Dr. Philip Handler has been president of the National Academy of Sciences for nine years. He has three more years to go as head of this most esteemed scientific body. Although he apparently enjoys his work, he recently told C&EN's Wil Lepkowski (C&EN, Feb. 13, page 20) that heading NAS can be a lonely job, "because the buck stops here. I have a continuing sense of being the scientific community's lawyer in town—a sense that it devolves on me to have the gut reaction to the scientific community on one issue after another." And, as Lepkowski himself put it, "[Handler] sees himself and the academy as elitist and one of the few remaining voices of reason that can command some kind of audience."

Handler took the occasion of the recent Washington, D.C., meeting of the American Association for the Advancement of Science to articulate some of these gut reactions and to speak out on the state of science today in a public lecture entitled "Pangs of science." Here, verbatim, is his prepared text.


C&EN staff photo

Pangs of science

Philip Handler, president, National Academy of Sciences

According to legend, Prometheus, who pitied the sad estate of mortals, defied the will of Zeus and stole fire from the sun in order to give that gift of power which made possible man the toolmaker, the traveler, and the food grower. Prometheus was condemned to torture and the gods on Olympus schemed to prevent mankind from fully possessing the fruits of its growing power. To this end, they created Pandora, whom they endowed with Aphrodite's beauty, Hermes' gift of persuasion, and Apollo's music to entice the heart of man. Endowed also with burning curiosity, inevitably she pried into the box which she had been sternly forbidden to open, a box which once opened could not be closed. And thence escaped a thousand plagues to scourge humankind until only hope remained. It was Bentley Glass who noted that the fact that Prometheus and Pandora are part of the same legend constitutes a great truth.

For most of the history of science, the knowledge and power that it brought were accepted and admired. Despite the horror of Hiroshima and Nagasaki, World War II was followed by two decades of euphoria. We gloried in the power that Prometheus had given us and came to assume that science and science-based technologies offered endless opportunity to alleviate the condition of man. But for the last decade, Pandora has increasingly claimed our attention as we became aware that technology can also engender unplanned secondary effects, "dysbenefits," which can subtract substantially from our evaluation of the benefit that was sought. The tragedy of Prometheus was not his defiance of the gods but his inability to foresee the full spread of consequences, leaving us, therefore, the children of Pandora.

To be sure, we still delight in each new technology; witness the extraordinary rate of diffusion of the pocket calculator, TV, and microprocessors for industrial control. But concern for the environment, malaise in the universities, criticism of the military/industrial complex, and indifference to what seemed almost routine walks on the moon were warning signs of a movement that has challenged the objectives of technology and internal standards of science.

For several decades, scientists, who pursued science for the pure joy of it, publicly associated science with spectacular technological progress. We found it facile to justify government support of basic research on the ground that it is the indispensable substratum of technological innovation, hence automatically to be taken as a public good. For having thus claimed credit for the benefits of technology when the public regarded technology as desirable and benign, science is now held, by some, to be responsible for the evils of technology grown out of control, a blind monster advancing according to its own internal logic, independent of democratic accountability. The claim of science to autonomy is seen as a claim for the autonomy of technology, for allowing technology also to develop according to its own logic. Associating science, therefore, with the threat of nuclear and "conventional" wars, as well as with deterioration of the natural and social environments occasioned by too rapid diffusion of unappraised new technologies, science as an institution is sporadically attacked by a coalition of those who denounce it as the expensive pastime of academics who show insufficient concern for efficiency and profitability, and those who see it as the instrument of military and economic domination. Both extremes demand that scientists should concern themselves more with the short-term "real needs" of society, while themselves perceiving these needs quite differently.

Mark you, science never was esteemed in the public mind for the values peculiar to science or even for the positivism which accompanied it. Historians may one day write that, in this era, the achievements and the spirit of science dominate the education, the employment, and the daily life of human beings. But of only a small minority of us. Indeed, the influence of superstition and belief in magic seem but little reduced. Twelve hundred U.S. newspapers publish daily horoscopes and 10,000 so-called astrologers find lucrative employment.

If the stream of antiscience pronouncements calling for a return to instinct, spontaneity, and "nature" were merely a literary revival of anti-intellectualism, the indictment would have little more effect than when science was the target of such mystic, romantic critics as Blake and Ruskin, even though it is hard to forget that anti-intellectualism also nurtured the worst political movements of this century. What is new in the present situation is that criticism of science no longer comes exclusively from outside. Numbers of scientists now join other intellectuals and the man on the street in voicing anxiety.

