Heart attacks from stress, via brain

The heart may rule the head in matters of love, but researchers are finding that in sudden heart attack deaths the brain often seems to rule the heart. Many heart-related deaths occur in apparently healthy people with no evidence of heart disease or artery blockage. And millions of people continue to live although they suffer reduced blood flow due to artery blockage by vascular heart disease. "There must be an additional factor in sudden cardiac death that is necessary to precipitate ventricular fibrillation [asynchronous heart muscle contractions that interrupt blood pumping], and in the case of those victims with perfectly normal hearts, this factor may even be sufficient," says James E. Skinner of Baylor College of Medicine.

The accused factor is stress, recognized by the brain and communicated to the heart. Skinner points out that bereavement, job insecurity and marital strife are all associated with an increased incidence of sudden death. The brain regulates changes in respiration and heart rate when an animal exercises or, for example, when it anticipates a need to fight or flee. Skinner suggests that the same "cerebral defense system" in modern urban life may actually increase vulnerability of the human heart to ventricular fibrillation and sudden death. Research both by Skinner and by Bernard Lown of Harvard University has shown that stressed animals are most vulnerable to fibrillations.

Now investigators are determining the anatomical basis of that brain influence and are investigating ways to break the stress/heart attack linkage. In experimental animals the brain's contribution has been both blocked and stimulated. Destroying one area of cells prevents a heart response to a stressful situation (hearing a tone forewarning a mild skin shock), Skinner told the meeting in St. Louis of the Society for Neuroscience. That same surgery, Skinner reports, prevents ventricular fibrillation in the heart of an animal with a blocked coronary artery. On the other hand, Richard Hall of the University of California at Los Angeles finds that electrical stimulation of the most highly evolved brain region, the frontal cortex, produces storms of heart action that irreversibly damage the heart muscle, while eliciting no significant behavioral response.

While the general path from stress to the heart is known, David H. Cohen of the University of Virginia School of Medicine is mapping the details. Starting at the heart, he hopes eventually to lay out the full circuitry of the brain involvement. In studies of pigeons, Cohen and co-workers find that nerve cells in a lower brain area, the medullary raphe, contact the spinal cord and the sympathetic preganglionic neurons that control cardiovascular function. Electrical stimulation of the brain neurons inhibits the activity of the sympathetic cells, and also decreases the birds' blood pressure dramatically. Because other research indicates that increased activity of the sympathetic cells increases the risk of heart fibrillation, medullary raphe activity should decrease heart vulnerability. This suggestion is supported by the observation that an increase in brain serotonin (the transmitter probably used in the raphe-spinal pathway) is associated with a decrease in heart vulnerability. "There is increasing evidence that the brain can have a tremendous input to cardiovascular function," Cohen says. "We need to learn the detailed connectivity, circuitry and neurotransmitters involved."

A drug to reduce the impact of stress would be welcome in this stressful world. While not expecting such a medicine for at least 10 years, the researchers do have some clues. Cohen says that serotonin may provide the pharmacological means of reducing sympathetic neuron activity, and thus heart vulnerability. Hall reports that prior treatment with beta-adrenergic blocking agents prevents heart damage during frontal cortex and hypothalamic "defense" region stimulation. Skinner suggests that the pharmacological solution may come from study of catecholamine neurotransmitters and cyclic AMP, which appears to mediate transmitter effects within the cells.

"First we must understand the functioning before we know which drug to use," Skinner says. "Then we could develop a pill that would enable people to lessen their cardiac vulnerability without moving back into the jungle." □

Suppressor T cells and diseases

Back in the "Dark Ages" of immunological research — say five years ago — only two major kinds of white blood cells appeared to serve as immunological defenders of the body. These were B cells and T cells. T cells, however, have since been found to consist of at least three different subpopulations — killer T cells (credited with killing tumors and other "enemies"), helper T cells (henchmen to the killer T cells) and suppressor T cells (moderates that keep killer Ts from going overboard in slaying the enemy) (SN: 4/29/78, p. 278).

More insights into the role of suppressor T cells in disease states are now reported by two separate groups of scientists in the October PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES. A vaccine called bacillus Calmette-Guérin (BCG) sometimes, but not always, helps cancer patients. The reason why it doesn't always help, it now appears, is that BCG activates suppressor T cells in the body and thus probably dampens killer T cells' ardor in attacking tumors. So report James A. Bennett and colleagues from Yale University School of Medicine. Suppressor T cells, on the other hand, are knocked off during autoimmune disease and thus appear to play a crucial role in such pathology. So report Anthony J. Strelkauskas and coworkers from Harvard Medical School.

In 1964, a Parisian physician did something that had never been done before. He gave BCG, a tuberculosis vaccine made of tuberculosis bacteria to children dying of leukemia. Animal studies had led him to believe that the vaccine might prime the children's immune systems against cancer. And he was right. Some of his young patients were alive 10 years later. Since then he and other researchers have given BCG to more cancer patients, often with ample success. However, BCG does not always help cancer patients. In fact, there is recent evidence that BCG may, on occasion, even decrease the immune responsiveness of cancer patients. Why is this? Bennett and his colleagues may have the answer. They have found that BCG activates suppressor T cells, either by increasing their production in bone marrow or by increasing their migration to the spleen. Thus, when BCG helps cancer patients, it may be because it has stimulated their killer and helper T cells into action, and when it reduces or impairs the immune systems of cancer patients, it may be because it has stimulated suppressor T cells into action. (All that has been known about BCG and T cells before is simply that BCG stimulates T cells in general.)

As for the role of suppressor T cells in autoimmune diseases, the first indication that they might be involved came three years ago when a Japanese researcher showed that there are defective suppressor T cells in patients with lupus erythematosus. Lupus is a well-documented autoimmune disease. Now Strelkauskas and his colleagues have found that patients with active juvenile rheumatoid arthritis — a possible autoimmune disease — have antibodies directed against suppressor T cells, whereas juvenile rheumatoid patients without active disease, as well as healthy persons, do not have such antibodies and possess suppressor T cells. Thus it appears that suppressor T cells and antibodies directed against them may play an important role in the pathogenesis of juvenile rheumatoid arthritis, although precisely how suppression of suppressor T cells might cause tissue inflammation remains to be explored. What's more, the finding indicates that there are distinct antigens (probably proteins) on the surface of suppressor T cells that the antibodies must react against. If such antigens can be defined, then perhaps antisera against them can be used to treat not autoimmune patients but cancer patients. The reason? The antisera would undoubtedly suppress suppressor T cells and allow killer T cells to attack tumors with full vengeance □