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Human Genetic Engineering

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ABSTRACT. The author addresses the new ethical and conceptual uncertainties posed by the application of gene-splicing techniques to human beings, an application of technology that raises complex ethical and social public policy issues. The author reviews the advances in the medical uses of gene-splicing, and addresses their consequences on (1) human genetic makeup; (2) intergenerational responsibilities; (3) the distribution of social benefits; and (4) the conception of what a person is. He describes the first two effects as posing new ethical uncertainties by being able to change the human gene pool, and with that change affect people's links to—and responsibilities for—their progeny. The latter two raise new questions of conceptual uncertainty concerning how these technologies will be distributed and to whom, and the resulting social and public consequences that arise from the potentially profound genetic changes possible to the individual. The author concludes by noting the need for circumspection to avoid the unfavorable effects of successes with this technology, which can be done, he notes, by using those goals and values that constitute the ethics and practice of medicine, namely, the application of science and art to human needs.

We are now in the middle period of public policy on genetic manipulation. Like the first stage, in which attention focused on the safety of laboratory experiments that altered the genes of microorganisms, the concerns at present involve safety, though on a larger scale: the creation of large quantities of recombinant DNA through industrial fermentation techniques for agricultural, manufacturing and pharmacological purposes, or the intentional release into the environment of plants and animals (beginning with bacteria) whose genes have been modified.[1] These developments have also spurred attention to social policy issues that underlie many areas of scientific investigation, such as the propriety of academic researchers and institutions having various connections with business enterprises, and the need to balance rewards to research sponsors (through patents and trade secrets) with fair access to the fruits of research on the part of the public, especially when public funds have contributed to the discoveries and when the benefits they provide may be matters of life and health for the people who need them.[2]

The unresolved status of many of the issues confronted during the first two stages will not prevent the arrival of the third stage, however. That stage—the extension of gene-splicing techniques to human beings—will be brought about not because public policy and ethical theory are ready for it, but because advances in biomedi-

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cal knowledge make it possible. Yet, unlike biomedical developments a decade or two ago, such as heart transplants, which burst upon the public unawares, the coming manipulation of human genes has been discussed for many years, among not only physicians and scientists, but also theologians, social scientists, philosophers, lawyers and members of the general public in meetings and in the popular media.[3]

Despite years of prior discussion, the barriers to resolving the questions in the third stage are even more formidable than those confronting participants in the first two stages. Divisions of opinion in the recombinant DNA debate thus far have turned on factors that are common in the formulation of public policy, namely, "occurrence uncertainty": what is the probability of certain things occurring and, given the likely consequences, who will benefit from, or be hurt by, different policies? Human genetic engineering also involves questions of occurrence uncertainty, but it presents two sets of questions not encountered in the early stages: ethical uncertainty and conceptual uncertainty. As the President's Commission observed, the first occurs "when no societal consensus exists as to whether certain applications of gene splicing are beneficial or undesirable."[4] Beyond the question whether a particular human use—like improving memory—would be socially and ethically desirable, even more basic questions are encompassed within ethical uncertainty because the determination of what constitutes a "defect" is itself not a definite concept, fixed for all times or all people.

The second new type of uncertainty "refers to the fundamental change in concepts that this new technology can engender."[5] For example, the opening of realms of therapeutic possibilities by the new genetics also destroys much of the security that had been provided by fixed landmarks; the exchange and manipulation of DNA among species challenges basic concepts and assumptions about what it means to be human.

Complex Issues

These added layers of uncertainty are among the important ways that human genetic engineering raises more complex ethical and public policy issues than even the highly contested issues that have already emerged in the pharmacological, industrial and agricultural research and development in recombinant DNA.

Of course, for the near future, issues of the latter type will continue to dominate discussions, because most of the direct human uses will be some years in coming. Nonetheless, those uses are not mere hypotheticals, and the issues they raise should not be dismissed simply because they are not yet as pressing or apparently prevalent as the nonhuman applications. Concern with those issues may partially result from the technical wizardry involved, but it can also be traced to worries about the potential misuses of these techniques. Furthermore, some people doubt the morality of any genetic manipulation in human beings or, at the least, believe that the burden of answering many concerns rests with the proponents of such efforts, which ought not to go ahead in the meantime.[6] These ethical and social concerns—about unacceptable uses or consequences, and about human gene splicing *per se*—will be addressed after a brief description of the medical background.