A principal cause of the malaise which has afflicted the western world for a decade has been awareness of damage caused by the very process of economic growth toward which national policies have been directed. To the extent that science is seen as connected with that damage, its image is no longer simply coterminous with the image of progress. Only yesterday, scientific activity could flourish innocently, unconscious of its role in processes that sometimes result in disastrous effects. Today, the movement called "technology assessment" demands that both science and technology prove their innocence in advance. It was Hannah Arendt who said, "The natural sciences are given credit for bringing about a demonstrable and increasingly swift growth of knowledge and power, but they can also be reproached for having increased, in scarcely less demonstrable manner, the instruments of death, despair, and nihilism. . . ."

Before her, Pasteur spoke of laboratories as "temples of the future and of well-being," and said that ". . . in those laboratories man learns how to read the works of nature, works of progress and universal harmony, whereas his own works are too often acts of barbarism, fanaticism, and destruction." Today, the works of science are seen by a vocal few to operate as much in the service of barbarism as in that of universal harmony. Yet, at this moment, when large computers are dedicated to increasingly sophisticated systems analyses of what the Club of Rome dubbed "the problematique," science is being translated into hundreds of imaginative new technologies; and powerful new insights emerge almost daily concerning the nature of matter, concerning the forces that mold the surface of the earth or give rise to climate and weather; concerning the history, structure, and future of the cosmos; concerning the elegant complexity of a living cell and the workings of that most remarkable of all objects, the human brain. It is a bitter irony that, at such a time, the protest movement appears to be growing significantly from within science itself. These voices may comprise a very small fraction of the scientific community, but the malaise is real. I sense that fewer and fewer scientists can now find unadulterated pleasure in their pursuit of scientific understanding.

The ground was laid long ago. André Malraux traced it back to the use of poison gas in World War I, which, he said, "for the first time showed the adverse side of science's balance sheet." What was not perceptible earlier was the discomfort which would arise from the fact that, as its pursuit became increasingly expensive, science, once symbolized by the ideal of the gifted English gentleman amateur, has associated itself increasingly with the authority and power of the state. This has been eloquently described by Jean Jacques Salomon, "The movement which, since the beginnings of modern science, has turned scientific research into a secularized profession leads, through science policy, to its transformation into a state institution if not a state religion. While the ideology of science conceives it as pure adventure of the mind, disinterested research as an institution autonomous in the social system appears illusory, even mystifying, in the face of the realities of the practice of research. For the scientist's position is bound up entirely with an inescapable ambiguity: Science claims to be an end in itself but it is recognized and supported only on account of its instrumentality."

Nothing so illuminates that transformation as the cases of Galileo and Oppenheimer. The former was a conflict between two different concepts of the nature and limits of knowledge, scientific analysis versus that which is alien to it, whereas in the latter, technical advice to the state was at odds with the political decision which it was called upon to inform.

Despite those changing circumstances, most scientists, nevertheless, "stick to their lasts." Indifferent to the conflicts others perceive in the relationship between science and the state, they pursue science at the frontiers of their disciplines; and it is they who advance those frontiers, the principal role of science. But a few scientists attempt to embrace a broader view, they evoke recourse to moral and aesthetic values which, we all can agree, must be preserved if both science and civilization are to survive. What is perplexing is that these values have led scientists to both sides of current attitudes concerning appropriate public policy regarding such matters as degradation of the environment, nuclear power, and research on recombinant DNA.

Risk vs. benefit analysis

Those who would be rational in such matters attempt their examination by formal risk/- or cost/benefit analysis. Perhaps the oldest such on record was that of Bernoulli, two centuries ago, who calculated that although, for an infant, the risk of death due to smallpox in the first 30 days after inoculation (it was not yet "vaccination") was 10 times natural risk, the chances of survival to age 25 after inoculation were increased 50 times over those who developed natural smallpox with a net population gain, 20 years later, of about 15%. But the great environmental problems of our day involve risks and benefits that accrue to different groups, and costs, risks, and benefits that are incommensurable. Costs are reckoned in dollars; benefits in aesthetic or material values; risks in human lives. Formal risk/benefit analysis may inform the decision maker, but decision necessarily continues to turn on value judgments; the acceptability of a given level of risk remains a political, not a scientific question. Hence, essentially political beliefs easily becloud seemingly scientific debate when scientists fail to recognize these boundaries.

