Issues in Science and Humanities
Whitney Humanities Center
Yale University
May 4, 2000

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I work at the junction of science as it is practiced, and science as it is studied, managed and funded. To most people who study science as well as practicing it, the practices of a science are the picture; the study, management and funding of a science are its frame, and the operating hypothesis is that those who manage the frame can move it around, but that they cannot paint the picture. That is, that managers can influence which problems get studied by those in the picture, but that they cannot have any real effect on the process – the model building and model testing – by which the work of science progresses.

I'd like to present evidence for the opposite: that the frame may determine not only the choice of topic for a science, but also the paradigm – the operating metaphor – on which a science's testable models are based. Further, I would like to argue that – far from a science being autonomous – it is not only the managers of science, but the public at large that may for better or worse help set these paradigms.

I will take my example from the field in which I worked productively for three decades: that aspect of cancer research which tries to understand the molecular mechanisms which drive a cell and its descendants to become a tumor. You can find these remarks enlarged upon in my new book, "The Missing moment: how the Unconscious shapes modern science," published in 1999 by Houghton Mifflin.

Just as every infection is an invasion of the body, every tumor is an insurrection from within. The cells of the body share a single heritage as the descendants of one fertilized egg, but the body is not a democracy. The human body is a society of a million billion cells, each living under the internal totalitarian control of its differentiated genome.

No cell has free will. Most are destined to sacrifice their lives for the sake of the greater good of the body, differentiating — filling themselves with proteins particular to one tissue and no other — until they no longer can divide, then dying in order that they may be replaced by younger, fresher versions of themselves.

The bodily insurrection and betrayal by a cancer are terrible to contemplate: if the body and the person are the same, how can one betray the other this way? Yet it happens, and not infrequently. About one in three of us will develop a cancer in our lifetime. Like all other failures of the body that occur primarily late in life, cancers are not of any particular interest to natural selection, so we find ourselves inhabiting bodies that are quite susceptible to betrayal as they age. Each year,

about a million and a half new cases of cancer are diagnosed and more than half a million people die of the disease in the United States; worldwide, cancer kills another seven million men, women, and children each year.

Current techniques for killing tumor cells with radiation and chemicals create the same Darwinian natural selection that takes place in the body of a person struggling with malaria or TB. As the tumor grows, throwing off a cloud of genetic variants, any mutant cells that can survive the body's defenses and medicine's assaults become the seeds of new, resistant tumors. Sometimes such mutants are overcome, and the tumor is eradicated. In other cases, the downhill slide ends with a painful death, a Malthusian – if not Darwinian – catastrophe for tumor and victim alike.

These similarities between cancer and infectious disease have generated similar dreams in the collective imagination of the scientific fields dedicated to understanding their respective causes and effects. Just as the fear of bodily invasion has been met by the dream of purifying the body from all microbes, a similar fear that at any time, in any place in the body, mutation in a single invisible cell may bring down the entire body has been met by the dream of being able to kill every last tumor cell. Until very recently that dream — as familiar as the dream of the perfect antimicrobial antibiotic — informed much of cancer research. It has yielded an equally familiar mixture of success and stalemate.

One aspect of cancer makes it a different sort of medical problem from any infectious disease and puts the dream of total victory wholly at cross-purposes with the actual possibilities for medical intervention. Cancers arise by mutation, and most mutations can be kept from happening in the first place. As a result most cancers — unlike most infectious diseases — are avoidable. Only a few percent of new cancers are the consequence of an inherited condition, and only a few more percent are the product of infectious agents. The ones that arise from infection can be prevented as well, by curing the infection. Eliminating the bacterial cause of stomach ulcers, for instance, also eliminates the associated risk of later stomach cancer.