Medical Uses of Gene Splicing

Remarkable progress has been made in improving health in the western world during this century. The initial triumphs resulted from public health measures, such as improved sanitation, water supply and immunization programs (as well as better food processing, nutrition and housing, which may not usually be considered matters of "health," although they have an enormous influence on it). More recently, dramatic steps have been taken to reduce the toll of trauma and acute diseases. The consequence is both a great lengthening of the average lifespan and improved functioning and enjoyment of life for many people. A further consequence, however, has been to throw the spotlight on the congenital, degenerative and chronic conditions, which now move to center stage as the major causes of disability and death in the United States. Since many of these conditions are "genetic"—or, at least, have a large genetic element—the search for diagnostic methods and treatments aimed at the genetic level will have increasing social as well as individual importance in the years ahead.

The techniques of genetic engineering—or "gene splicing"—are first being applied to human genetic diseases through a traditional route, namely, the production of enzymes and proteins for exogenous treatment of genetically based diseases like diabetes or growth failures by means of recombinant DNA-produced insulin and human growth hormone, respectively. Once the relevant gene can be identified, extracted from its place in the nucleus of human cells, spliced into a microorganism, and then caused to manufacture its gene product, a new way to produce plentiful quantities of formerly hard-to-obtain material is a reality. The ability of bacteria (often the "host" for a recombinant DNA chain) to multiply rapidly—a single cultured cell can become a billion copies in less than 15 hours—would seem to endow the gene-splicers with a biological Midas touch.

Gene Splicing Techniques

As formidable as this capability may seem, however, it is still rather conventional compared with more direct use of gene splicing techniques in diagnosis and manipulation of human genetic diseases. In the diagnostic area, the technique holds great promise for genetic disorders or carrier status that until now have not been readily diagnosable because present testing methods look for gene products, rather than for the genes themselves, and such biological markers are not always discernible.

The techniques can be briefly sketched.[7] Basically, they involve the use of enzymes as scissors to cut DNA chains and then the use of various methods (such as gel electrophoresis) to discern differences in the resulting pieces of DNA. In some cases, as has already been shown with some hemoglobin disorders, a restriction enzyme site occurs right at the relevant gene, while in the variant ("defective") gene the restriction site is absent, so that when the DNA is cut, a segment of a different length is produced, which indicates the presence of the defective gene. In other cases, the cutting-point is in a stretch of DNA adjacent to the gene of interest; then it is necessary to do familial studies to find this linkage. Recently, for example, a research team headed by James Gusella of Harvard announced an absolutely stun-

ning use of the molecular genetic techniques—specifically, the use of restriction fragment length polymorphisms—to detect a marker on Chromosome 4 that appears to be closely linked to the gene for Huntington's disease.[8] This is a rare progressive neurodegenerative disorder with autosomal dominant inheritance; the first symptoms usually occur after the patient's child-bearing years. The primary defect is not yet known, but the symptoms—progressive motor abnormality and intellectual deterioration—are well studied, and are clearly devastating, leading to an early death. Although the potential to do presymptomatic—indeed, even prenatal—screening will raise ethical problems (about confidentiality, and particularly about autonomy), it is also plainly a great step forward in identifying the Huntington's gene itself and understanding its mechanism.

Besides diagnosing genetic defects, gene splicing may also make it possible to cure them—not in the way insulin injections "cure" diabetes, by counteracting its harmful effects on the patient, but by providing the genetic blueprint for a previously diabetic patient's body to make its own insulin. If this means of treatment—sometimes termed gene therapy or gene surgery—proves possible in human beings, it would offer a wholly new and potentially much less expensive way of treating many illnesses; if it makes inheritable changes, it would move another step beyond any current treatment (which is addressed to individual patients) and would become the treatment of future generations as well.