Awareness of the need for environmental protection burst upon us in the 1960's. With sudden public awakening to the fact that the environment had been used as a free good came a rush to put into place protective policies and programs, and to internalize the associated costs in the price of goods and services. Although various technologies, in retrospect, appeared to have been mixed blessings, for most of the U.S. public the benefits have far outweighed the negative features and the additional costs which must be imposed were generally accepted.

As these events have proceeded, I have been disturbed by the facile identification of science as the primary culprit because it was progenitor of the technologies whose unregulated use has resulted in despoliation of field, stream, and atmosphere. That identification is particularly ironic since science is usually required both for recognition of the problems and for suggestions for their management, largely because those forms of pollution which are today of greatest concern relate frequently to substances undetectable by the human senses. For example:

Phosphate is an integral component of all living cells, but when present in agricultural runoff or in municipal wastes, it becomes a nutrient for the growth of algae which flourish, die, and are decomposed by oxygen-consuming bacteria, yielding stinking anoxic streams and eutrophied lakes.

Smog is the consequence of sunlight acting on invisible, unsmellable constituents of automobile exhausts. Invisible sulfur dioxide from power plants interacts with micron-sized smoke particles to produce sulfate aerosols which are alleged to be the primary health hazard from air pollution, although the magnitude of that hazard remains highly uncertain. Invisible carbon dioxide, now increasing in the atmosphere from the combustion of fossil fuels, may be becoming the most dangerous of all atmospheric pollutants in consequence of the "greenhouse effect" and its consequences to world climate.

But mark you, the possibility of such an effect came to attention only because of knowledge of the fine structure of the infrared absorption spectrum of CO_2, established by those desiring to understand the stretching frequency of its C=O bonds. And the greenhouse effect could be predicted only by use of elaborate computer models of the atmospheric radiation balance and global atmospheric circulation patterns.

Perhaps the most subtle instance is the threat of reduction by chlorofluorocarbons of the stratospheric ozone column which protects us from the sun's ultraviolet radiation and thus from skin tumors. Without the stimulus of an hypothesis growing out of fundamental research in atmospheric chemistry, no one would have thought to seek an effect of pollutants on stratospheric ozone. (The most recent calculations indicate that effect to be about twice as great as had earlier been proposed. And I should take this occasion to note that the hypothetical effect upon ozone of nitrogen oxides arising from the use of nitrogen fertilizers and from combustion processes now seems rather unlikely.)

These various gases constitute a new type of societal problem; their effects have been predicted by scientific theory, they have not been demonstrated. This effect on ozone may be the paradigm of what may prove to be an increasingly common characteristic of modern pollution problems: The human consequences can appear only after so long that, if they are to be forestalled, they must be predicted from theoretical considerations or laboratory observations well before they become significant. Prototypical are substances whose ingestion may result in the appearance of cancer only after 30 or 40 years, and even then in only a very small percentage of the exposed population. In the absence of a guiding hypothesis, such cancer, like that indirectly resulting from chlorofluorocarbon release, will appear to have occurred on so random a basis as compared with background fluctuations that causality will not be demonstrable, analogous to the presumed effects of widespread exposure to low doses of radiation.

The point is that science, the progenitor of technology, is also its conscience—and should not be maligned!

Debate has barely begun

Meanwhile, the great carcinogenesis debate has barely begun. The assertion that environmental factors contribute significantly to carcinogenesis rests on distinct historic differences in the geographic incidence of various forms of cancer; the presumably responsible environmental carcinogens have rarely been identified. For example, the extraordinarily high incidence of gastric carcinoma in Japan was prevalent when first such records began to be kept. But Nisei Japanese in the United States show no more gastric carcinoma than do any other ethnic groups within our population. The carcinogen in Japan is unknown. What is so frustrating is the fact that gastric carcinoma, once also a fairly frequent form of cancer in the United States, now essentially has disappeared here and we are at a loss to account for this phenomenon. We are doing something right and don't even know what it is! Or are we, since the incidence of cancer of the colon and bowel has increased while that of gastric carcinoma declined?

What seems certain is that only a minuscule fraction of the environmental factors that have contributed to the patchy distribution of carcinogenesis in the recent past was due to chemicals made and utilized by man; they have been present in nature. The future is less certain.

