Moral and Legal Decisions in Reproductive and Genetic Engineering

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Man has long known that he can modify the genetic bases of organisms by controlling their breeding patterns. The application of such knowledge to the development of specific breeds of dogs or of wheat strains particularly suitable to cultivation is quite old. Mendelian and post-Mendelian genetics increased this ability by providing a rational model for the observed effects and thereby increased the ability to predict. This ability, when combined with advanced knowledge in the physical sciences, led to an understanding of many of the major mechanisms for the genetic transmission of information. Finally, this newest knowledge is rapidly providing the means for the manipulation of that hereditary information itself.

Imminence of the Developments

The ability to change the hereditary information content of a human cell is not a matter for the future: it is presently available. In 1971 Merrill, Geier, and Petricciani showed that a gene—a unit of hereditary information—from a bacterium could not only be introduced into human cells but could be caused to function in them. Nor need we any longer simply search for a gene that we may wish to manipulate: in 1972 a human gene was synthesized by Kacian and his associates. These techniques are still laboratory exercises; but the time-span from first demonstration to practical application is not likely to be longer than for similarly important developments in the physical sciences. Transistors, for instance, were in general use within less than a decade of their initial development.

An additional line of research is likely to accelerate the application of genetic manipulation, or genetic engineering, to man. This is what may be termed reproductive engineering. Reproductive engineering is any deliberate manipulation of the procreative part of the life cycle. Much of this is already in daily use in such forms as conception control and artificial insemination.

Genetic and reproductive engineering tend to be synergistic. Consider, for example, the production of genetically mosaic mice; that is, mice whose heredity is literally a patchwork. This condition is achieved by fusion of very early embryos of different strains. This requires at least four interacting techniques: (i) the exact timing of pregnancies, (ii) the manipulation of the eight-cell embryos in vitro, (iii) the production of exactly timed pseudopregnancies in the recipients, and (iv) the safe implantation of the mosaic, tetraparental embryos into the pseudopregnant females. The technique of transferring very early embryos from the uterus of one female to the uterus of another—this is called inovulation—itself has implications, to be discussed later. Another potential synergism between the two kinds of engineering may soon appear in the form of the insertion of genes into sperm prior to the use of that sperm in artificial insemination.

A warning should be added here, however. In all of these processes highly specific techniques must be used. This means that one kind of manipulation may be possible at a particular time while another, and apparently closely related, procedure remains out of reach. For example, it is now possible to insert a gene into a human cell; but to remove a specific gene is not yet possible, and indications are that it may remain impossible for a long time. It follows that only a person well acquainted with both the scientific literature and the conceptual basis of these activities is in any position to estimate the time scale for a future development.

Uniqueness of the Developments

These new scientific developments, which have been and are being incorporated into the technology of our society, pose serious moral and legal questions. That, of course, is not in itself new; scientific developments, when more or less broadly applied, have always raised such questions. (Recent examples include the fluoridation controversy and the legal aspects of artificial insemination.) What is new is the nature of the questions raised by the development of genetic and reproductive engineering: the manipulations of man, in these fields, will be vastly more fundamental than any previous ones. In some instances the manipulations will be irreversible, not only with respect to the individual but also with

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respect to all his descendants and to the population. In such circumstances wrong decisions can lead not only to the death of the individual but also to extinction of the species. Other incorrect decisions could seriously degrade the quality of life through control of thought, of liberty, and of motivation.