Such steps have not yet been successfully undertaken, but they are coming closer every day. Several recent developments are particularly important regarding human applications. First, because scientists do not yet fully understand how genes are regulated, it has been difficult to induce expression of foreign genes inserted into human cells—that is, to get the gene to function and program the cell to produce the relevant protein. Remarkable progress has been made lately, however, and scientists have been successful in getting recombinant genes to function in multicell animals and even in correcting a gene defect—a feat accomplished in fruit flies through the discovery of what are termed "transposable elements."[9] Although the counterparts of these elements have not yet been found in man, this experiment points the way to the future therapeutic uses of gene splicing. Second, there is the question: Can the changes brought on by gene splicing be passed on to subsequent generations? In experiments with mice, this important effect has now been demonstrated.[10]

The Two Categories

Gene splicing in humans can be divided into two categories: ***somatic cell treatment*** and ***germ cell treatment.*** It is likely that somatic cell treatment will initially be directed at single gene mutations, which are now known to cause more than 2,000 human disorders. For disorders that involve an identifiable cell product of a discrete subpopulation of cells, treatment might consist in removing some or all of these cells, genetically altering their genes, and then reinserting the cells into the patient. Thus, the technique is in effect organ transplantation—except that the physicians would alter a patient's own organ, rather than using another human being's organ.

From the viewpoint of medical ethics, this may be no small matter, because of the greater uncertainties, but conceptually it seems to me no different—provided that we have agreement on what constitutes a "disease" for which "therapy" is appropriate. Indeed, the criticism that was directed at the first attempt to use recombinant DNA techniques to treat patients with a genetic disease was of the same type that could be leveled at any experiment undertaken prematurely and without the necessary approval of an institution's "human subjects" review board.

That experiment, conducted by Dr. Martin Cline of the UCLA Medical School on two thalassemic patients in Israel and Italy in 1980, was condemned, and Dr. Cline was punished by the National Institutes of Health's cancellation of research funding, because his laboratory results and animal tests did not demonstrate sufficient likelihood of success to justify going ahead clinically.[11]

Since then, other researchers have pressed ahead, both to develop better animal "models" of the hemoglobin disorder, and to find ways around the problems that kept the altered DNA in Dr. Cline's experiment from having a beneficial effect. It seems likely that more experiments will take place in the near future, and that the initial experiments are likely again to involve an organ (like bone marrow) that can be physically removed, altered genetically, and returned to the patient's body.[12]

If only certain cells were altered, the recombinant DNA would be limited in its effect to those cells, and the individual's genetic material would otherwise remain the same as it always had been. Were an attempt made to change a person's genes to involve other methods of introducing the new genetic information, however, a large number of cells, including the germ-line cells, could be affected. This might occur if the new genetic material were introduced systemically (because the affected organ cannot be removed for separate treatment outside the body) or if the disease in question had to be treated early in development, because it affects many organs or is manifested irreversibly before birth.

For example, if the gene splicing took place at the zygotic stage, it would probably affect all cells in the body. Although treatments of this sort are almost certainly further in the future than other therapeutic uses of gene splicing, they raise much more troubling issues. First, there are the special ethical problems of creating human beings with the intention of altering them—entirely without their consent.[13] Second, social and biological concerns arise because any deleterious changes, rather than being limited to one person or one generation, would become part of the human genetic inheritance.

As important as social and ethical issues of this sort are, their mere recitation ought not to be substituted for careful analysis; valid objections to particular uses of gene splicing need not provoke wholesale rejection of the techniques themselves. It is worthwhile remembering that, a little more than a decade ago, the field of genetics was seen by many of its practitioners to have reached a plateau; problems remained to be explored, but mostly at the interstices, not the frontiers.[14] Gene splicing changed all that, and the exploration of gene functioning in higher organisms that splicing permits "turns out to be full of surprises."[15] The knowledge produced—about everything from the theory of evolution to the process of aging—may hold more for science than the practical applications of gene splicing hold for technology, at least in the near future. Therefore, calls for bans on areas of research

—which could easily chill other types of research—ought to be greeted very skeptically.

Decision-makers should remember that the key that they are told to put out of reach may be the one that could open storehouses of knowledge of unimaginable dimensions. Thus, the mere possibility that the key may also fit a biological Pandora's box—while enough to demand that public and scholarly attention be paid—is not enough to impose a moratorium on carrying the work forward into the medical realm.

