SHOULD MAN CONTROL HIS GENETIC FUTURE?

by Donald Huisingh

In recent years, many scientists have begun to emerge from the ivory towers of pure scientific research and to become actively engaged in discussions with nonscientists. The scientists are beginning to realize their ethical responsibilities and obligations. Their concern has developed most rapidly since the discovery of the awesome power of atomic energy. This event has emphasized the need for scientists to inform their fellow citizens about the findings of science and the implications they may have for their lives and those of future generations.

Today scientists are speaking to representatives from all walks of life, including politicians, theologians, economists, and laymen in general. As concrete examples, three separate symposia dealing with "Man and His Future" have been held within the last four years.[1] The speaker lists were comprised primarily of physical and biological scientists.

None of the speakers claimed to have final answers about what direction man should take in the future. Most of them indicated various alternatives and discussed the probable results, but few grappled seriously with the quandaries that are likely to result in the pursuance of any particular course.

It is not surprising that most scientists are reticent to speak about the moral and ethical considerations of their work. They have tended to relegate religion to certain discrete times and places in their lives and to do the same with their science. Thus, few have had to grapple earnestly with the fundamental moral and ethical problems their work may raise. Furthermore, more scientists (I for one) came through undergraduate and graduate training in the physical and biological sciences with little formal experience in the social sciences. Scientists also appreciate the necessity to specialize and are aware of the pitfalls of speaking beyond their specialty, so they have tended to shy away from the territory of the moralist and the ethicist.

I feel uncomfortable in the role I try to fulfill in this paper: to write about the "Ethical Issues of Genetic Manipulation." I am not an ethicist, nor am I primarily a genetic specialist. In what follows, however,

Donald Huisingh is associate professor, Department of Plant Pathology, North Carolina State University at Raleigh. This paper was originally prepared for presentation to the Experimental Study of Science and Religion at North Carolina.

I will first attempt to sketch briefly some of the alternatives science has made or is likely to make available to man to enable him to manipulate and direct the future of the human race. Second, I will discuss the problems involved in employing some of these alternative means and suggest tentative guidelines in their development and application.

Possible Approaches to Genetic Manipulation

There are three main categories of proposed approaches to genetic manipulation. They are: (1) euphenic engineering, (2) genetic engineering, and (3) eugenic engineering.

By *euphenic engineering,* Lederberg[2] refers to the modification or control of expression of the existing genetic information (genes) of an organism so as to lead to a desirable physical appearance (phenotype).

Genetic engineering is defined as the change of undesirable genes to more desirable forms by a process of directed mutation.

Eugenic engineering involves the selection and recombination of genes already existing in the "gene pool" of a population. The term eugenics was originally coined by Sir Francis Galton in 1883 to designate his aspiration to improve the human race by scientific breeding.[3] The word is derived from the Greek root, *eugenes,* which means "well born."

Euphenic Engineering. Euphenic engineering in its simplest forms already is common practice. For example, lack of the capacity of an individual to produce insulin results in a disorder called diabetes. The expression of this genetic abnormality can be prevented by regular injections of insulin. Similarly, normal blood constituents such as gamma globulin now are supplied routinely to individuals who do not have the genetic information to synthesize these necessary blood components. Two other genetic defects lead to mental retardation because of the accumulation of harmful metabolic products. The diseases, phenylketonuria and galactosemia, result from an individual's inability to utilize the amino acid phenylalanine and sugar galactose, respectively. These diseases do not develop if the afflicted individual's intake of these molecules is restricted by careful control of his diet.

In these examples, expression of available genetic information was manipulated so as to minimize deleterious effects. As the factors which regulate and control gene action are more thoroughly understood, it is very likely that many other types of euphenic engineering will be possible. Suggestions of what the future may hold are evident by the following examples. It has been found that an injection of the anterior pituitary growth hormone into developing rats increased their brain size by

76 percent and increased their capacity to learn by an equivalent amount. There is one report of a similar response in a human child that received an injection of this hormone in its fourth month of fetal development. There is also a report of work being done in South Africa in which pregnant women are placed in decompression chambers for varying periods of time. The children which result are said to be superior to their siblings in intellectual capabilities.