All remaining new cancers — nine out of ten, or more — will be neither caught nor inherited. They will be the result of avoidable habits and preventable exposures that, given the will, can be changed at any time without the need for any further basic research. Tobacco smoke is the classic avoidable inducer of cancers, but far from the only one. Foods laced with pesticides, pollutants in the air and water (both at work and at home), radiation and drugs that cause mutation: all of these cause cancer, and all can be avoided. The risks of cancer from any of them are cumulative, so cancers tend to appear in older people. Thus prevention requires the earliest possible intervention. The same mother's milk that concentrates protective immune cells and antibodies also concentrates these chemicals and delivers them to a nursing infant, where they can reach much higher concentrations than are typically found in adult tissue.

This is the first irony: the science of preventing cancer is thus simpler and easier than the science of curing it. Prevention works, and it has no clinical side effects. With very little in the way of either cash or cachet, the strategy of prevention —

changes in diet, reduction in tobacco use, exercise programs — has led to a modest overall reduction in cancer deaths in the 1990s. Four percent fewer men and one percent fewer women died of cancer in 1995 than 1991. Perhaps a few lives were saved by genetic detection coupled with prophylactic surgery, but most were saved by people changing their habits to avoid cancer in the first place. Most escaped by staying away from tobacco. The different behaviors of men and women demonstrate this: a few decades ago, women took to cigarettes in great numbers as men were pulling back. In the 1990s, as the rate of lung cancer in men declined by more than six percent, it increased by almost the same percentage in women.

The unconscious fantasy that motivates much of today's cancer research is plainly visible in any country's budget for cancer research. Prevention is hardly mentioned. Instead, genes associated with higher risk are sought, on the premise that one day the information will provide better drugs to kill every last cell of the tumor that will inevitably arise. This agenda is woefully incomplete at best and absurd at worst. For instance, to discover precisely which chemicals will cause cancer when they enter the bloodstream, and then — instead of working to remove these chemicals from everyone's food, air, and water — to study the genetics of the liver proteins that detoxify them, is to be in a waking dream.

Driven by this dream of total victory after total war, scientists have wrapped cancer research in a variety of military metaphors over the decades. Each change in the scientific agenda of cancer research has been presented as a restatement of this war aim: to kill every last cancer cell. Untethered to the reality of cancer as avoidable, the rhetoric of cancer research has changed as well, always realigning the strategies of the cancer war with the nation's priorities. We have been through three different wars on cancer of this sort and are currently in the midst of a fourth, genetic, war today.

In the 1930s, the diagnosis and treatment of the disease were left in the hands of local doctors and hospitals. The major national charity concerned with the disease, the American Society to Control Cancer, opened the first war when it began to use volunteers to raise money for a small number of “cancer hospitals” around the country. In the depths of the Depression, with armies being formed all through Europe and Asia for what would be World War II, the charity moved from the genteel to the military. Its president recruited support from the General Federation of Women's Clubs to form the Woman's Field Army, the WFA. This female organization, with two million mostly middle-class women for troops, and with officers from Commander Eleanor Roosevelt to thousands of captains and lieutenants throughout the country, was organized to fight cancer not with guns nor with scalpels but with knowledge.

Learning that the disease was almost always fatal even in the best hospitals, and knowing that the few cures and remissions were almost always accomplished for cancers detected at an early stage, the WFA fought cancer with posters, radio announcements, newspaper advertisements, and the like, stressing self-examination and early detection as the best — if not the only — weapons against the disease.

The first war on cancer came to an end as World War II did, when Congress, prodded in good measure by the leaders of the WFA, created the first federal

establishment for basic research on cancer and for developing new treatments, the National Cancer Institute. This new laboratory, funded by Congress with money from what had been the Office of Scientific Research and Development during the war, soon had millions of dollars for cancer research. Private funds also increased, especially after Mary Lasker — whose healthy fortune came from her family's success at creating effective advertisements for, among other items, cigarettes — disbanded the WFA and converted the American Society to Control Cancer into a fund-raising operation, the American Cancer Society.

The second war on cancer was nuclear. Radiation was to be not only a fearsome new weapon of destruction but also a clean new knife that would remove all traces of the disease from a sick person's body. Life magazine's way of explaining this new treatment was to show a cancer cell under a mushroom cloud. As an editorial in a 1947 issue of the Journal of the American Medical Association blithely put it, “Medically applied atomic science has already saved more lives than were lost in the explosions of Hiroshima and Nagasaki.”

