Cancer and the body's defense system

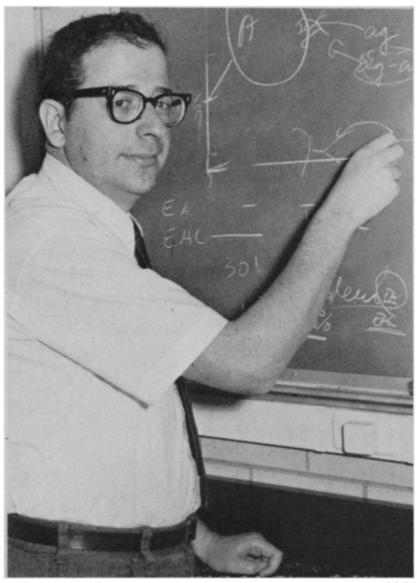
Research on cancer and research on immunology have converged into study of the body's complex strategies against foreign invaders

by Joan Arehart-Treichel

After the brain, the immune system is probably the most complex system in the body. It defends the body against bacteria, viruses and other foreign invaders. Immunological research has galloped during the past decade. So it is not surprising that immunological research and cancer research should converge.

Actually the normal role of the immunological system is not completely understood. The mechanisms of cancer are understood even less. Still, immunologists and virologists are getting some important insights into how immunology and cancer mesh.

If there is anything investigators have learned during the past few years it is that cancer is linked with suppression of immunological defenses. For example, 420 patients who received organ transplants and immunosuppressant drugs were followed for 10 years. Some 5.5 percent of them developed cancer within subsequent months. However, "It is unlikely that immunosuppression alone is a sufficient cause for the development of cancer," says Robert S. Schwartz of the New England Medical Center Hospitals. Martin S. Hirsch of the Massachusetts General Hospital agrees. "Many studies," he says, "indicate that immunosuppression alone is not enough for cancer to develop. Virus induction of cancer must also be present." Asserts Herman Friedman of the Albert Einstein Medical Center in Philadelphia, "I do not believe that anyone has the answer at present."



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Herberman: The body's dual defenses.

Whether immunological suppression is enough for cancer to develop or not, investigators are learning that immunological responses to malignancy are complex indeed. Ample evidence suggests that more than one defense factor is involved. For example, leukemia patients have been found to produce both antibodies and lymphocytes. When patients relapse, both antibodies and lymphocytes disappear. Mice make lymphocytes and antibodies in response to an injection of cancer virus, Ronald B. Herberman of the National Cancer Institute has found.

Lymphocytes are cells that are made in the thymus and bone marrow. Lymphocytes then pass into the lymph nodes and spleen. They are released from these tissues in response to infection. Because lymphocytic responses to infection are not immediate but long-range, they are known as delayed hypersensitivity. Antibodies are proteins that are released by lymphocytes in bone marrow. Antibodies are released right away in response to infection. They are known as humoral immunity. That both lymphocytes and antibodies are released in response to cancer signifies that cancer requires both immediate and long-range destruction.

Whether lymphocytes or antibodies are more crucial in the fight against cancer, researchers aren't sure. If a poll were taken, lymphocytes would probably win. For example, Karl and Ingegerd Hellstrom of the University of Washington took lymphocytes from a patient with a spontaneous regression of a tumor and put them with some of the patient's tumor cells. The lymphocytes killed the tumor cells. When antibodies from the patient, along with lymphocytes from the patient, were put with the patient's tumor cells, the cells were killed more swiftly. But the antibodies alone could not kill the cells.

Immunologists and virologists are getting a better idea of what it is that immune factors react to in cancer. The enemy appears to be cancer antigens. These are proteins or sugars that appear in the blood or on the surface of cells in cancer victims. Electron microscopic techniques are helping virologists distinguish viral antigens from cell-surface antigens. The antigens may be made by cancer viruses. Antigens may fight for places on cells, David W. Weiss of the Hebrew University-Hadassah Medical School in Jerusalem, suggests. Different kinds of antigens are linked with different kinds of cancers or even with the same kind of cancer. Herberman, for example, has found that more than one kind of antigen is present in animals with viral-induced leukemia.

Whether these antigens actively participate in the cancer process is not known. But the antigens are known to form complexes with antibodies. The role of these antibody-antigen complexes is controversial. Some evidence suggests that the complexes abet cancer by tying up lymphocytes and antibodies in arm-to-arm combat. If fresh immune forces are added to the complexes, the complexes can be unblocked and cancer can be overcome.

For example, a patient with cancer of the lymph nodes had antigen-antibody complexes in her blood. After the nodes were excised, the complexes disappeared. Later the complexes reappeared, and sure enough, the patient had a relapse. Lymphocytes can unblock complexes, Klein has found. Antibodies can too, the Hellstroms report. They found that antibodies could unblock complexes taken from patients

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Zbar: Priming the immune system.

with breast and colon cancer. If antibodies are given to animals with cancer, the complexes in their blood disappear and cancer regresses, Hans Olaf Sjögren of the University of Lund reports. Control animals that do not receive antibodies keep their complexes and their cancer.

While investigators are trying to get a better understanding of the role of immune factors in cancer, they are also exploring the possible value of immunotherapy for cancer. Since 1964, bacillus Calmette-Guérin, a strain of tuberculosis that has been used as an antituberculosis vaccine for many years, has been injected into animals and patients with cancer. BCG has induced a number of cancer remissions. There is evidence that BCG licks cancer by priming a cancer victim's immune defenses. Berton Zbar of the NCI found that the cell walls of the tuberculosis bacteria are just as effective as whole bacteria in bringing about a cancer retreat. This suggests that when the bacteria are injected into a host, the host regards sugars on the walls of the bacteria as foreign. The host makes lymphocytes against those antigens. The lymphocytes are then deployed to fight cancer.