There is rising anxiety for the potential carcinogenic effects of the thousands of organic compounds now utilized for diverse purpose in our civilization. Substance after substance—pesticides, food additives, industrial intermediates—has been screened for carcinogenic activity and its use challenged. Only rarely have the data enabled confident decision. More frequently, we are confronted with compounds that are mutagenic in bacterial assays but without other known effects, compounds which are mutagenic and which induce neoplasia in only one sex of one strain of mouse and are without effect on rats and rabbits; one material, arsenic, seems carcinogenic in humans but is without effect in test animals. For only a handful of compounds is there a convincing, consistent body of laboratory and epidemiological data. Using necessarily limited numbers of test animals, in many cases positive carcinogenic effects have been obtained only at dosages immensely greater than those

C&EN staff photo

that might be encountered in the human environment. How shall one regard experiments in which no lesions are seen in animals receiving one half the maximum dose? For chemical carcinogens as for radiation, we do not know whether the dose/response curve, in intact animals if there were enough data to construct one, would go neatly through the origin or, in consequence of the metabolic activity of the liver or of enzymic repair mechanisms for damaged DNA, would drop to zero at some threshold exposure level. When evidence of adverse effects on humans is lacking, I could wish that those engaged in such studies would behave as do scientists generally and refrain from publication until they have completed a sufficient series of coherent studies to enable rational decision, rather than announcing each experiment in turn, generating public alarm that can neither be justified nor assuaged. Once a compound has been called into question, publicly, decision concerning its use becomes unavoidable. The sensible guide would be to accept substantial hazard only for large benefit, little hazard for small benefit, and no hazard if it can be avoided without penalty. But in most cases, to date, quantitative assessment of risk is entirely lacking. Hence, conservative value judgments, minimizing the possibility of risk, must prevail, as they have.

Under these vexing circumstances the public discourse is sometimes strident. Years ago, Maurice Arthus, one of the founders of immunology, warned that the scientist who publicly adopts a doctrine for reasons that are not patently scientific has based his or her arguments on personal articles of faith. Wrote Arthus, "... to persist in one's faith becomes in a sense a question of honor. Having adopted such a public position the protagonist... becomes like the attorney who defends a client in spite of the evidence of his crime, like the politician who exalts his party even for its mistakes and vile actions which he proclaims to be acts of virtue and of courage. He automatically sorts the facts newly brought to light. He retains those, even the modest ones, that seem to prove him right and neglects the others, even the clearest and most precise and convincing ones, if they appear to indict him. Blinded by his passion, that is by his immoderate love for this theory, he has recourse to all means, honorable or not, in order to defend it, for to him, all means have become legitimate. He has ceased to be a scientist and has become a partisan." How reminiscent of the recent history of DDT, diethylstilbestrol, cyclamates, and the Sanguine antenna.

Whereas man's activities have badly scarred some areas of the earth's surface, this process is being brought under increasing control—enlightened modern agricultural, lumbering, and mining practice can actually improve the aesthetic quality of the environment. Witness the glories of the European countryside. For most environmental pollutants that have been called to attention, we are concerned with potential but as yet undemonstrated hazard. Statistically speaking, relatively few persons have been known actually to have been seriously damaged by man-made chemicals. We can only be sure of those injured in a series of dramatic but relatively small episodes, e.g., carbon tetrachloride, kepone, vinyl chloride, dibromochloropropane, and asbestos fiber as well as mercury, beryllium, lead, and several polycyclic hydrocarbons. It is perhaps informative that the examples which most readily spring to mind are those instances in which toxicity to humans was noted before studies in laboratory animals. We have become highly conscious of such problems; the Environmental Protection Agency, the National Cancer Institute, the Occupational Safety & Health Administration, and a host of other institutions, public and private, are alert and vigilant.