This second cancer war lasted as long as the first one, all through the Korean War, the early Cold War, and the period of nuclear proliferation, until the early 1960s. The side effects of radiation had become clearer by then. The appearance of radiation-resistant tumor cells in many patients meant that this war, like the propaganda war, was not going to end in complete victory. The answer was a new declaration of war, in terms well adapted to the politics of the day: a war against invasion by aliens.

This third war began about the time that the first nuclear test-ban treaties were being signed by the Cold War superpowers, a time when competition between them shifted to proxy wars fought on the territory of small Third World countries like Vietnam. In 1962 the Rockefeller University scientist Peyton Rous was profiled in Life in a cover story headed “New Evidence That Cancer May Be Infectious.”

Even though neither the most fearsome aspect of the disease — its capacity to strike at random — nor the striking propensity of some families to develop one or another kind of tumor fit easily into the model of contagion, the metaphor fit the times. It was the centerpiece of the successful campaign, led by Mary Lasker and the American Cancer Society, to establish the twenty-one comprehensive cancer centers throughout the United States. These were backed by the heavy artillery of the third war, the Special Virus Cancer Program, a vastly expensive federal effort to find and eradicate — search and destroy — the viruses that were now argued to be the cause of much human cancer. To win the war, the budget of the National Cancer Institute was increased from $140 million to $1 billion in a decade.

By 1975, the war on cancer viruses was going no better than the war on Viet Cong insurgents. Neither war was going to be won by the forces of the United States government, and Congress was no longer willing to support either. By 1980, the Special Virus Cancer Program had been partially disbanded. The remainder was kept going more as a support program than a high-priority research effort until a real virus, HIV, began to kill people. The AIDS crisis gave the government a clear use for the program, its facilities as well as its rhetoric. Although little in the way of curing human cancer had come out of the third war, many of the facts about how HIV works and many of the agents that slow its

progress came from the redeployment of its weapons and troops. About a tenth of the NIH budget, about $1 billion per year, has gone into research on AIDS in the 1990s.

The fourth war on cancer, declared as the Cold War ended, focused on the discovery of genes that are specifically mutated in cancers. These genes liberate a line of cells to grow from a differentiating tissue cell that otherwise would have died without offspring. The genes fall into two classes: genes that would lead to the death of a cell that has suffered significant damage to its DNA, and genes that would lead to the death of a cell by normal, terminal differentiation. One gene of the first class, called p53, makes a protein that will make a cell that has received damage to its DNA commit suicide, shriveling it up in a process called apoptosis. The p53 protein is missing or inactive in a remarkably large fraction of all human tumors, regardless of tissue. In the absence of this rather severe quality-control agent, a clone of cells will not only be able to grow despite mutations suffered throughout its chromosomes, but it will also be able to accumulate new mutations — including ones conferring resistance to chemotherapy — at an escalating rate.

In this fourth war, the enemy has ceased to be an alien and became a home-grown, misguided, camouflaged militia fighter. This most recent shift in emphasis in the military metaphor is particularly inward and repressive. Today's war on cancer is heavily invested in checking IDs and passports; that is, it recognizes the genetic differences that create and identify cancer cells, so it can better monitor the success of treatments designed to root them out and kill them.

An unexpected second front in the fourth war was opened in the 1990s with the discovery that some of the genetic differences that convert a normal cell into a cancer cell could also be inherited through the human germ line. Families in which such a mutation can be inherited have remarkably high frequencies of particular sorts of cancer. While avoidable stem-cell mutation is responsible for the vast majority of cancers and germ-line mutation is responsible for only a few, scientists on this new front imagined all cancers to be problems of family inheritance rather than random misadventures. Instead of being a threat to all and therefore a social problem, cancer became a personal problem for those at higher risk because of their genetic endowment.