Concerns with Consequences

A wide range of potentially troublesome results have been raised by critics of human genetic engineering.[16] Four deserving special attention are the effects on (a) human genetic makeup; (b) intergenerational responsibilities; (c) distribution of social benefits, and (d) the conception of what a person is.

Evolution and the Human Genome

In the early years of recombinant DNA research on microorganisms, many critics shared the view expressed by biologist Erwin Chargaff, who challenged the right of workers in this field "to counteract, irreversibly, the evolutionary wisdom of millions of years."[17] The objection focused on the notion that the inability of different species to mate and produce fertile offspring must offer a natural protection that scientists should not circumvent, lest they destroy an adaptive advantage.

There are several problems with this view, however. First, the scientific theory of evolution contains no notion of a plan or endpoint, so "wisdom" is a misleading metaphor—one set of genes is not necessarily more desirable than another. Even genes well adapted to a particular time and place may be maladaptive—perhaps lethal—under other circumstances. Whatever role "species barriers" played in evolution thus far would not mean that they are necessarily of continuing value.

Furthermore, the ability to move genetic material readily might itself become the means of ensuring species survival if, as philosopher Stephen Stich has argued, a time could come "when, because of natural or man-induced climatic change, the capacity to alter quickly . . . genetic composition" will be needed to forestall a catastrophe.[18]

This is not to say that all concerns about effects on the human gene pool should be dismissed. While it is not possible to know which particular genes would prove advantageous in a changed environment, population geneticists regard the loss of even minute advantages as serious, since the cumulative effect over generations can give a species marked benefits. Moreover, in the face of a sudden change in the environment (such as the introduction of a novel pathogen), a species is more likely to survive if its members possess greater heterogeneity. It seems unlikely, however, that therapeutic interventions aimed at eliminating genes in a form that is deleterious to an individual (*e.g.*, a person who is homozygous for an autosomal recessive disorder) would have a significant impact on the rate of the gene's occurrence in the population, especially given how rare most deleterious genes are. (This would also

be true if genetic alterations of germ-line cells were limited to affected individuals; obviously, a much more dramatic impact on a gene's frequency would follow in the unlikely event that the germ cells of *all* carriers were altered—an issue that is also raised by screening aimed at carriers of dominant disorders.)

Medical geneticists tend to be much less concerned with any of these changes than are population geneticists, "because they believe that it should be possible to make up, through environmental manipulation (including medical treatment), for the loss of any advantage provided by a variant in any probable future environment."[19] Nonetheless, as scientists (aided by the tools of molecular genetics) learn more about the beneficial effects of gene variants—distinct from other environmental and inherited causes—it would seem desirable to take the diminution of the frequency of such variants into account in weighing the costs of a gene splicing program.

Intergenerational Responsibilities

Human genetic manipulation would add considerably to the challenges that other developments in reproductive and genetic medicine have already presented to traditional notions of parental and societal obligations toward children. In some circumstances, these obligations may seem to be expanded; in other ways, contracted.

Already the ability to predict genetic defects in unborn children has led some prospective parents to choose to terminate a pregnancy (and perhaps to "try again"). For the family involved, this result may be a great blessing, justified in ethical as well as practical terms, especially when the fetus that was aborted would have had a painful existence. Nonetheless, the rapid acceptance of prenatal diagnosis ought not to obscure the fact that, when used with selective abortion, it upsets the traditional norm that children are to be accepted unconditionally, even when their birth creates a burden, like one of life's other mysterious tragedies. To the extent that gene splicing greatly expands the range of prenatal diagnoses, it will accelerate the rejection of traditional attitudes and reenforce a growing sense that human imperfections need not be tolerated.

The use of genetic engineering for therapeutic rather than merely diagnostic ends could have even more far-reaching effects on people's links to, and responsibilities for, their progeny. It may no longer be seen as appropriate for "responsible parents" simply to accept the result of the natural lottery by which characteristics are now determined; instead, they may be expected to "correct" genes that cause diseases and to "augment" other genes to give their children opportunities for higher levels of physical or cognitive functioning. On the other hand, knowing that future generations may employ an even more advanced technology to alter or to replace characteristics passed on to them could weaken people's sense of genetic continuity.