It will be only a matter of time before many additional manipulations will be feasible, especially as we learn selectively to switch on or off at will the action of desirable or undesirable genes at specified periods in a person's life. The possibility of controlling the realization of the hereditary potential of the individual is impressive.

Genetic Engineering. Genetic engineering is in its infancy in its applications to humans, but information already available suggests at least three possible approaches: (1) transduction, the virus-mediated transfer from one cell to another of genetic material; (2) transformation, the incorporation of a segment of DNA from one cell into the genetic material of another cell; (3) directed induction of mutations of specific places on the chromosomes (gene loci).

An example of transduction in humans was reported recently by Rogers of the Oak Ridge National Laboratory. He showed that the Shope virus, which causes tumors in rabbits, also induces the synthesis of a distinctive form of the enzyme arginase which lowers the concentration of the amino acid arginine in the rabbit's blood. Dr. Rogers wondered if this virus would also lower the arginine concentration in human blood. Because one may not infect human beings with animal viruses for experimental purposes, he had to get an answer to this question indirectly. He compared the blood of a number of people who had worked with, and therefore been exposed to, the Shope virus with the blood of randomly selected individuals as controls. He found that many of the researchers working with the virus were carrying "virus genetic information." They had lower arginine levels than controls and had specific antibodies against the distinctive form of arginase, indicating that the virus DNA had supplied the information for the synthesis.

The Shope virus, Rogers suggests, is a harmless "passenger" virus in these people. It is possible that there are other such viruses. Perhaps some of them carry genes that would be useful in the treatment of genetic diseases. It is conceivable that a harmless virus might even be utilized as a vector for specific information in the form of tailor-made DNA that could be attached to the virus and transferred by the process of transduction.

Szybalska of the McArdle Cancer Laboratory at the University of Wisconsin has reported that human cells in tissue culture can be transformed.[4] She found that the genetic ability to synthesize inosinic acid pyrophosphorylase could be transferred to cells that lacked this capacity by the application of DNA containing the appropriate genetic information.

Bentley Glass[5] in commenting on Szybalska's work has stated: "It may be feasible and possible in the near future to treat a germ cell defective in some gene with DNA from one known to be sound in that respect. By so doing it may be possible to improve the genetic content of the individual's reproductive cells and hopefully improve the performance of his progeny." This may be feasible, but not necessarily either advisable or wise. Within just a few years, however, we must decide whether to permit such engineering of human reproduction.

Tatum believes that "genetic engineering" by directed mutation can be seen as a possibility in humans. In microorganisms we already are learning techniques for producing mutations in a nonrandom fashion by the use of chemical mutagens such as nitrous acid and synthetic molecules related to nucleic-acid bases. These latter analogues are incorporated into DNA and upset the replicative process so as to cause the replacement of the original natural base by another one—thus producing a mutation.

Another potential approach to directed mutation is through the synthesis in the laboratory of a desired molecule of DNA. This tailored DNA molecule, if it can be isolated in pure form from an organism or cell, can probably be replicated by already known enzymatic processes to any needed quantity. This new or modified gene can then be introduced into the mammalian cell in culture as in bacterial transformation.

Eugenic Engineering. Muller very pointedly says that while genetic engineering may have some applications in the future, it will be a long time before many of the technical difficulties are removed and the methods will be applicable to a sizable segment of the population.[6] Further, he indicates that euphenic engineering, while it may be extremely beneficial to the individual, does no good for the human race as a whole. On the contrary, by keeping a genetically defective person alive and allowing him to reproduce, we are increasing the frequency of deleterious genes in the population. Muller suggests, therefore, that we ought to employ a technique which is already possible: eugenic engineering through choice of desirable germ plasm.

