## LETTERS

### Evolution, Epidemiology, and Recombinant DNA

In attempting to assess the hazards of incorporating eukaryotic DNA into bacteria it is not enough simply to set up hypothetical scenarios: we must also try to judge critically the underlying assumptions. The first assumption is that these experiments will breach an ancient barrier between eukaryotes and prokaryotes and will thereby produce a radically novel class of organisms.

Principles from evolution and bacterial ecology offer our best guides for judgment. Bacteria in nature have long been exposed to DNA from lysed mammalian cells—for example, in the gut and in decomposing corpses. *Escherichia coli* can take up DNA after damage to the cell envelope, and one would expect random phenotypic variation to produce such damage occasionally (perhaps at frequencies of $10^{-5}$ to $10^{-10}$). Homologous DNA is efficiently incorporated after entry, because its potential pairing with long regions of host cell DNA facilitates enzymatic crossover. Indeed, genetic recombination between bacteria (transformation) has even been observed in the human host. Incorporation of nonhomologous DNA is much less efficient but nevertheless can occur, presumably by transient pairing between adventitious short regions of complementarity. For example, deletions based on such "illegitimate recombination" occur at frequencies of about $10^{-9}$.

With such low frequencies of both entry and incorporation, one could not expect to demonstrate natural hybridization between bacteria and man. Nevertheless, its scale almost certainly compensates for its inefficiency. Every person's gut is a huge chemostat, and the total population excretes about $10^{22}$ bacteria per day. Hence over the past $10^6$ years human-bacterial hybrids are exceedingly likely to have already appeared and been tested in the crucible of natural selection. If so, experimental DNA recombination will not be yielding a totally novel class of organisms.

A second assumption is that some of the recombinant strains are likely to spread and cause epidemics. Evolutionary principles are again pertinent. Nature selects for genetic balance: the contribution of a gene to Darwinian fitness depends on the rest of the genome. In bacteria, specifically, the introduction of a substantial block of foreign DNA would almost always lower the growth rate. With the short generation time of bacteria such a difference would lead to rapid outgrowth by competitors (unless the introduced genes promoted adaptation to alterations in the environment, such as the wide use of an antibiotic).

This argument is reinforced by a large body of epidemiological and experimental evidence. To cause communicable disease a potentially pathogenic organism must be able to survive in nature, in competition with other strains. It must also be able to be transmitted to a host, reach a susceptible tissue, and express its toxic potentialities there. Much current anxiety seems to be based on unawareness that microbial pathogenicity and communicability are complex and depend on a balanced genome. *Escherichia coli* carrying a gene for diphtheria toxin would be poorly suited to cause a diphtheria epidemic.

While bacteria carrying mammalian genes are thus unlikely to menace the public health, the risk of laboratory infection is much larger, since a heavy infecting dose of even a poorly communicable organism can cause disease in an individual. But this danger resembles that encountered with known pathogens, and it can be minimized by similar means. Perhaps the most valuable outcome of the current debate would be the requirement that those working on recombinant DNA be trained and supervised like medical bacteriologists.

I conclude that the risks in research on recombinant DNA require reasonable precautions but do not warrant public anxiety. A greater danger may be that the presumed analogy to nuclear weapons will lead to demands for virtually absolute freedom from risk. Yet the analogy to our mastery over infectious diseases is more apt. And if this field had faced similar demands, from its start, we might still be losing one-quarter of our children to communicable diseases. Is the balance of risk and benefit in research on recombinant DNA so much more unfavorable?

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### Preserving National Forests

The article by Constance Holden on national forest management (News and Comment, 2 Apr., p. 36) and the subsequent letter by J. N. Duffield (7 May, p. 506), following preceding articles in the special "Materials" issue of *Science* (20 Feb.), lead us to present some comments on this subject.

A fundamental confusion exists about the meaning of the word "forest." Your contributors use it for any tree-covered area. We believe there is a basic distinction between the real forest—a complex, natural, or eventually seminatural ecosystem—and tree plantations—man-made, simplified ecosystems.

Tree plantations are oriented toward maximum timber production, which is not usually compatible with other uses of forests. They are more unstable ecosystems that need energy-intensive intervention (fertilization, pest control) like agricultural land, in which category they in fact belong. Thus the main issue is not how to manage the national forests, but whether parts of them should be replaced by even-aged tree plantations, which in modern sylviculture is the usual destiny of clear-cut areas. Before such a choice is made, the more or less definitive loss of uses other than timber production must be considered and the possibility of obtaining valuable timber from suitably managed real forests should not be forgotten. For such forests, the Randolph-Brown bill as presented by Holden seems satisfactory. The criticism of selective cutting by Duffield is not relevant. The situation he describes (cutting of all the best trees) is certainly damaging; however, selective cutting can be a technique involving the preservation of a sufficient number of the best trees as seeds producers, a successful practice in several European forests.

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### Notable Americans

Radcliffe College is sponsoring a supplement to *Notable American Women*, a reference work published in 1971 by Harvard University Press. The first three volumes contained over 1300 articles about women who died between 1607 and 1950. To fill a gap noted by scholars and general readers alike, the supplement will include approximately 400 articles on women who have died since 1950.

The editors of *Notable American Women* invite readers of *Science* to suggest the names of women scientists and physicians who ought to be included. The date of death and a standard or obituary reference (when available) should be given for each candidate. A brief statement of why the individual is important would also be helpful.

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