity

*New connections have become evident between mental states and physical health.*

As a by-product of recent research into the immune system, stimulated by the AIDS epidemic, new information has come to light on the relationship between mental states and health. In studies of the immune system in particular, a great many reports, of varying validity, have suggested that factors such as stress could influence immune response and susceptibility to cancer and infections.

An article in the March 8, 1985 issue of *Science* magazine reviews the current state of knowledge of the interconnections between the nervous and immune systems.

It has been known for a number of years that the epithelial cells of the thymus have receptors for acetylcholine, a chemical responsible for transmission of nerve impulses from one nerve cell to another.

Karen Bulloch of the State University of New York at Stony Brook has found that the autonomic nervous system sends nerve fibers to the thymus gland in a very specific pattern, which is similar in mice and men as well as chickens and lizards. The thymus gland is now recognized as a key factor in the changes associated with aging, among other immune functions.

The nerve effect on thymus epithelial cells, which secrete the hormone thymosin, is probably responsible for the development of the T-cells, or thymus dependent lymphocytes. In mice with deficient T-cell function, the nerve pattern of the thymus is abnormally sparse.

Other researchers have demon-

strated that the spleen, lymph nodes, and bone marrow, as well as the thymus, have specific patterns of nerve fibers. These organs are also important parts of the immune system.

The nerve fibers in these organs end in areas which are rich in T-cells and avoid areas rich in B-cells, which are antibody-forming cells derived from the intestinal lymph glands.

The T-cells themselves have been shown to have two sets of receptors for neurotransmitters, the chemicals responsible for transmission of impulses from nerve to nerve. One set is for acetylcholine, and the other for norepinephrine (adrenaline).

On the other hand, there is now evidence that the immune system is closely linked to the nervous system, including the brain. Studies by Hugo Besedovsky at the Swiss Research Institute show that immune responses alter the rate of firing of neurons (nerve cells), and Besedovsky has hypothesized that the immune system informs the brain about invading foreign antigens.

The suggestion has been made that soluble chemicals released by the activated immune cells cause these changes in neuronal firing. These include interferon and the interleukins which also regulate immune cell function. This has led Allan Goldstein and Nicholas Hall of the George Washington University School of Medicine to suggest the name "immunotransmitter" for these substances.

Goldstein, who has done the most extensive work on thymus hormones,

has evidence that thymic hormones have effects on the brain. One such hormone, thymosin a1, acts on the hypothalamus at the base of the brain to stimulate the pituitary gland to secrete ACTH, which in turn stimulates the adrenal gland to produce steroid hormones. Steroid hormones, in turn, have long been known to suppress certain aspects of immune function. Along with this however, thymus hormones also promote maturation of lymphocytes, making them less susceptible to steroid suppression.

Since the lymphocyte maturation occurs early in the immune response and the steroid production later, this provides a mechanism to prevent immunologic overreaction.

Psychological stress, such as depression, bereavement, or even anxiety about academic exams, has been shown to alter immune function in a documentable way. One manifestation, familiar to many, is the activation of latent herpes virus infections resulting in the "cold sores" which appear in certain individuals under stress.

In other cases this can result in painful attacks of "shingles" caused by another herpes virus.

Another aspect of psychological effect on the immune system comes from work at the University of Rochester School of Medicine and Dentistry which indicates that animals can be conditioned to suppress their own immune responses. Although the research has shown potential benefits in autoimmune disorders, which are characterized by overactivity of the immune system, this "conditioning" approach generally increased the death rate of such animals.

The work points to the need to fund much more extensively this area of research, for new discoveries here have the potential to relieve all kinds of diseases—and to extend human life.