Immediately, the term eugenics elicits a negative response on the part of many people, because to them eugenics and racism are synonymous. To others, eugenics means voluntary or mandatory sterilization of individuals who carry certain genetic defects. This latter approach to eugenics has been termed negative eugenics. Though such responses are understandable if the negative point of view of eugenics is maintained, Muller observes that they are readily modified by sincere thinking individuals if positive eugenics and the positive point of view are considered.

What is meant by positive eugenics? Muller develops his arguments for the application of artificial insemination with selected germinal material as a technique in positive eugenics. He says, "For any group of people who have a rational attitude towards matters of reproduction, and who also have a genuine sense of their own responsibility to the next and subsequent generations, the means exist right now of achieving a much greater, speedier, and more significant genetic improvement of the population, by the use of germinal selection, than could be effected by the most sophisticated methods of treatment of the genetic material that might be available in the twenty-first century."

The idea of artificial insemination per se is not new, nor is it completely objectionable. In the United States in 1962, more than 10,000 children were "fathered" by this method.[7] In most of those cases, the husband was either sterile or was carrying some genetic defect. The seminal donors were chosen by the doctor from men with body build and other morphological features similar to the husband, so that the resulting progeny would pass as the natural offspring of the legal family. The donor's anonymity was maintained to avoid paternity suits. According to Muller, we have among such couples many who would be happy to play a role in the decision of what germinal material is to be employed. "We are thus missing a golden opportunity to begin to consciously improve the genetic complement of the human race," Muller contends. According to him, intelligent germinal choice ought to be encouraged as the most effective way of rapidly achieving evolutionary improvement of the human race. Therefore, semen banks should be established, and the husband and wife ought to be permitted to select semen from donors of highest proven physical, mental, emotional, and moral traits. In order for a sound judgment to be made of the genetic potential of an individual donor, at least twenty years should be allowed to elapse after the donor's death before the deep-frozen semen is used. The men who earn enduring esteem can thus be called upon to reappear age after age through their preserved semen.

In addition to semen banks, it will soon be possible to store human ova as well. It is already possible to fertilize the human ovum in vitro and to implant the resulting embryo into the womb of a foster mother. It may also be possible in a few years to permit the embryo to develop to "normal" maturity in artificial glass wombs.

In fact, Dr. Daniele Petrucci of Bologna, Italy, has already done extensive experimental work with human embryos in vitro. Apparently, some technical difficulties still exist, because none of the embryos have lived beyond fifty-nine days.[8] There are also theological and legal difficulties; he was told by irate church officials and local legal authorities to discontinue this type of experimentation or be tried for murder. It takes little stretch of imagination to see that soon someone somewhere will make the necessary breakthrough and it will be technically possible to develop human beings in the laboratory from the sperm and eggs of any man or woman without restriction to time or place of the donor. In this way wide numbers of individuals could be produced by genetic selection from especially able parents. Further, as euphenic engineering progresses, it will be possible to nurture the developing embryos in different types of environments and thereby condition their mental constitutions. It will not be necessary for a woman to endure the discomfort and pain of carrying a child during the prenatal period. She would, of course, not get much psychological pleasure out of visiting the laboratory where her child was developing.

Does this sound too futuristic and too much like something taken from Huxley's *Brave New World*? Many people do not think so. In fact, in September 1965, the president of the American Chemical Society, Dr. Charles C. Price of the University of Pennsylvania, urged at the society's national meeting in Atlantic City that the United States make "creation of life" in the laboratory a national goal.[9] He was speaking of creation of life *de novo* from simple inorganic and organic molecules, a feat far more complicated and difficult than merely growing an embryo to maturity in vitro.

I have tried to indicate some of the types of possibilities that are or may be feasibly applied in directing the future of man. Many questions and problems present themselves. Guidelines are needed to help the scientist choose what types of research he ought to be engaged in, to aid the technologist to select the techniques he should make available to the population at large, and to enable the politician to cope with the social, legal, and political problems which will arise as these techniques are used. With this "Biological Bomb" already about to explode, the need to face the complexity of the problems involved takes on acute, do-it-now urgency.