Roles in Controlling the Applications

Unfortunately the track record of those who, in my opinion, should be developing the moral positions, public policies, and legal constraints concerning these developments is not good. With few exceptions the moralists, theologians, sociologists, political scientists, legislators, legal scholars, and judges, whose job it is to integrate new developments into a sustained, viable, and sound fabric of society, have not only failed to be prepared for the introduction of new, science-derived technologies into the culture but have even reacted, at best, rather sluggishly. Their reaction time has sometimes been slower than that of the general public, as is shown by the widespread acceptance of certain developments long before they are placed in a definite legal and moral framework. An example is the debate about "when and whether to pull the plug" of the machine keeping a terminal patient more or less alive. This debate commenced seriously only well *after* the machines had come into common use and is still often being conducted in terms hardly useful to the person who must make the decision: the physician on the ward. Another example of the failure to develop an adequate set of moral stances has to do with genetic counseling and the individual and societal risks arising from the reproduction of persons who are sustained by medical skills in the face of hereditary defects. Should an 11th commandment have been promulgated: "Breed not, ye who carry defects"?

One popular reaction to this lack of guidance has been a feeling that research in these fields should be stopped because "it's too dangerous." Of course it is not the research itself that is dangerous but the application of the results within a society that has developed neither the broad principles nor the specific directives to make these applications wisely.

By default, the natural scientist himself has had to fill the vacuum with his own inexpert opinion so frequently that the impression is now abroad in some circles that this, too, is a part of his job. The job of the natural scientist is to make the discoveries; that of the technologist is to develop applications; and that of the social scientist and humanist is to suggest whether, how, and under what conditions the work of the other two ought to be applied.

As a well-informed citizen the natural scientist should have, of course, the same opportunity and at least the same responsibility to contribute to the decision-making process as any other well-informed citizen. But he is not an expert in, and should not be expected to act as if he were an expert in, the delicate processes of weighing the data or of drawing conclusions and making recommendations. He does, however, have responsibilities in this constellation of events beyond those of the ordinary person. First, he should give plenty of advance notice to the humanists and social scientists of forthcoming developments likely to require their attention. In doing so he must put all his expertise to work to differentiate between science and science fiction, lest the world react like those to whom the shepherd cried "wolf" too often. Second, he must be prepared to give the relevant details of new developments to his colleagues in the humanities and the social sciences. He must do this with due regard for (i) relevancy, lest he either swamp or impoverish the communication channels; (ii) scrupulous accuracy, lest he mislead his listeners; and (iii) intelligibility of language, lest he be misunderstood. Finally, he ought to monitor the tentative and the definitive pronouncements of the humanists and social scientists so as to detect early any misinterpretation or lack of facts that may have distorted their work.

The need for careful formulation of moral and legal positions on new developments *before* their widespread use is now more critical than ever before: the changes are more fundamental in nature, are less likely to be reversible in the individual or in his descendants, and, most importantly, are changes in human nature itself. As Leon Kass (1971) has pointed out, ". . . both those who welcome and those who fear the advent of 'human engineering' ground their hopes and fears in the same prospect: *that man can for the first time recreate himself*. Engineering the engineer seems to differ in kind from engineering his engine." (Kass's emphasis.)

Aspects of Human Engineering

The "human engineering" of which Kass speaks—it is inclusive of what is here called genetic and reproductive engineering—differs from previous kinds of changes in several respects. Consider its influence on human conduct. The traditional methods of modification have had three important characteristics: (i) they used symbols, especially as embodied in speech and art, as their primary vehicle; (ii) they allowed considerable choice to the individual as to the acceptance of at least parts of the modifications offered; and (iii) their effects could, to a great degree, be reversed in both the individual and his progeny. In contrast, the changes brought about by human engineering are largely nonsymbolic, because they modify the conduct-controlling mechanism directly. For example, the human engineer would *not* seek to educate or train a victim of Down's syndrome (the so-called mongolian idiot) to the point of self-sufficiency but rather would eliminate the chromosomal defect or, alternatively, would block fertilization or development of eggs carrying the defect. This is, incidentally, in sharp contrast with one of the most advanced of the old-style techniques, Skinnerian operant conditioning.