The result has been a stream of regulations, each well intentioned, each, indeed, commendable. But in the absence of persuasive data concerning the magnitude of risk, if any, to humans, the sum of such regulation can engender public cynicism, ensnarl life in the workplace, and slowly paralyze the economic life of the nation. Hence, I applaud the evolution of the Clean Air Act as amended, from reduction of risk to zero, regardless of cost, to decision based on comparison of marginal cost with marginal benefit of pollution abatement. But that returns to the scientific community the burden to quantify the risk and relate health effects to exposure levels. A decade ago it was necessary, even desirable, to flag public attention to potential hazard and proceed as if the hazard were a clear and present danger. It is time to return to the ethics and norms of science so that the political process may then proceed with some confidence. At the current stage of scientific understanding of almost every matter where science and technology affect public policy, decision must be taken in the face of uncertainty. The public may wonder why we don't already know that which appears vital to decision—but science will retain its place in public opinion only if we steadfastly admit the magnitude of our uncertainty and ignorance. And we shall lose that place if we repeatedly dissemble and argue as if all necessary fact is in hand—whether the problem be dietary prevention of atherosclerosis, the health effects of air pollution, or the economics of solar energy. Scientists best serve public policy by living within the ethics of science, not those of politics.

Shibboleth of the antiscientists

Nuclear power ranks with nuclear weapons as the shibboleth of the antiscientists. The controversy surrounding nuclear power has been conducted by scientists who, on both sides, have done much to inform that debate. To be sure, there remain technical issues that have not been resolved to the satisfaction of *some* scientific critics: the effectiveness of technical means for preventing diversion, by governments, of weapons-usable materials from the fuel cycle, or their theft by terrorists; the safety aspects of reactor design including protection against the consequences of deliberate sabotage; the long-term management of nuclear wastes and the release of long-lived radioactive effluents from fuel reprocessing plants. Presumably, generally acceptable solutions to these questions will ultimately emerge. But even when they do, debate will continue and the scientific community, like the country generally, will remain divided precisely because decision will turn not on scientific questions but on social and political value judgments.

The best estimate of the risk associated with the complex nuclear fuel cycle for light-water reactors is approximately 0.5 death per gigawatt per year—about 1/200th that stated to be associated with an equivalent electrical supply generated by coal combustion. But these figures are not strictly comparable. 0.5 death per gigawatt per year is the statistically prorated effect of the loss of life in major accidents postulated to occur with very low frequency in many reactors over a long period. No such event has yet occurred. We hope that none will. Apart from the possibility of such major events, there is an essentially zero death rate due to nuclear power. Controversy, therefore, centers about the appropriate public approach to the rare major accident. An event that would result in a thousand fatalities once in 10,000 years could be stated to subject society to a risk of loss of 1/10th of a person per year—absurdly trivial as compared to crossing streets, eating steak, or taking baths. But some view the possibility of a large-consequence accident, however low its probability, as intrinsically unacceptable. How society should weigh infrequent catastrophic events in comparison with frequent small events cannot be settled by any objective criterion known to me, and scientists should not suggest this to be a scientific question.

Public distrust of the institutions and individuals responsible for the management of nuclear energy programs in the past will cast a long shadow into the future. Even granting that there can be developed essentially acceptable technical solutions to the problems of reactor safety, waste management, and the safeguarding of weapons-usable materials, many will question whether human institutions can be relied upon to implement and monitor them on a long-term basis; many will be skeptical that international institutions for the management of the nuclear fuel cycle will provide sufficient assurance against the proliferation of nuclear weapons.

To these judgments must be added concern for the future of a democratic society if the safeguarding of nuclear facilities—reactors and reprocessing plants—will perpetually require rigorous security measures. That prospect led Alvin Weinberg to propose minimization of the numbers of such vulnerable facilities by construction of large, well-guarded, self-contained power parks, each to contain a considerable number of reactors, a commensurate reprocessing plant, and waste disposal facilities, each park to supply power to a rather large geographic area. An extension of this notion was proposed by Haefele, who proposed that several islands, where the ocean itself could be used as the coolant, be dedicated to clusters of breeder reactors and their associated reprocessing facilities, their output to be converted to either hydrogen or methanol which could then be shipped to the mainland. I mention it because such an arrangement, like Weinberg's scheme, would minimize the intrusion of the necessary security measures on the rest of society.

For others, their views of the desirable character of future society condition their rejection of nuclear power. For them, nuclear power stands as the most visible symbol of centrally, bureaucratically managed technology for which the average citizen has surrendered control to experts who cannot be held accountable. A segment of the younger public also dislikes nuclear power and particularly the breeder reactor because it offers the likelihood of continuation of a high-growth, materialistic society that, in their view, will ultimately prove disastrous to both the physical and social environment of man. Arguments concerning the safety of nuclear power are lost on this group which affirms the "technological imperative": "What can be done, will be done." Believing that *development* of a given technology makes its ultimate *deployment* inevitable, they say, "Stop it now." These critics of modern technology, and with it of modern science, espouse an alternative but perhaps scientifically equally sophisticated "soft" technology that emphasizes decentralization, local self-sufficiency, and small-scale enterprises controlled by consumers and craftsmen. Household solar energy, windmills, and renewable resources, generally, have become the positive symbols of this school; in its way, it holds the fascination of the Israeli kibbutz. However strong the attraction of this vision of an alternative life style, it can be available only to a relatively small group drawing on the resources of a larger affluent society and seems an unrealistic goal for the bulk of an already overpopulated modern society.