Problems and Guidelines

The possible approaches to genetic manipulation we have discussed raise many ethical questions, including: (1) What is the essence of human life? (2) Is the human body a sacred vessel of man's soul and spirit, or is he merely at that position in biological evolution to know that he is a part of evolution and can do something about his own future evolution? (3) What absolute human values are we eager to retain? (4) What values are only relative in a particular sociological, theological, and political framework and as such should change with future evolutionary changes? (5) What are man's biological rights and responsibilities as individuals and as members of the species *Homo sapiens*?

If we accept the possibility of improving man by germinal and oval selection, the following questions arise: (6) Are there any truly ideal genotypes? (7) What are objective criteria by which they can be selected? (8) Who singly or collectively could objectively select individuals who fulfill these criteria once they are agreed upon? Since the eugenic approach would necessarily be a long-term project, it would have to have built-in mechanisms to ensure that the goals and objectives did not change with every new generation. This would necessitate the development of breeding plans. (9) Could such plans for the population be pursued without at the same time taking away much of the freedom of the individual? (10) Should the individual's freedoms and rights be secondary to the supposed good of the human race as a whole?

Let's take a look at what might happen if we subject man to a program of planned eugenics. William Shockley in a discussion of this subject stated, "I believe the difficulty with planned eugenics is that we are forced to think of ourselves and other people as being not solely warm, living human beings with whom we can establish personal relationships, but as *objects* which can be thought of and dealt with statistically and analytically."[10] He goes on to say, "My own reaction reminded me of a quotation expressing the same feelings in T. S. Eliot's *The Cocktail Party*":

> Nobody likes to be left with a mystery.
> But there's more to it than that. There's a loss of
> personality;
> Or rather, you've lost touch with the person
> You thought you were. You no longer feel quite human.
> You're suddenly reduced to the status of an object—
> A living object, but no longer a person.
> It's always happening, because one is an object
> As well as a person. But we forget about it

As quickly as we can. When you've dressed for a party
And are going downstairs, with everything about you
Arranged to support you in the role you have chosen,
Then sometimes, when you come to the bottom step
There is one step more than your feet expected
And you come down with a jolt. Just for a moment
You have the experience of being an object
At the mercy of a malevolent staircase.
Or, take a surgical operation.
In consultation with the doctor and the surgeon,
In going to bed in the nursing home,
In talking to the matron, you are still the subject,
The centre of reality. But, stretched on the table,
You are a piece of furniture in a repair shop
For those who surround you, the masked actors;
All there is of you is your body
And the 'you' is withdrawn.[11]

Do we dare withdraw the "you-ness" from human beings? Do we have the option to treat man as a manipulable object or is he to be treated as an inviolable individual at the center of reality? Is there something here that we must strive to retain? Is it possible that in the process of attempting to call the shots for human evolution, one will destroy those attributes that make him human? Muller says, "No, for by selection of individual sires who have demonstrated a genuine warmth of fellow-feeling, a cooperative disposition, a depth and breadth of intellectual capacity, moral courage, an appreciation of nature and of art, a healthful, vigorous constitution, and highly developed physical tolerances and aptitudes; the progeny of such progenitors are bound to be more human, not less."[12]

The question of our ability to select objectively such qualities looms as a great obstacle; but the problem of finding anyone with all of these attributes in desirable proportions is even more formidable. Besides that, it is believed that everyone carries an average of four to ten recessive lethal genes which express themselves only in the homozygous condition or only in the presence of certain modifier genes or under certain environmental conditions. Even the best phenotype may have these genes lying hidden.