All this is pretty tenuous, though. R. L. Simmons and his colleagues at the University of Minnesota gave BCG to cancerous mice. Their tumors disappeared but later returned. "If what we gave was immunotherapy," Simmons says, "the mice should have been cured forever." What is needed, Zbar stresses, is evidence that lymphocytes interact with bacteria antigens. Such evidence would be strong support for the theory that BCG primes immune defenses that in turn fight cancer.

However promising BCG treatment, it has several drawbacks. One is that it has raised false hopes in many cancer patients. Thousands of patients have called the NCI seeking such treatment. But BCG is usually effective only against new tumors. Also, BCG preparations vary markedly in composition and effectiveness. The side effects from BCG can be severe, Frank Spark of the University of California at Los Angeles, reports. And sometimes BCG can enhance rather than snuff cancer, add Friedman and George Mathé of the Institute of Cancerology and Immunogenetics in Villejuif, France.

"We need more animal studies," Zbar asserts, "so that we can approach clinical treatment with more confidence." Weiss agrees. "Despite the clinical urgency of immunotherapy for cancer," he says, "there must be solid groundwork for both scientific and ethical considerations. Immunological intervention may lead to heightened or suppressed tolerance. One cannot jump in this area." □

OFF *the* BEAT

This is the first appearance of a new SCIENCE NEWS *column titled "Off the Beat." In it, our staff editors will present informal items, personality notes, comments or anecdotes related to science—things we would like to share with readers that don't quite fit our definitions of news but that nevertheless seem likely to be of interest. We hope you find it adds dimension to your view of the world of science.—Ed.*

'Ascent of Man': Science with a dramatic flare

Broader and more deeply involved than Kenneth Clark's award-winning "Civilisation" series, Jacob Bronowski's "The Ascent of Man" dramatizes the rise of science from the humanoid's first stone tool to the latest theories on life and the universe. The 13-part film series is currently showing in Britain on BBC-TV.

Washington audiences, who were given a tantalizing glimpse of four of the films in conjunction with the Copernicus celebration in May (SN: 5/5/73), will get a chance to see the entire series this fall. The Smithsonian Institution will begin a program of Wednesday night showings for 13 consecutive weeks starting Sept. 19.

As for the rest of the United States, Time-Life Films, the series co-producer, hopes shortly to find a sponsor to bring "Ascent" to American television.

The films represent an important step in the ascent of television programming. Following Clark's peripatetic style, Bronowski and the series producer, Adrian Malone, take the viewer several times around the world, portraying the nature of scientific discovery through a whirlwind of exciting visuals. A discussion of steelmaking gives rise to a demonstration of samurai swordsmanship. The slow-motion agony of an athlete at full gait is contrasted with a child's first halting steps. A war game of 350 Uzbek horsemen recreates the epochal sweep of their ancestors, the hordes of Genghis Khan.

Most of all, Bronowski emphasizes the process of science, rather than the results, celebrating the "triumph of the process that takes nature apart and puts it back together in ingenious ways." From the beginning, he stresses the hand of the scientist as well as his brain. "Pleasure in one's own skill is the driving force of the ascent of man," he says.

Scientists whose faces most of us recall only from vacuous formal portraits suddenly gain personalities. An irascible Newton broods away the plague years in a country cottage, while he formulates a mathematics to unlock the secrets of the universe. Bronowski walks through the dim vaults of the Vatican archives and triumphantly holds up the documents proving Galileo was framed. He explains relativity in a conversational tone while sipping beer in the pub where Einstein first argued the theory with his friends, then takes the viewer onto the rickety tram Einstein rode home, for a simulated ride approaching the speed of light, to show relativity at work.

The dramatic climax of the series comes in the 11th installment when Bronowski tackles head-on the question of the social responsibility of science. Kneeling in the slough of Auschwitz where the ashes of perhaps 4 million prisoners were dumped, he blames the carnage on ignorance and arrogance, which, he asserts, is contradictory to all that science stands for. "Science is a very human form of knowledge," he says as he scoops up a handful of the mud and ashes that contain the remains of his own family.

The tone is tough; the details, explicit. When an old man of the nomadic Bakhtiari tribe of Iran grows too weak to ford a river under his own power, he calmly sits down to die. His relatives, the tribesmen and the camera crew all leave him. Only the camera looks back. With no concession for sentiment or squeamishness, a child is shown being born in pain and blood and mess. Yet that sense of wonder emerges from these details, without which, Einstein said, a man or a scientist is "as good as dead."

Sometimes scientific precision gives ground to visual effect in the series, and Bronowski's own halting, spontaneous style, though generally effective, sometimes rambles in a way that makes his train of thought hard to follow. The final installment of the series particularly suffers from this fault. Women are generally as absent in the films as in the title. Oriental science is cavalierly dismissed, and present youthful interest in oriental religions is considered a "retreat."

But such failures must be expected in a work so boldly personal as this. Like Clark, Bronowski is primarily concerned with whether Western science and civilization can survive. "It is a lack of confidence, more than anything else, that kills a civilization," Clark said. Echoing this sentiment, Bronowski laments what he calls a "loss of nerve" among some scientists. Ethnocentrism aside, "Ascent of Man" is conceived—in words Bronowski applied to the work of another scientist—with "immense integrity and at least a little genius."

—John H. Douglas