Is cancer man's middle name?

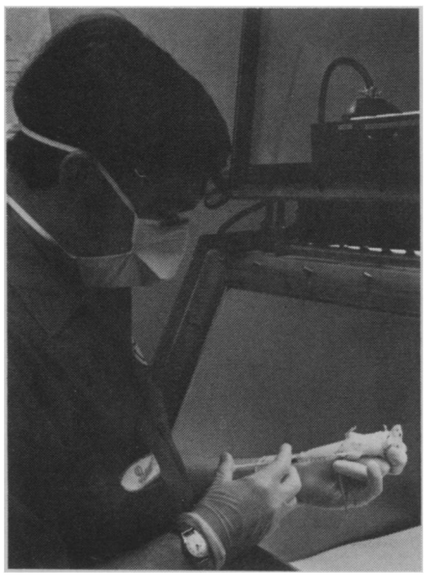
Evidence gathers that cancer is inborn, switched on by hormones, DDT or radiation

Something interesting, or disturbing, depending on how you look at it, has been brewing in cancer research laboratories during the past three years. It is the growing experimental support for a theory that cancer is not transmitted horizontally—victim to victim, say—but vertically by genetic inheritance. Cancer is no less than a malevolent component of man's genetic makeup. Only when the cancer genes are turned on by outside agents does a cell become malignant and grow into a tumor. The thrust of this hypothesis, in other words, is that every man carries the seeds of his own destruction, perhaps waiting to be activated by a variety of internal or external factors.

The overwhelming bulk of support for this theory, until recently, was limited to work on tissue cultures. Certain suspected markers of cancer, such as group-specific antigens and the reverse transcriptase enzyme, have been detected in certain cells in culture, but not in others. The cells containing the markers are not necessarily active cancer cells, nor do they always contain any cancer-causing virus. More interestingly, the markers were coaxed out of the cell lines by chemicals and radiation, further underscoring the possibility that certain outside factors might turn on cancer genes and cancer markers.

Then, last September, Alfred Hellman and A. K. Fowler of the National Cancer Institute reported they were able to activate one of the markers of cancer—the group-specific antigen—in live animals, not just in cell cultures, by injecting them with hormones. Again, no suspect cancer virus was detected in tissues from the animals. Here was still more evidence for the oncogene theory. (Oncogene is a general term for a tumor-causing gene.)

In the forthcoming (August) PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES, Hellman and Fowler, with George Todaro and D. C. Reed, also of NCI, will be presenting still further ammunition for the oncogene theory. They have now activated two kinds of cancer markers in live animals —group-specific antigens and the reverse transcriptase—using not just hormones but radiation and DDT. These



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Reed gives mouse hormone injection.

results appear to be the strongest yet supporting the notion that quiescent cancer genes are waiting for outside signals—hormones, environmental chemicals or radiation—to switch cells into uncontrollable reproduction and tumor formation. In the past, when hormones, chemicals or radiation were capable of inducing tumors in experimental animals, researchers tended to assume that these factors trigger cancer directly. Now it appears quite possible that these factors only activate genes that turn a cell into a cancer cell. Also, there is a high incidence of cancer in people during periods when there is hormonal fluctuation—prepuberty and postmenopause. Such hormonal activity might turn on cancer genes.

However elegant and though-provoking the oncogene theory evidence is, though, there are serious questions that still require answering. How do viruses fit in with the theory? Viruses have been used many times to induce tumors in animals. But, as Hellman points out, only in certain laboratory situations can chemicals, hormones or radiation be used to coax whole viruses out of tissues or whole animals. Far more often, only markers of these viruses, such as antigens or reverse transcriptase, appear. The preponderance of partial versus full viral expression, he and other oncogene proponents contend, argues for activation of latent oncogenes. Partial or full viral expression, in other words, is nothing other than oncogenes transformed; these oncogenes are built into a cell from conception, rather than transmitted into it during its lifetime.

What role does the group-specific antigen really play in cancer? The antigen has been found in some viruses known to induce cancer in animals and provides a marker for these viruses. Yet it has also been found in animal fetuses during normal embryological development and in certain reproductive tissues at the time of sexual maturity—both periods of rapid cellular proliferation. Might the antigen be expressed in any cellular growth, not necessarily the cancerous kind? Or might the antigen express itself upon hormone activation, independently of either normal or abnormal cellular reproduction? "The challenge we are faced with," Hellman says, "is proving the group-specific antigens we have found in animals are the same as those found in viruses, and that these are then related to cancer in man."

The role of the reverse transcriptase enzyme in the oncogene theory is especially nettling. Since the enzyme was discovered two years ago, it has been identified in some animal tumor viruses, in cancerous tissue from animals, from human leukemia tissue, from normal human tissue. Enzyme taken from leukemia tissue was recently found to copy tumor-virus RNA in the test tube, then make DNA that hybridizes with the viral RNA. Is this activity a sign that the cell has been infected with an RNA tumor virus, or that the enzyme is a normal cell enzyme that just happens to copy and hybridize with tumor-virus RNA? Or does the enzyme's presence mean that cancer genes have been activated in the tissue? If so, why is the enzyme capable of interacting with a tumor virus' genetic material? To further complicate (or clarify) matters, the NCI researchers now have preliminary evidence that the enzyme may be genetically determined. □