Many nations of both the industrialized and developing worlds already have cast their lots firmly with nuclear power and several are driving toward the commercialization of the breeder reactor. Breeder reactors may well be inevitable in the future of the U.S. as well, but years of debate lie ahead. The date of decision will turn on international agreement to on-site inspection, the success of conservation in braking growth of demand for electricity, the magnitude of oil fields yet to be found, the success of secondary oil recovery, the economic feasibility of various coal technologies, and the rate of penetration of other energy technologies. The latter, in turn, will depend upon whether the economically uncompetitive costs of such technologies—oil shales, solar electric, solar production of liquid fuels—will find acceptance as a charge to what must be regarded, psychologically, as the national security accounts rather than the cost of energy. Regrettably, this debate and the factors that will influence decision come rather late; if breeders prove to be required by 1995, it is already too late to start on the development of a commercial reactor that can be on line by that time. We have entered the transition from the age of hydrocarbons to the age of dependence on essentially infinitely available energy resources. It will be a turbulent half-century at best. How it will turn out depends on whether we muster the political will to do all that is required, particularly to mount and sustain the necessary R&D program. And the country will need all the science it can muster to support development of benign new technologies so that the nation will be able wisely to choose among truly feasible and economic alternatives, and not be in the hapless position of choice among a set of unacceptable technologies.

Recombinant DNA is newest battleground

The newest battleground concerning science is truly about science and how it is seen in U.S. society, viz., research utilizing recombinant DNA, the technique in which a fragment of the genetic material of one species is inserted into that of a second species. This esoteric but simple technique, the most powerful tool now available for illuminating the structure and functioning of the genetic apparatus, evoked a crescendo of concern, which is now diminishing somewhat. The public was frightened by tales of imaginary hazards reminiscent of "The Andromeda Strain"—a book written to be entertaining, not believed. And the statements of a handful of scientists, few of whom were currently close to this field of research, were taken as evidence that "the scientific community is itself divided."

The earliest expressed concern was for the possibility that in the course of such research there might be generated a microorganism that would escape laboratory control and, being of a new species, might prove to be dangerous to man, to domestic animals, or to the environment.

Since first the matter arose, I have had difficulty in imagining that this research could engender any risk greater than that which is daily accepted by those who minister to persons afflicted with genuine viral or bacterial infection. Every day the world over, thousands of technicians with a modicum of training in sterile technique have cultured and manipulated genuine, virulent, pathogenic bacteria taken from the urine, stools, sputum, and blood of patients. And they have done so, all things considered, with a remarkable overall safety record. That risks exceeding those of everyday, unregulated, routine hospital practice may attend any experiment with recombinant DNA that a knowledgeable investigator might reasonably wish to perform has never been made clear to me. Nor are the viruses to be utilized in these studies man-made objects. They are abroad in nature. They have been harvested and studied with none of the physical containment facilities now demanded, and largely without incident. I have difficulty in believing that a fragment of such a virus placed in an innocuous bacterium transforms it into a raging beast, unmanageable by standard cautious laboratory procedure.

A panel of the National Academy of Sciences that examined all aspects of this question concluded that: "The body of evidence acquired or adduced over the last few years clearly indicates that recombinant DNA research, performed under the NIH guidelines, presents no real risk to public health. Past experience teaches that no manifest epidemics have ever arisen from laboratory work even with extremely pathogenic and contagious organisms, whereas recombinant DNA work uses nonpathogenic organisms with diminished communicability. Knowledge of the biology of EK-2 hosts and vectors gives confidence that, when the research is in the hands of trained workers, no untoward events will occur. We conclude with the majority of scientists that many of the concerns first expressed in 1973 have been satisfactorily answered.

