Letters

On the Dangers of Genetic Meddling

A bizarre problem is posed by recent attempts to make so-called genetic engineering palatable to the public. Presumably because they were asked to establish "guidelines," the National Institutes of Health have permitted themselves to be dragged into a controversy with which they should not have had anything to do. Perhaps such a request should have been addressed to the Department of Justice. But I doubt that they would have wanted to become involved with second-degree molecular biology.

Although I do not think that a terrorist organization ever asked the Federal Bureau of Investigation to establish guidelines on the proper conduct of bombing experiments, I do not doubt what the answer would have been; namely, that they ought to refrain from doing anything unlawful. This also applies to the case under discussion: no smokescreen, neither P3 nor P4 containment facilities, can absolve an experimenter from having injured a fellow being. I set my hope in the cleaning women and the animal attendants employed in laboratories playing games with "recombinant DNA"; in the law profession, which ought to recognize a golden opportunity for biological malpractice suits; and in the juries that dislike all forms of doctors.

In pursuing my quixotic undertaking—fighting windmills with an M.D. degree—I shall start with the cardinal folly, namely, the choice of *Escherichia coli* as the host. Permit me to quote from a respected textbook of microbiology (*1*): "*E. coli* is referred to as the 'colon bacillus' because it is the predominant facultative species in the large bowel." In fact, we harbor several hundred different varieties of this useful microorganism. It is responsible for few infections but probably for more scientific papers than any other living organism. If our time feels called upon to create new forms of living cells—forms that the world has presumably not seen since its onset—why choose a microbe that has cohabited, more or less happily, with us for a very long time indeed? The answer is that we know so much more about *E. coli* than about anything else, including ourselves. But is this a valid answer? Take your time, study diligently, and you will eventually learn a great deal about organisms that cannot live in men or animals. There is no hurry, there is no hurry whatever.

Here I shall be interrupted by many colleagues who assure me that they cannot wait any longer, that they are in a tremendous hurry to help suffering humanity. Without doubting the purity of their motives, I must say that nobody has, to my knowledge, set out clearly how he plans to go about curing everything from alkaptonuria to Zenker's degeneration, let alone replacing or repairing our genes. But screams and empty promises fill the air. "Don't you want cheap insulin? Would you not like to have cereals get their nitrogen from the air? And how about green man photosynthesizing his nourishment: 10 minutes in the sun for breakfast, 30 minutes for lunch, and 1 hour for dinner?" Well, maybe Yes, maybe No.

If Dr. Frankenstein must go on producing his little biological monsters—and I deny the urgency and even the compulsion—why pick *E. coli* as the womb? This is a field where every experiment is a "shotgun experiment," not only those so designated; and who knows what is really being implanted into the DNA of the plasmids which the bacillus will continue multiplying to the end of time? And it will eventually get into human beings and animals despite all the precautions of containment. What is inside will be outside. Here I am given the assurance that the work will be done with enfeebled lambda and with modified, defective *E. coli* strains that cannot live in the intestine. But how about the exchange of genetic material in the gut? How can we be sure what would happen once the little beasts escaped from the laboratory? Let me quote once more from the respected textbook (*1*): "Indeed, the possibility cannot be dismissed that genetic recombination in the intestinal tract may even cause harmless enteric bacilli occasionally to become virulent." I am thinking, however, of something much worse than virulence. We are playing with hotter fires.

It is not surprising, but it is regrettable that the groups that entrusted themselves with the formulation of "guidelines," as well as the several advisory committees, consisted exclusively, or almost exclusively, of advocates of this form of genetic experimentation. What seems to have been disregarded completely is that we are dealing here much more with an ethical problem than with one in public health, and that the principal question to be answered is whether we have the right to put an additional fearful load on generations that are not yet born. I use the adjective "additional" in view of the unresolved and equally fearful problem of the disposal of nuclear waste. Our time is cursed with the necessity for feeble men, masquerading as experts, to make enormously far-reaching decisions. Is there anything more far-reaching than the creation of new forms of life?

Recognizing that the National Institutes of Health are not equipped to deal with a dilemma of such import, I can only hope against hope for congressional action. One could, for instance, envision the following steps: (i) a complete prohibition of the use of bacterial hosts that are indigenous to man; (ii) the creation of an authority, truly representative of the population of this country, that would support and license research on less objectionable hosts and procedures: (iii) all forms of "genetic engineering" remaining a federal monopoly; (iv) all research eventually being carried out in one place, such as Fort Detrick. It is clear that a moratorium of some sort will have to precede the erection of legal safeguards.

But beyond all this, there arises a general problem of the greatest significance, namely, the awesome irreversibility of what is being contemplated. You can stop splitting the atom; you can stop visiting the moon; you can stop using aerosols; you may even decide not to kill entire populations by the use of a few bombs. But you cannot recall a new form of life. Once you have constructed a viable *E. coli* cell carrying a plasmid DNA into which a piece of eukaryotic DNA has been spliced, it will survive you and your children and your children's children. An irreversible attack on the biosphere is something so unheard-of, so unthinkable to previous generations, that I could only wish that mine had not been guilty of it. The hybridization of Prometheus with Herostratus is bound to give evil results.

Most of the experimental results published so far in this field are actually quite unconvincing. We understand very little about eukaryotic DNA. The significance of spacer regions, repetitive sequences, and, for that matter, of hetero-

chromatin is not yet fully understood. It appears that the recombination experiments in which a piece of animal DNA is incorporated into the DNA of a microbial plasmid are being performed without a full appreciation of what is going on. Is the position of one gene with respect to its neighbors on the DNA chain accidental or do they control and regulate each other? Can we be sure—to mention one fantastic improbability—that the gene for a given protein hormone, operative only in certain specialized cells, does not become carcinogenic when introduced naked into the intestine? Are we wise in getting ready to mix up what nature has kept apart, namely the genomes of eukaryotic and prokaryotic cells?

