IMMUNOLOGY

Cancer and Immunology

Immunologists are frustrated so far in efforts to explain cancer in terms of the body's natural defenses.

by Barbara J. Culliton

Most people do not get cancer.

Though they fill their lungs with cigarette smoke and breathe polluted air, statistics show only one person in four is likely to get cancer.

Science does not know why some people don't succumb any more than it knows why others do, but the hypothesis that some individuals are immune to cancer is an intriguing thought which has contributed to widespread interest in immunology as a vital, active field of cancer research.

Immunologists who have committed themselves to ferreting out the intricacies of the human body's system of immune responses are looking for a relationship between cancer and the body's capacity to defend itself. If they find one, they can turn their knowledge into ways of preventing and curing not only cancer but a host of other disorders that may be associated with the immune system. Already they know a lot.

The human immune system is a two-step operation: first recognition and then response to anything foreign. If it is working efficiently, it responds to the presence of antigens—foreign proteins—by producing specific antibodies to destroy the invaders before they have a chance to disrupt the normal functioning of the body.

Recognition is as important to the smooth operation of the immune system as is rejection or response. The body cannot fight an enemy it doesn't know is there and when an antigen is not recognized as foreign, as may be the case with cancer cells, tolerance is established. And the body's tolerance of a deadly invader can be fatal.

Though immunologists know that recognition and response take place, and that tolerance may have been established if they do not, they have yet to learn the how of these phenomena. The mechanisms by which the immune system works remain one of the central mysteries of immunology.

Usually the human body knows enough not to produce antibodies to itself; that is, it tolerates itself. Most cancer cells do not appear to be immunogenic; they don't trigger antibody formation. This phenomenon shows that cancer cells are seen as part of the "self" the body naturally tolerates. They are, perhaps, so like normal cells in some unidentified way that they can spring up without being caught.

The other possible explanation for toleration of cancer cells is that there is recognition of a foreign body, but no response, and the one without the other is virtually useless.

Although there is no clear cut evidence to support this theory that cancer patients tolerate the antigens of their own cancer cells the hypothesis is an attractive one to researchers.

But there is not even proof that all human tumors possess antigens. There are circumstantial grounds for believing that at least some tumors do. Occasionally cancerous growths show spontaneous remission, lying dormant for years before they reappear, suggesting the existence of mechanisms that inhibit the growth of human tumors.

Researchers are finding it reasonable to postulate the tumor inhibiting mechansim as rooted in immunological activities. But they are unable so far to do more than postulate.

There is, however, additional promise in the realization that many cancer victims show impairment of immune responses. Whether their cancer is responsible for the immune deficiency or the deficiency responsible for the cancer is still open to question, according to Dr. Eugene Van Scott of the National Cancer Institute, Bethesda, Md. Either way, however, it is a problem of immediate clinical significance: if scientists understood it they'd be a step closer to a remedy.

Another link of potential clinical importance is the observation that the effectiveness of the immune system seems to decline with age, and correspondingly, the incidence of cancer is higher in older persons.

Experimental and clinical evidence to date suggest that the power of the immune response to alter the course of cancer is rarely sufficient to reverse permanently the growth of advanced cancer cells. But it may be able to slow the growth down and may be valuable in treating what is called "minimal residual cancer." That means, treatment by immunological methods may be useful in knocking out the last traces of disease in a leukemia patient, for example, who has been effectively cured by drug therapy or in a patient whose cancer has been effectively removed by surgery but in whom the statistical probability of recurrence is high.

National Cancer Institute

Cancer: doesn't trigger antibodies.

One of the greatest obstacles in the road to successful pursuit of the potential applications of immunology to cancer research is the fact that the tools of science are somewhat limited and overcoming those limitations is no simple thing.

"The immune response is hard to quantify," says Dr. John Fahey of the National Cancer Institute. "You may respond to one level, someone else may respond to another. There is no precise normal range of immune response, even within the same species." Because of this, the value of animal experiments is subject to grave limitations. To a certain extent, mice do make ideal animal models for studies of immune responses because one can breed identical strains and thereby do away with individual variations in immunological behavior in laboratory tests, Dr. Nathaniel I. Berlin, also of the Cancer Institute, points out. But it is difficult to extrapolate this data to man who is so extraordinarily variable in his biological responses.

Therefore, one leans toward increased use of clinical trials in the search for truth. This is an area in which things get sticky, but a recent report from the World Health Organization, "Immunotherapy of Cancer," calls for more consideration of tests on humans. In spite of the value of experimental data obtained from animals, "It should be recognized that cancer in man often differs considerably in its biological behavior and its response to therapeutic measures from the usual experimental models of cancer in rodents. This makes a continuing search for additional and more appropriate models necessary and may justify clinical therapeutic trials for which a firm basis of animal studies has not yet been achieved."