Furthermore, by blurring the line between what counts as a serious defect or disability and what is "normal functioning," gene splicing may alter our perception of what society owes to children, particularly those burdened by handicaps. Today's norm may become tomorrow's deficit; those problems that could have been genetically corrected at some prenatal or even preconceptual point may be seen as matters

of human choice (comparable to the problems or disadvantages that result from a wide range of parental choices about their children's schooling, health care, and general upbringing) and hence less demanding of the beneficial or charitable impulses of society.

The interrelationship between genetics and social and psychological behavior and attitudes is complex and poorly understood. Yet it is apparent that people's impressions of sharing constitutional similarities with their kin reenforces family solidarity and a sense of mutual obligation. "If genetic engineering makes use of reproductive technologies such as artificial insemination and *in vitro* fertilization, it will increase the strains on this concept of lineage."[20] Consequently, the possibility of using genetic technologies to correct defects creates uncertainties both about what effects on intergenerational relationships are likely and about how to evaluate their ethical effects.

Distribution of Social Benefits

In the third area of possible effects, one moves from those that illustrate ethical uncertainty to those that also raise questions of conceptual uncertainty. The core ethical concern is that of fairness. Human gene splicing confounds our attempts at distributive justice at two levels: What is distributed, and who deserves it.

Most of medicine—and all that seems heroic or praiseworthy—aims to hold back death, relieve suffering, and overcome disability. The things that provoke the need for medical intervention are viewed as disruptions in our personal universe and labeled as such—scourges, plagues and disasters (or, in the cooler terms of medicine, diseases, disorders and syndromes)—whether they originate within the body or as the result of some external contagion or accident. Thus, the targets of medicine are relatively clear to the practitioner, researcher or bureaucrat, as well as to the ordinary citizen-patient.

The potential of genetic engineering (admittedly, a more remote potential than its application against single-gene defects) to alter "adequate" or "normal" functioning would cast medicine into an uncomfortable role. To the extent that it has already been cast into that role on occasion, it seems obvious that those occasions—for example, cosmetic surgery or prescription of drugs to enhance athletic performance—have been marked with controversy and a general sense of dis-ease by many in the field. And even those earlier examples have been grounded in a firm sense of what was normal and a recognition of the artificiality of manipulation.

Gene therapy blurs such lines. While it may be "normal" (in the sense of inheritance of certain genes from a person's parents) for a person to be afflicted with sickle-cell anemia, it is not "normal" for the population as a whole, and most people with this genetic makeup will not experience an adequate level of health without medical intervention, if even then. The replacement of the functioning of the sickle-cell genes with genes that would program the production of normal hemoglobin would seem an obviously beneficial use of gene splicing.

But it is also not normal, in the sense of *average*, for a person to have 160 IQ or to be able to run 100 meters in under 10 seconds. It would, however, be surprising were someone to suggest that, when "abnormal" genes occur that provide the bases

for these abilities, they should be removed. But what about the reverse—for example, giving the hypothetical genes for mental acuity to someone who has an IQ of 100, to push the person to 160? If a society is deciding where to expend funds for research and treatment, should such an alteration be included among those things that a society that desires to be fair will encourage—or prohibit? Or neither? How, indeed, can one conceptualize any notion of equity in the area of health if the notion of some adequate level (in terms of both resources and outcome) is wholly indeterminate?

Even if it were agreed that an increase in intelligence or athletic abilities were a medical good, like a means of overcoming sickle-cell anemia, that ought to be made available, who would deserve to get it? This is the second problem posed for anyone seeking to be fair about human gene splicing. The usual answer to such a problem is to seek a means of distribution that is either rationally related to the good being distributed, or that is completely neutral (such as a lottery). The latter would seem an odd way to distribute a form of medical treatment (or "enhancement"), yet the former is likely to be impossible, as Michael Shapiro has noted:

> What if intelligence could be engineered upward? Who would merit this increase in merit? The very oddity of the inquiry calls into question the continued use of intelligence as a basis for resolving competing claims—say, for admission to educational institutions or for access to the intelligence-raising technology itself.[21]

Thus, if genetic engineering ever moves beyond the treatment of generally recognized diseases and comes into use to alter more complex characteristics, it will pose the very old problem of distributive justice in a very novel, perhaps unanswerable way. Indeed, it could "call into question the scope and limits of a central element of democratic political theory and practice: the commitment to equality of opportunity."[22] Would true commitment to equality require in the end mandatory genetic alterations to give everyone the same (or equally functional) genes?