Let's assume, however, that we found outstanding individuals of the types desired. What is the probability of improving the heritage of the human race appreciably? To answer this, I quote from Bentley Glass's article, "Human Heredity and the Ethics of Tomorrow":

The fertilized egg contains 46 chromosomes, 23 of them inherited from the egg and 23 from the sperm. The number of different genotypes that might be present in a single fertilized egg, if there were only 23 differences between the genes in the two sets of chromosomes in the father, and 23 other differences between the genes in the two sets of chromosomes in the mother, i.e., one difference per pair of chromosomes, would be $(2^{23})^2$. That is to say, the mother could potentially produce 2^{23} or 8, 388, 608 genetically different sorts of eggs, and the father an equal number of sperms with different genotypes. Hence there is the possibility through random fertilization of nearly 70 trillion genotypes of offspring. That would amount to about 2,300 times the present population of the entire world. This means that the variety of human genotypes is essentially inexhaustible and that there is only an infinitesimal chance that any two persons will be identical in all genetic respects with the exception of identical twins, triplets, etc.[13]

Besides this, many of the desirable attributes of man are inherited not as single genes but as multiple genes.

Thus, even if we were capable of selecting outstanding semen and ova donors, a large degree of variability would be expected in the progeny. There would, however, be a large number of genes held in common by the offspring. Not only would it be undesirable sociologically to have large numbers of humans of very similar genotypes, but biologically it may even prove to be disastrous, because nature puts a premium on variability. Let me cite two examples of what could happen if homogeneity were achieved in a large segment of the human population.

Wheat breeders have selected, crossed, backcrossed, and selected again for desirable agronomic qualities in wheat. A few years ago, they came out with a variety which they said had tremendous genetic potential for productivity and also carried a high degree of disease resistance. In a few years, thousands of acres of America's rich wheat lands were planted with this variety of wheat. But, in 1952, a new race of wheat stem rust appeared which completely overcame the disease resistance of this variety. Two years later only a few acres of this wheat were to be found anywhere in the country. That variety of wheat was fine in the old environment but not in the new one; so too is the possibility with man. New strains of bacteria, fungi, and viruses are arising all the time. If there were a large number of people who held many genes in common, they could all rapidly succumb to a new strain of microorganism that was pathogenic against those genes.

An example from the genetics of fruit flies also is relevant here. In a certain strain the female flies have been shown to pass on through their eggs a virus which infects the developing young. This virus makes the individuals susceptible to CO_2 and has been called the CO_2

lethality virus. Similar transovarian transmission of viruses in humans is possible, and if the ova of several individuals were widely used, the likely results are obvious.

This discussion of the application of eugenics for human betterment has been based upon the following assumptions: (1) we could objectively agree what qualities to select for, (2) we could quantify and select these qualities, and (3) genetics is the most important factor in determining that an individual have or develop the desirable traits listed earlier.

Without going too deeply into the nature versus nurture argument, I would like to cite the statements of two noted authorities. Nobel laureate Dr. Francis H. C. Crick, physical biologist at Cambridge University and winner of the Nobel Prize in 1962 for his contribution to our understanding of the physical arrangement of DNA, is reported to have said, "Humans probably will not be improved or altered by genetic manipulation in the future; education and environment are more important than genetics."[14]

Dr. Bentley Glass, in a similar tone, says:

> Modern man has been on the earth for an immense stretch of time, at least 40,000 years, and maybe several hundred thousand, without much change in his skeletal anatomy. We are therefore justified, I think, in regarding all his tremendous human advance in culture and civilization, in material power and relative understanding of nature, as having occurred with little if any, genetic change. The great advances made by modern man, therefore, reflect no change in his biological heritage but represent a new phenomenon, the advent of cultural transmission, the accumulation of knowledge and its transfer from one generation to the next. Equal opportunity must be coupled with freedom of the individual if it is to lead to fullest development of the potential of the genotype.[15]

Thus two outstanding experts in the area of genetics seem to say that it is not desirable, nor is it likely to be fruitful, to involve human beings in Muller's grand genetic experiment. I concur with that conclusion. Most people never approach a realization of their genetic potential even for short periods of time because their society has not provided the educational opportunities for them to develop fully their intellectual capabilities. In additional cases the sociological mores, the political machines, and the theological institutions have erected further barriers to the individual's progress. In short, their individuality, personality, and humanity have never been developed. We ought to concentrate on maximizing the nurture of every individual so that he more nearly realizes his existing genetic potential, and move very cautiously into the area of germinal selection experiments.