The second contrast between the old and the new techniques lies in the fact that the individual frequently will have no power to adopt or reject a particular modification. The modification will have occurred before he became an individual—either in the gametes or the early embryo that produced him or in an ancestral generation. To the extent that the change is in the hereditary material itself, it may be an irreversible change for either of two reasons: the technique for reversing it may not be available—at present a gene may be added but not subtracted—or else the desire to make the reversal at some future date may have been blocked genetically at the same time that the other changes were made.

A further consequence of the difference between the old and the new techniques is that the new techniques have the effect of removing literature, mythology, religious liturgy, etc., one more step from the real seat of power. Once, long ago, a speech—a curse—was expected to kill an enemy. Later a speech was expected to inspire soldiers to kill the enemy. In the future a speech might cause technicians to change the genes of some persons so that, under certain conditions or at a certain age, these persons simply die.

"Now" and "Soon" Examples

What, then, are some of the more likely of these human-engineering techniques? I wish here to deal only with those that are either available right now or have a great likelihood of becoming available in the next few years. Due to the highly technical nature of the work, long-range prophecy is likely to be unprofitable.

One technique that fits the human-engineering category, although it is neither reproductive nor genetic, is that of the direct control of man's neural system by electrical or drug stimulation of specific parts of the brain, as detailed so well by Delgado (1969). One need only read his book to discover the tremendous power available here and the need to develop a proper framework for that power.

Other nonreproductive and nongenetic methods are those devised for the prolongation of life by what, at any point in time, would be considered "extraordinary" means: heart transplantation, heart prosthesis, and the like.

In the realm of genetic engineering itself, one must at least mention genetic counseling—already widespread and rapidly spreading—because serious moral problems crop up almost daily in this work. If a prospective child has a risk of 5% that he will be seriously defective, should the parents reproduce? Or, if conception has occurred, should an abortion be done? What if the risk is 10% or 30% or 60%? What if the risk is essentially zero that the child will be affected but quite substantial that the child will transmit the deleterious gene?

Let us turn now to questions of genetic engineering in the strictest sense. Here we are dealing with techniques that change "human nature" and are transmissible directly to the offspring. Under what conditions should such techniques be used? The technique for inserting a gene or a group of genes into sperm is likely to be practical within a very few years. Suppose two persons are defective in the gene for the production of the enzyme parahydroxylase: their child may suffer from the disease phenylketonuria (PKU). It should be possible soon to introduce the normal, active gene into the sperm of the father and thereby assure that the cells of the offspring have, each, at least one properly functioning gene for this enzyme. Should this procedure be done? Consider not only that normal offspring will be produced but that both of the defective genes will be available to, although perhaps not active in, further progeny.

In the eugenic uses of genetic engineering that I have mentioned here, most of the arguments seem to be on one side: because it is highly likely that both the individual and society will benefit from the engineered changes, and because either short-term or long-term deleterious effects are unlikely, the judgment probably will be that the procedure should be carried out. But let's take a less simple case. There is good evidence for a hereditary component in the origin of schizophrenia and schizoid conditions (Heston, 1970). Very likely we are dealing with a multigenic inheritance pattern here. Therefore there may be a defective gene that facilitates the appearance of a mild schizoid condition. It is not unreasonable to suppose that it should become possible to insert a gene into the fertilized egg—a gene that would "correct" the defective gene. At first sight this would seem to be another clear-cut case for the use of the technique. But there are reasons to suppose that mild schizoid tendencies are useful in a wide range of endeavors, from painting and composing to scientific research. It is obvious that, without *much* further information, both the long-term and the short-term benefits cannot be weighed properly against the possible harm. And remember that once such a corrective gene has been introduced, it may not be removable! In such an equivocal situation what ought to be the rules for the application of the technique? I submit that, in such a situation, the role of the biologist is to provide the raw information and, perhaps, an indication of the probabilities of the various consequences. Then the humanists and social scientists should formulate the rules, subject to revision as more information or better techniques become available.