The Concept of Being Human

The notion of such radical changes in people's genetic makeup raises yet another set of social and ethical issues, namely the challenges that genetic engineering poses for the concept of being human. This has several facets. On the individual level, a person's sense of identity could be called into question by genetic changes; more generally, changes of degree at some point become changes in kind.

The first of these possible effects might be viewed simply as a matter of change in psychology. Although people now think of themselves (and others) as relatively fixed in their capabilities, characteristics and personalities once they pass adolescence, dramatic changes are not unknown (as unwelcome as they often are to those who have anticipated a certain stability in their relationships with others). But even such changes are either viewed as a further manifestation of a person's true inner self or, when they are not, are resisted by others and perhaps subjected to medical intervention, designed to restore the person to his or her "true self." Compared to the methods now available, genetic engineering could well be faster and more se-

lective, and almost certainly could extend well beyond anything now attempted through psychotherapy (including psychopharmacology).

> Here again, uncertainty about possible shifts in some of people's most basic concepts brings with it evaluative and ethical uncertainty because the concepts in question are intimately tied to values and ethical assumptions. It is not likely that anything so profound as a change in the notion of personal identity or of normal stages of development over a lifetime is something to which people would have clear value responses in advance.[23]

The second and more general change in the concept of being human comes down to the ancient question: What is human nature? Can it be described by those characteristics that are uniquely human? This would appear to be a very narrow category, since most "human genes" and many "human characteristics" are found in other species. Would the addition of new capabilities to an otherwise human creature render it nonhuman? What of a genetic subtraction of a few capabilities—such as the ability to record and study the past and plan beyond the immediate future?

The very notion of a ***direction*** of change implicit in the preceding questions itself poses a problematical point: that humankind knows what an improvement or a degradation in its nature would be. The notion of betterment has long been attractive to geneticists. Herman J. Muller was one of the leading scientific spokesmen for this view; his notion of the desirable genetic traits changed with fashions in politics, however.[24] The coming of a means to manipulate the genes directly (rather than through the random chances that attached to Muller's proposals for selective breeding) offered human beings the opportunity to "rise above their nature," as Robert Sinsheimer observed in the late 1960s.[25]

Nonetheless, in time, Dr. Sinsheimer came to doubt the wisdom of many proposed uses and investigations of genetic engineering.[26] Even if the power to make genetic changes were not seized by an evil government (always a danger with any great power—but the fault is in the powerful government, not in the science it seizes), it might cause harm despite its user's benign intent. Indeed, 20 years ago, C.S. Lewis described the arrival of "one dominant age" that could overcome all influences of the past while simultaneously pre-ordaining the actions and capabilities of all subsequent generations.

> Man's conquest of Nature, if the dreams of the scientific planners are realized, means the rule of a few hundreds of men over billions upon billions of men.[27]

It is by no means certain that it will ever be possible to change the genetic basis of all or even the most important human characteristics in a predictable, inheritable way. Compared to the immediate threats of nuclear holocaust and ecological degradation, the social and ethical difficulties posed by developments in human genetic engineering seem remote and perhaps insignificant. Yet events in science have a way of overtaking the unwary. Although the large degree of uncertainty in outcome that marks each of the possibilities discussed here prevents their definitive evaluation in ethical and social terms, it is none too soon to begin attending to the important matters of ethical and conceptual uncertainty raised by the mere possibility that physicians will soon be able to make direct—and directed—genetic changes in human beings.

The Need for Circumspection

Science fiction is seldom great literature, and since Nathaniel Hawthorne is, without question, a great writer, it is not surprising to discover that, while one of his stories may look, to our modern eyes, like science fiction, it is actually a moral tale. Nonetheless, the morality carries a large message about scientific ethics, especially as applied to the potentialities of human gene splicing.