Much more could be stated in summary about other possible approaches to the future of man. For example, it seems likely that negative eugenics should be continued, but it poses the ethical problem of selection of some individuals as not being fit to reproduce. In some extreme cases few people would disagree that some individuals do not have the right to reproduce because of their load of genetic defects. However, very few people would agree where the cutoff point should be.

I anticipate that genetic engineering will be found to be helpful in modifying the genetic information of individuals, but it is not likely to be a significant factor in the human population as a whole. On the other hand, progress in euphenic engineering and the provision of favorable conditions for human development and self-actualization are likely to be the most significant ways by which man will direct his own evolution. There will be many facets of the "scientific engineering" of man which will pose serious ethical problems. The politicians, lawyers, theologians, social scientists, and the general public must all be informed of the alternatives which will be available to them. They must be informed of the possible benefits and problems in order to be in a position to make intelligent use of the new tools science will provide.

What general guide will all these people use in deciding whether a particular type of research should be engaged in or whether a particular practice should be condoned and used? I would like to paraphrase what John Baillie has to say in his little book, *Natural Science and the Spiritual Life*. The future of man is secure only as long as the virtues of humility, tolerance, and impartiality are retained as absolute standards. Within this framework we should use scientific advances as tools to serve society.[16]

The time ahead is uncharted. No one has been there, so there are no experts. Each of us whose body and brain may be modified or whose descendant's characteristics may be predetermined has a vast personal stake in the outcome. We can help to insure that good will be done only by looking to it ourselves. We must be careful to retain the individuality of the individual and the personality of the person, or else the humanity of the human may be lost.

NOTES

1. See J. D. Roslansky, ed., *Genetics and the Future of Man* (New York: Appleton-Century-Crofts, 1966); T. M. Sonneborn, ed., *The Control of Human Heredity and Evolution* (New York: Macmillan Co., 1965); and G. Wolstenholme, ed., *Man and His Future* (Boston: Little, Brown & Co., 1963).
2. See Wolstenholme, pp. 263–73.
3. Anram Scheinfeld, *The New You and Heredity* (Philadelphia: J. B. Lippincott Co., 1950), p. 679.
4. Elizabeth H. Szybalska and W. Szybalska, "Genetics of Human Cell Lines. IV. DNA—Medicated Heritable Transformation of a Biochemical Trait," *Proceedings of the National Academy of Sciences* 48 (1962): 2026–34.
5. C. Stern, *Principles of Human Genetics* (San Francisco: W. H. Freeman & Co., 1960), p. 753.
6. See Sonneborn, pp. 100–122.
7. See Wolstenholme, pp. 258–62.
8. "Control of Life. I. Exploration of Prenativity," *Life*, September 10, 1965, pp. 60–79; "Control of Life. II. Gift of Life from the Dead," *Life*, September 17, 1965, pp. 78–88; "Control of Life. III. Spare Parts for People," *Life*, September 24, 1965, pp. 66–84; and "Control of Life. IV. The New Man—What Will He Be Like?" *Life*, October 1, 1965, pp. 94–111.
9. "Control of Life. IV. The New Man—What Will He Be Like?" *Life*, October 1, 1965, p. 94.
10. See Roslansky (n. 1, above), pp. 96–97.
11. T. S. Eliot, *The Cocktail Party* (New York: Harcourt, Brace & World, 1950), pp. 29–30. Reprinted by permission of Harcourt, Brace & World, Inc.
12. See Wolstenholme (n. 1, above), pp. 247–62.
13. Bentley Glass, *Science and Ethical Values* (Chapel Hill: University of North Carolina Press, 1965), p. 101.
14. "Little Change Likely," *Industrial Research* (March 1967), p. 36.
15. Bentley Glass, "The Ethical Basis of Science," *Science* 150 (1965): 1254–61.
16. John Baillie, *Natural Science and the Spiritual Life* (New York: Charles Scribner's Sons, 1952), pp. 34–43.