The worst is that we shall never know. Bacteria and viruses have always formed a most effective biological underground. The guerilla warfare through which they act on higher forms of life is only imperfectly understood. By adding to this arsenal freakish forms of life—prokaryotes propagating eukaryotic genes—we shall be throwing a veil of uncertainties over the life of coming generations. Have we the right to counteract, irreversibly, the evolutionary wisdom of millions of years, in order to satisfy the ambition and the curiosity of a few scientists?

This world is given to us on loan. We come and we go; and after a time we leave earth and air and water to others who come after us. My generation, or perhaps the one preceding mine, has been the first to engage, under the leadership of the exact sciences, in a destructive colonial warfare against nature. The future will curse us for it.

ERWIN CHARGAFF
350 Central Park West,
New York 10025

References

1. B. D. Davis, R. Dulbecco, H. N. Eisen, H. S. Ginsberg, W. B. Wood, Jr., *Microbiology* (Harper & Row, New York, ed. 1, 1967), p. 769.

The recombinant DNA research controversy is permeated by the assumptions that (i) the work will go ahead; (ii) benefits outweigh the risks; (iii) we can act now and learn later; and (iv) any given problem has a solution. We therefore had better take those steps necessary to ensure that the April meeting of the Recombinant DNA Molecule Program Advisory Committee at the National Institutes of Health (NIH) is *not* the "last look before the leap" (News and Comment, 16 Apr., p. 236).

Several serious questions must be addressed.

On what basis were the scientists on that committee chosen so that a mutually reinforcing group was able to vote down almost every safety suggestion requested by NIH director Donald S. Frederickson? Why was there no committee discussion about or reference to the myriad reports, statements, letters, and varied data submitted to the committee from throughout the United States by eminent scientists stressing the necessity for (i) more stringent control measures; (ii) centralized P4 facilities; (iii) rejection of *Escherichia coli* as host; or (iv) postponement of recombinant DNA research? When and why was it decided that the work will go ahead merely pending guideline ratification?

As recently as this past February, after NIH's public hearings on recombinant DNA research, David L. Bazelon, Chief Judge of the District of Columbia Court of Appeals, advised that Frederickson, in assessing the varied testimonies covering a spectrum ranging from laboratory safety procedures to ramifications of interference with evolution, should set forth in great detail the reason for each step he takes or does not take. Yet at the April meeting, the advisory committee reviewed the details of laboratory containment facilities and procedures as if the public hearings had never taken place. That the benefits outweigh the risks of recombinant DNA research was taken as a matter of course, not a matter of discussion. This "act now and learn later" approach gave rise to a vote for the use of an "enfeebled" strain of bacteriophage (lambda), predicated in the proposed guidelines on its use with "enfeebled" *E. coli* bacteria. Yet we cannot predict whether, within the human organism, either host or vector, or both, will not later revert to greater strength.

We should seriously question whether these DNA committee meetings are window dressing for those scientists, many currently involved in recombinant DNA research, who are committed to pushing this research ahead with as little impediment as possible. Producing guidelines serves not only as a sop to Cerberus but distracts from the basic alternatives of (i) postponement of research and (ii) open, unbiased discussions of benefits and risks. We should be wary of self-imposed guidelines which experimenters may cite as a defense in lawsuits for punitive monetary damages. It is none too soon to consider federal legislation that would prevent limiting the liability of the experimenter, laboratory, institution, manufacturer, distributor, and direct agent in the case of disease, injury, or death resulting from recombinant DNA research.

There are striking parallels between the recombinant DNA and the nuclear energy controversies. Thirty years ago, when nuclear energy development was initiated, the problems of waste transport and disposal, sabotage, weapons proliferation, and low-level radiation were either not foreseen or not deemed worthy of consideration.

Proponents of nuclear energy defined the problems and proposed their own solutions. Questionable data were classified and talk centered on design criteria, reactor safety, and regulation. The unquantifiable problems—the genetic risk to future generations, human fallibility, the vulnerability of centralized electric generation, acts of malevolence, the threat to civil liberties by massive security measures, and the economic investment and subsidies required—were not addressed.

In like manner, proponents of DNA research have set up the question of laboratory containment as the pivotal problem, for which their guidelines will be the solution. What scientist would claim that complete laboratory containment is possible and that accident due to human fallibility and technical failures will not inevitably occur?

It is therefore essential that open discussion include the entire range of problems in the field of genetic engineering and take into account the biohazards of accidental release of uncontrollable new organisms, the implications of interference with evolution, reduction of diversity in the gene pool, the imposition of complex medical decisions on individuals and society, and the inherent fallibility (not to mention corruptibility) of inspection, enforcement, and regulatory bodies.

We have the unique opportunity now, *before* the intellectual and economic investment in the development of recombinant DNA research grows much greater, to assess the benefits and risks. Such assessment should include acknowledgement that not all problems necessarily have solutions and that problems will arise that cannot possibly be foreseen. The vast number of human and technical variables precludes adequate anticipation of the problems of new technologies. At a recent recombinant DNA conference, NIH deputy director for science DeWitt Stetten, Jr., warned that ". . . the real hazard is the one no one around this table has dreamed of yet, and this you cannot specify against."

FRANCINE ROBINSON SIMRING
Committee for Genetics,
Friends of the Earth,
72 Jane Street, New York 10014