The story I have in mind concerns events in the life of a young man, Giovanni Guasconti, who went many years ago from the south of Italy to study at the University of Padua. The garret he rents overlooks the garden of Dr. Rappaccini, an eminent physician, whom Giovanni observes tending his strange flowers and plants with the assistance of his lovely daughter, Beatrice. Pietro Baglioni, another eminent professor of medicine at the university, advises Giovanni to avoid Rappaccini, who "cares infinitely more for science than for mankind." In words that ring with greater resonance today than they can have in Hawthorne's time, Professor Baglioni says that Rappaccini's

> patients are interesting to him only as subjects for some new experiment. He would sacrifice human life, his own among the rest, or whatever else was dearest to him, for the sake of adding so much as a grain of mustard seed to the great heap of his accumulated knowledge.

Giovanni—partially, one senses, out of the irresistible attraction he already feels for Rappaccini's daughter—objects that this reveals a "noble spirit." "Are there many men," he wonders, "capable of so spiritual a love of science?"

Yet Hawthorne seems to take a harsher view of the scientist, for in the end Dr. Rappaccini's research leads to tragedy. His work—in what seems so prescient for today—involves the creation of artificial forms of life, albeit not (so far as we are told) through genetic engineering. The plants in Rappaccini's garden display

> an appearance of artificialness indicating that there had been such commixture, and, as it were, adultery, of various vegetable species, that the production was no longer of God's making, but the monstrous offspring of man's depraved fancy, glowing with only an evil mockery of beauty.

Like the plants in her father's garden, lovely Beatrice turns out to be possessed of man-made qualities, and, like them, it turns out that the central quality is being poisonous—her sweet breath literally kills insects, and ordinary flowers wilt in her hands.

The power possessed by Beatrice is so great that her father has kept her closed off from the world in his garden (which one might thus liken to the first P-4 laboratory!). Wishing to overcome Beatrice's total isolation from people, Dr. Rappaccini alters Giovanni to be like her; when Giovanni discovers this, he turns on Beatrice and condemns her—an early example of what is now called "blaming the victim." Finally, Beatrice and Giovanni—wishing to become normal humans again—decide to take an antidote supplied by Professor Baglioni.

Perhaps sensing the danger for a person with poison taking an antidote, Beatrice insists on going first. She rebuffs her father's claim that she has been "endowed

with marvelous gifts against which no power or strength could avail an enemy," and then she dies, "the poor victim of man's ingenuity and of thwarted nature, and of the fatality that attends all such efforts at perverted wisdom," as Hawthorne writes.

It is hard to know whom to pity more—poor Beatrice, who is dead; Dr. Rappaccini, who has lost his precious child, and perhaps his experiment as well; Giovanni Guasconti, who is left facing life alone in the poisonous garden—or death at his own hands; or perhaps Professor Pietro Baglioni—in the role of societal watchdog—who was able to prevent generalized harm from arising from the experiment only by a step that led to the death of its subject, the lovely Beatrice.

In a way, Hawthorne's "Rappaccini's Daughter" has more to say of relevance to the situation of gene splicing than does Mary Shelley's story of Dr. Frankenstein and his monster, which was the dominant metaphor of the early years of gene splicing. We may have less to fear from a monster run amok than from the unfavorable effects of our successes. But we need not suffer Dr. Rappaccini's fate, if we remember the human values and goals that ought to guide the human uses of genetic engineering—just as they do elsewhere in that application of science and art to human needs which we call medicine.