"Indeed, it is probable that most recombinant DNA work using enfeebled *Escherichia coli* systems could be carried out safely without any special precautions. Consequently, the public and its representatives and legislative and administrative office should consider carefully the risks of overregulating this kind of endeavor. . . . The financial cost of overly cautious containment and enforcement, the delay in achieving benefits, and the penalties incurred by restricting freedom of inquiry are real risks to be considered in setting up regulations."

Ironically, the very enzymic "cut and paste" procedures used in the laboratory have been found to occur constantly in nature, with plasmids moving back and forth among unrelated bacterial species and being remodeled by identical mechanisms. Indeed, Elwell and Falkow were led to state that, "While committees of scientists and laymen banter about recombinant DNA around conference tables, nature has been conducting experiments prohibited under the NIH guidelines for recombinant DNA research."

Two other themes that appear in the literature opposing this field of research may actually constitute the hidden agenda of some of those who continue to raise concerns for safety. Some argue that man should not knowingly intervene in the workings of biological evolution. Others suggest that this research could be a major step along a trail that ultimately could lead to the capability of genetic manipulation of man himself. Both groups argue that it would be best to prevent the development of this capability by halting all possibly contributing research at its earliest stage, viz., all research with recombinant DNA. Their position is that there are some facts that man should not seek to learn. The most complete presentation of this position was offered by an Australian, Prof. Julius Stone of the law faculty of the University of New South Wales. He argues that, as soon as a scientist can see some direct pathway from the work on which he is engaged to an evil outcome at some future date, no matter how remote, he should abandon the field. And indeed, that most distinguished immunologist, Sir Macfarlane Burnett, appears to have said, "It is a hard thing for an experimental scientist to accept, but it is becoming all too evident that there are dangers in knowing what should not be known."

More dangerous to live in ignorance

To Dr. Burnett I reply that it must be far more dangerous to live in ignorance than to live with knowledge. Prof. Stone and Prof. Burnett forget that the uses of science are indeed unpredictable. They ignore the intrinsic value of knowledge of our own genetic mechanisms, the immediately obvious practical applications of research in this field, and the applications which must lie beyond the horizon of our imaginations. Conversely, the ugly possibility to which they address themselves could occur only at the end of a long and extraordinarily difficult experimental road and in full view of many observers. There will be ample opportunity to prevent the feared outcome, whereas termination of the entire enterprise at this stage denies to posterity all of its potential fruit.

Nor can I easily condone any abridgment of the freedom of scientific inquiry. This is not an ancient freedom. Commencing about 400 years ago, the very concept developed slowly with the growth of science itself. Hopefully, the day is past when anyone would seriously argue that a democratic government should prohibit free expression of new ideas simply out of fear of the ideas themselves. Totalitarian governments may fear new ideas even as they fear their own people. But the freedom openly to espouse and debate new ideas has been the essence of liberty and the guardian of democracy, enshrined in the Bill of Rights of our Constitution. Freedom of speech, of religion, of the press, and of assembly historically came to be cherished precisely as the power of the scientific search for truth freed mankind from dogmatic religious and political thought. Scientific inquiry has challenged the dogma of an authoritarian world for the past 400 years. It has freed men's minds as it eased their toil. At the half-way mark, after two centuries of science, it was Thomas Jefferson who said, "There is no truth on earth that I fear to be known."

Abridgment of the freedom of inquiry of scientists, therefore, would constitute the first step along a trail which must inevitably lead to loss of those other freedoms that we cherish.

For scientists, experimental research, empirical observation, and the testing of hypotheses against the reality of experience are inseparable aspects of free inquiry. Neither law nor tradition confers an absolute right of freedom from all restraints. We have readily accepted various such with respect to scientific inquiry, as, for example, those regarding the use of human subjects. But we need accept no constraints other than those found absolutely essential to protect against injury other values that we cherish.

The objective of some who have proposed regulation of recombinant DNA research is to use the power of government for the suppression of ideas that may otherwise flow from such research. That would take us back to an era of dogmatism from which mankind has only recently escaped. But it would be a feckless course. In the long run it is impossible to stand in the way of the exploration of truth. Someone will learn somewhere, sometime.

Civilization a zero-sum game

As Harvey Brooks has noted, the pessimists among scientists, particularly the ecologists and the systems analysts, see doom as the inevitable consequence of population growth, resource depletion, and environmental pollution. For them, civilization is a zero-sum game in which some can benefit only by taking from others. Viewing industrial societies as unwilling to share their capital resources with the developing world, they see nuclear holocaust as inevitable. And such statements necessarily color public attitudes toward the scientific endeavor.