The other type of human engineering—reproductive engineering—also will require much thought and study. Although less likely to have permanent or irreversible effects, its points of action are even more closely bound up with our general ideas of morality and proper conduct than are those of genetic engineering. This is evident from the arguments raging around the two early forms of reproductive engineering presently in use: conception control and artificial insemination. Neither legal nor moral opinion has been stabilized or universalized in respect to these. What are and what should be the legal and moral positions vis-à-vis the following procedures, all but one of which have already been carried out in nonhuman organisms?

1. Artificial insemination with sperm from donors selected for particular qualities.

2. Artificial inovulation in which an egg produced by the wife and fertilized by the husband is transferred to a foster uterus.

3. Artificial inovulation by transfer of an egg produced by a donor, and fertilized either by the husband or a sperm donor, into the uterus of the wife.

4. Insertion of the nuclei of ordinary body-cells into eggs whose own nuclei have been removed, producing thereby any desired number of individuals with exactly the same genetic constitution as that of the donor of the nuclei—a procedure called cloning.

5. Cloning by causing ordinary body-cells to act as if they were fertilized eggs, thereby (again) producing any desired number of persons having the same hereditary makeup as the donor of the cells.

So little thinking has been done about the last two of these possibilities (outside the realm of science fiction, anyway) that we can hardly even list the individual or social advantages and disadvantages that might accrue from having a large number of genetically identical individuals. We are even less in a position to give these possibilities the calm and deliberate weighing that ought to lead to acceptable patterns of application.

Prospects and Challenges

The following general conclusions can be drawn:

1. Specific modification of individuals, by action on the genes or on the reproductive patterns and for individual or social purposes, is now possible and is increasingly and rapidly becoming feasible.

2. These techniques differ fundamentally from older approaches based on restricted breeding patterns–classical eugenics and Hitlerian eugenics, for example—in two critical respects: they are fast and they work. Even the insertion into man's heredity of what might be termed socially specific genes is a rather close—an uncomfortably close—probability.

3. We need to develop ways of adjusting these possibilities, of restricting their use within morally and socially acceptable patterns.

4. To do this will require a rejuvenation of the humanities and the social sciences and a reshaping of the relationship between them and the natural sciences.

Athelstan Spilhaus (1972) has said: "Just as technological invention cannot remove the need for social invention, neither should our slowness in changing outmoded social practices, institutions, and traditions be allowed to slow technological realization of potential benefits to all." Unless we rearrange our houses so that we can get to work immediately and unless we *do* get to work immediately, the genie (or gene) will be out of the bottle before we know the magic formulas that control it. And to permit this kind of genie to be out of control or to be misused is (to use the words in an unusual but meaningful combination) to *commit extinction*—first of freedom, and then of the species.

As teachers we have additional duties: to inform our students of these developments and to help them make the questions raised by these developments a prime order of business in their lives. We may confidently expect their lives to encompass the period during which most or all of the developments outlined here, as well as others, will be brought into practice. Those who are presently our students will be the ministers, the judges, the political scientists, the philosophers, the legislators, the teachers and, yes, the biologists, in charge. We and they had better start to think fast about how to handle that charge.

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Cell Energy System Duplicated

A part of the mysterious process by which cells produce energy has been duplicated in the laboratory by Efraim Racker, a Cornell University biochemist and molecular biologist.

The accomplishment is considered a breakthrough in the field of energy metabolism and membrane research. Scientists have been attempting for years to unlock the secret of the complex mechanism by which cells, the basic units of life, produce energy.

A major portion of the energy used in animal cells is produced in tiny "power plants," the mitochondria. The membrane of mitochondria contains enzymes that burn food and release an energy-storing molecule, adenosine triphosphate (ATP).

Three distinct enzyme systems cooperate to generate three molecules of ATP for each oxygen atom used in the burning process in which food is changed into energy. Racker isolated the third of these enzyme systems from mitochondria taken from beef hearts; and by combining the enzymes with phospholipids and membrane proteins Racker was able to reconstitute small round structures that produced ATP during the burning process.