Notes

1. *See generally* M. Rogers, *Biohazard* (1973); N. Wade, *The Ultimate Experiment* (1977); "NIH Guidelines for Research Involving Recombinant DNA Molecules," *Fed. Reg.* 41 (July 7, 1976), p. 27902 (first version of frequently revised rules on experimental safety); Fox, "Despite Doubts RAC Moving to Widen Role," *Science* 223 (1984), p. 798.
2. *See e.g.*, the article by Peter Hutt in this series for *Technology In Society* (Vol. V, no. 2, pp. 107–118); *Commercialization of Academic Biomedical Research*, Hearings Before the Subcommittee on Investigation and Oversight and the Subcommittee on Science, Research and Technology of the House Committee on Science and Technology, 97th Congress, 1st Session, June 8, 1981; Culliton, "Pajaro Dunes: The Search for Consensus," *Science* 216 (1982), p. 155.
3. *See generally* M. Hamilton, ed., *The New Genetics and the Future of Man* (1972), pp. 109–175; M. Lappé and R. Morison, eds., *Ethical and Scientific Issues Posed by Human Uses of Molecular Genetics, Annual of the New York Academy of Science* 265 (1976) pp. 1–208; J. Little, ed., *Prospects for Man: Genetic Engineering* (1979); Roblin, "Human Genetic Therapy" in G. Chacko, ed., *Health Handbook* (1979), p. 103; Anderson and Fletcher, "Gene Therapy in Human Beings: When Is It Ethical to Begin?," *New England Journal of Medicine* 303 (1980), p. 1293; J. Cherfas, *Man-Made Life* (1982), pp. 228–234.
4. President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research, *Splicing Life* (Washington, DC: U.S. Government Printing Office, 1982), p. 22.
5. *Ibid.*
6. This appears to have been the position of the three religious organizations whose objections to President Carter about the "fundamental danger triggered by the rapid growth of genetic engineering" led to the request that the President's Commission study the field. See *President's Commission, supra*, note 4, pp. 1, 95–96 (Appendix B). *See also Human Genetic Engineering*, Hearings Before the Subcommittee on Investigation and Oversight of the House Committee on Science and Technology, 97th Congress, 2nd Session, November 16–18, 1982 (especially comments of R. Shinn, R. McCormick and J. Beckwith).
7. *See generally ibid.*, pp. 238–278 (comments of Y. Kan and M. Skolnick); Wyman and White, "Restriction Fragment Length Polymorphism in Human DNA," *77th Proceedings of the National Academy of Sciences* (1981), p. 6754.
8. Gusella *et al.*, "A Polymorphic DNA Marker Genetically Linked to Huntington's Disease," *Nature* 306 (1983), p. 234.
9. Marx, "Still More About Gene Transfer," *Science* 218 (1982), p. 459.
10. Wagner *et al.*, "Microinjection of a Rabbit B-globin Gene Into Zygotes and Its Subsequent Expression in Adult Mice and Their Offspring," *78th Proceedings of the National Academy of Science* (1981), p. 6376.

11. Williamson, "Gene Therapy," *Nature* 298 (1982), pp. 416, 418; and Wade, "UCLA Gene Therapy Racked by Friendly Fire," *Science* 210 (1980), p. 509.
12. *See generally* Roblin, *supra,* note 3.
13. R. Ramsay, *Fabricated Man* (1970).
14. Cherfas, *supra,* note 3, pp. 24–25.
15. Judson, "Thumbprints in Our Clay," *The New Republic,* September 19 & 26, 1983, p. 12, 15:

    > The problems for which the techniques of genetic engineering are indispensable are the most interesting in biology, perhaps in all of science. This technology is popularly presented as irresistible for its practical benefits. Far more significantly, it is irresistible for fundamental science.

16. *See generally* J. Rifkin, *Algeny* (1983).
17. Quoted in Cavalieri, "New Strains of Life—Or Death," *The New York Times Magazine,* August 22, 1976, pp. 8, 68.
18. Stich, "The Recombinant DNA Debate," *Philosophy and Public Affairs* 7 (1978), p. 187.
19. President's Commission, *supra,* note 4, p. 64.
20. *Ibid.,* p. 65.
21. Shapiro, "Introduction to the Issue: Some Dilemmas of Biotechnology Research," *Southern California Law Review* 51 (1978), pp. 987, 1001–02.
22. President's Commission, *supra,* note 4, p. 67.
23. *Ibid.,* p. 68.
24. Allen, "Science and Society in the Eugenic Thought of H.J. Muller," *BioScience* 20 (1970), p. 346.
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26. Dixon, "Tinkering with Genes," *Spectator* 235 (1975), p. 289.
27. C.S. Lewis, *The Abolition of Man* (1965), p. 71.