The optimists, myself included, see the further development of scientific understanding as the means for expanding the planet's energy resource base, for converting nonrenewable resources into an infinite resource base, as a means of so managing affairs that the goal of an equitable, harmonious world need not be denied to mankind. But the path is perilous. Success demands an endless stream of greater and lesser appropriate decisions, with little forgiveness for error. Brooks offers us the image of civilization traversing an ever-narrowing ridge towards the peak of a better human existence but with a precipice of possible disaster ever closer on each side. The scope of human choice and freedom widens at the same time that the possible price of error escalates. I regret that, vaguely sensing this circumstance, public attitudes seem to be shifting from seeking means of accomplishing the greatest possible good to settling for pathways that risk the least harm. With Dr. Brooks, I find it difficult to believe that the frailty of human institutions will deny us the realization of the opportunities which lie within our intellectual and moral capacities. I continue to believe that science will enable us to avert catastrophe—although it may be nip and tuck.

I can, however, be unabashedly optimistic concerning the prospects for continuing great discoveries in science. Consider only two fields, astronomy and biology. Until recently, man's experience of the heavens was limited to that revealed to him by radiation in that portion of the electromagnetic spectrum to which his retina is sensitive. For only a few years, sensors on the ground and in space have explored earth's surround as 'seen' in the gamma ray, x-ray, ultraviolet, and radio portions of the spectrum. The image thus revealed stretches the human imagination as has no other vision in history. And patently the best is yet to come. I can hardly wait for the large space telescope to be placed in orbit!

Having more or less successfully managed those diseases occasioned by vitamin deficiencies, endocrine dysfunctions, and bacterial infections, while almost eliminating those virus diseases preventable by immunization, medical research now seeks to address those major degenerative disorders to which humanity remains almost helplessly subject: cancer, cardiovascular disease, multiple sclerosis, arthritis, nephritis, muscular dystrophy, schizophrenia, and the rest, including hundreds of genetic disorders. None are necessarily the natural condition of our species. What must be resisted is the public impulse to address these problems directly before the time is right, to engage in feckless attempts to apply the inapplicable. As in the past, the stage must again be set by fundamental biological research before there can be hope for the next cycle of successful management of disease. And we are so engaged.

It is difficult to communicate the excitement or the dimensions of the current explosion of biological understanding, understanding of metabolic regulatory mechanisms, of genetic mechanisms and their defects, of the nature of the cell surface, of how cells communicate with other cells. Immunologists, molecular biologists, cell biologists, and pathologists—biochemists all—obsessed with the structure and function of cell membranes have discovered that they are all really working on a common set of problems—the mechanisms that govern the orderly development and differentiation of tissues and organs and how errors in this process are controlled. Neurobiologists, faced with the seemingly hopeless task of dealing with an overwhelmingly complicated circuitry without a wiring diagram, now have quantitative understanding of the mechanism of the nervous impulse, of the manner of connection between nerve cell and nerve cell, between nerve cell and end organ, knowledge of physiological activators and inhibitors, and recent awareness that the brain is an essentially endocrine tissue. Understanding of the brain is suddenly perceived as a difficult but inevitably successful rather than as an impossible task. There has never been a time like it, and we stand on the brink of understanding the mechanisms of diverse diseases. In due course, this will surely permit us to cope with some of our oldest afflictions. It is a remarkably bright panorama giving cause only for cheer.

Our current malaise, then, stems in considerable part from a few bad experiences and from the time delay in meeting the high hopes and expectations raised in the minds of those who appreciate the great power of science and the force of technology. Those expectations have taken on a new light as science has also revealed the true condition of man on earth. I see no alternative but to address vigorously the principal questions of science itself, and to use our ever-widening understanding and sophisticated technology with grace and charity and wisdom, recognizing that there will always be questions to be asked and problems to be managed if not solved.

We are not omnipotent but neither are we unwilling foils of powerful forces over which we have no control. To be sure, new problems seem always to arise as we solve old ones. But we have learned not to seek a perfect world. Our joy must be found in those acts by which we exercise our unique human capabilities to eradicate what we abhor and to promote that which we value and cherish. For myself, I retain my faith that science, which has revealed the most awesome and profound beauty we have yet beheld, is also the principal tool that our civilization has developed to mitigate the condition of man. Science is the hope in Pandora's box. □