The earlier cancer wars produced two-edged weapons, but at least drugs and radiation did stop some tumors in their tracks. Human germ-line genetics has not yet added much to the arsenal of such weapons, but it has already given new force to the old business of fortune-telling. DNA-based fortune-telling may serve as an early warning for someone who will then be able to catch a genetically inevitable clone of cancer cells as soon as it appears. But it can also mislead others into thinking that because they are free of a germ-line mutation, they are somehow protected from the more common sorts of cancer that grow from random stem-cell mutations.

A sure sign of the unconscious at work is the inability to give up a set of useless behaviors or habits that serve to alleviate a hidden fear or need. In this case, the hidden fear is obvious: scientists do not want to get cancer. For a scientist to be able to diagnose certain death in a number of strangers while remaining personally free of the risk and unfazed by the information, confirms the dream that science can be a way to avoid death. Dangerous variants of growth-control

genes are rare except in tumors; only a small fraction of the population inherits them. The tools that detect inherited propensities pick up very rare events, so the scientists who develop them are unlikely to be given a bad prognosis by their own hand; it is only a little bit magical for them to think that they have warded off the disease. As a result, a preventable disease that can strike anyone has begun to be reinterpreted as an inherited disease, one that cannot be escaped if one was unlucky in one's ancestors.

Avoiding cancer is a better and cheaper outcome than curing cancer. By focusing on the human genetics of susceptibility to cancer, scientists have escaped into their own fantasy of avoiding the risk of the disease. As a result, cancers that might be avoided by all of us today if we took the necessary political steps are coming to be regarded as the unavoidable future consequences of someone else's genes. Genetic medicine will be more than a fortune-teller only when the information it yields is coupled to a mature strategy for preventing the vast, preventable majority of cancers. We are not there yet, and it is difficult to see how preventive strategies can become part of a current genetic war on cancer in a country that has not yet even made medical care a right and privilege of citizenship.

In an impassioned defense of basic research written for Scientific American at the height of the congressional budget debates of 1994, the renowned nuclear physicist Victor Weisskopf made the case for science as an agent of medicine's transformation, the bridge connecting an inadequate earlier medicine of empty altruistic gestures to a current medicine of treatments and cures: “Human existence depends on compassion and knowledge. Knowledge without compassion is inhuman; compassion without knowledge is ineffective.”

For people who have an incurable tumor and for their families, there is no reason that compassion without knowledge cannot be effective; it is what they most need. For those with cancer and all other diseases that cannot be cured, the other half of Weisskopf's syllogism fails as well: certain kinds of scientific knowledge about cancer — the fact that one has inherited the certainty of developing an inoperable tumor, for instance — simply cannot be conveyed with compassion and may be intrinsically inhuman. In terms of our current science, the implications are plain. If it were not for the unconscious need of everyone, even scientists, to push the real meaning of an incurable disease away from consciousness, basic research would be able to contribute to that last stage of life instead of turning away from it in abject terror disguised as a lack of interest in a hopeless patient.

This is the second and final irony of our current situation: it is not even good science for us to act as if genetic knowledge was final knowledge. Though the differences in DNA sequence between any two people underlie and provide a biological foundation for the notion of human individuality, individuality is more than genetic. Because our brains are capable of sustaining consciousness and memory only by changing in response to the world, each of us is as different in terms of brain chemistry from all other people as our lives are from all other lives. Consciousness not only assures that each of us is doubly unique, it also allows our experiences — and therefore certain changes in our bodies and brains — to be remembered and experienced for many generations. It provides our species with a

second channel — teaching and learning — for transmitting differences between individuals over times much longer than an individual lifetime.

Learned experience is the only biological channel of this sort we know of, one that does not need to encode differences in DNA in order to preserve them for many generations. Like the DNA-encoded differences in our genes, the different lessons learned in life can be transmitted perfectly or imperfectly; like mutations in genes, changes in what is learned or taught can become fixed in later generations. The second channel gives our species a unique advantage in competition with other forms of life: what may take millions of years and tens of thousands of generations to appear through DNA can be learned – even by the managers and practitioners of a science– in less than a single generation. It's about time for biomedical science to begin to use that channel to understand itself.