ALFRED CUSCHIERI

SCREENING FOR GENETIC DISEASES: WHAT ARE THE MORAL CONSTRAINTS?

Now that the Human Genome Project (HGP) is an ongoing and rapidly progressing reality, and human genetic engineering is expected to become standard procedure, the inevitable question is how will these procedures be applied. The inevitable and much debated answer is eugenics. It is often looked upon as positive eugenics, directed perhaps, towards achieving human beings endowed with optimal characteristics of physical strength and beauty, intellectual genius and longevity. There is of course the immense and probably insoluble problem of determining which human characteristics, among nature's rich and superb diversity, can be improved and what constitutes the hypothetical physical and intellectual excellence that one might envisage and enhance.

Assuming, purely for the sake of argument, that it would be possible to achieve this excellence, for ourselves and for our future offspring, through genetic engineering, there would immediately arise two significant moral problems. The first would arise from the great likelihood that the vast majority of us would rush to be genetically engineered, creating the moral problem of who should have priority. The second is, that those of us who did not have the privilege of being genetically engineered, or did not have the natural endowment of perfection, would somehow be considered as inferior, second-rate human beings raising the other serious moral worry of discrimination.

Being simply a practicing geneticist who sees an abundance of problems of genetically induced misery, I must confess that my competence in speaking about achieving such perfection is limited. My eugenic priorities dictate that I limit myself to a discussion of the prevention and correction of genetic diseases as a contribution to eugenics for the future. As a geneticist who witnesses some of the most distressing diseases which affect mankind, including the birth of congenitally malformed infants and serious, incapacitating and often lethal genetic diseases; who feels the psychological trauma experienced by parents as a result of the knowledge that one or both of them were agents in the genetic transmission of disease, I cannot help but think that negative eugenics (or the prevention of genetic disease) is, and will remain for a considerable time, the priority

E. Agius and S. Busuttil (eds.), Germ-Line Intervention and our Responsibilities to Future Generations, 3–11.

with respect to future generations. The great strides currently being made in the field of genetic screening is directed precisely towards alerting geneticists to the presence of disease-producing genes as a first step in the prevention of genetic disease and thus contributing to eugenics concerning future generations.

It cannot be denied that the development of human genetics and its remarkable achievements have been spurred on by the relentless quest to find the underlying causes of genetic and inherited diseases and to find remedies for these hitherto untreatable conditions. This is the present ambition of most geneticists and scientists, as can be witnessed by their contributions to the immense literature on genetics. It is a positive contribution: to improve the present gene pool which is the one that will be passed on to future generations.

Given the considerable advances taking place in gene technology, the prospects of genetic engineering and particularly of germ-cell engineering, can we feel confident that we will live up to our responsibilities towards future generations? Is there cause for concern when one considers the prospects of positive eugenics, of creating clones and designer babies? In trying to assess the gravity of the situation one should start by assessing what the present generation of geneticists and scientists are doing and what direction is being taken, because this is what is within our capabilities to oversee. It is our responsibility to guard the present gene pool and ensure, in the most cautious and enlightened way possible, that nothing is done which may be detrimental to future generations, and that necessary measures are taken to implement any positive measures for its enhancement. Should we concern ourselves with what might happen in the future and think of ways in which such eventualities might need to be dealt with?

My thesis is that the greatest positive contribution that we can make to future generations lies in the present. Genes are transmitted one generation at a time. The present genes are the ones which can be modified by the present generation of geneticists and scientists in ways that could be beneficial or detrimental to future generations. How scientists might behave or react in the future is not within our control. However, it is within the responsibility and control of the present generation to criticize the values that emerge from the vast and rapidly expanding field of human genetics and genetic technology, and perhaps to set the trend in the development and evolution of thought regarding future projects.

Consequently, I will not here pursue the philosophical questions that

arise should we conduct genetic interventions to enhance desirable characteristics, but I shall dwell on the more mundane and practical issues of what we can do, and what we are doing now, and how we could benefit future generations.

The HGP is the major landmark and turning point of the present time. It is meant to ensure that there is a complete map, catalogue, and sequence of the 100,000 (or probably much more) estimated genes in the human genome, how they function, and how they interact with one another. The project is also expected to provide important information about the large amount of non-coding genetic DNA which apparently does not carry genetic messages in the conventional sense, that is genes for the synthesis of proteins. This vast amount of largely unexplored DNA certainly holds many yet untold secrets about gene interaction and control. The HGP is expected to provide a better understanding of the common heritable traits which do not appear to be attributable to single genes, such as stature, intelligence, obesity, and others. Above all, it is expected to form the basis and the main reference point for investigating inherited and acquired disease, human development, and evolution.

When the HGP is completed we would be in a position to say that we understand human life much better than ever before; that we have a grasp on the mechanisms operating in the human genome. Equipped with all this knowledge man would have control over his own genome and would be able to manipulate it. However, we need not wait until the project is completed. The HGP has already started, and although there is still a long way to go to its full realization, it has already yielded results and its effects are already being felt.

The genes for a number of serious diseases have already been mapped, cloned, and sequenced. This has made possible genetic testing for quite a number of genetic diseases. Genetic testing has already been with us for quite some time. The moral and ethical problems encountered in the course of such testing are therefore not new. However, their magnitude has increased and will continue to increase in proportion to the increase in our knowledge of genes and their mutations.

Advances in genetic technology not only increased the number of tests for genetic diseases, but also made the testing simpler and less costly so that large scale genetic screening has become a possibility and can even be extended to populations.

The greatest moral problems that arise from the ability to test for human genetic disease are (as Baroness Warnock points out) problems of

knowledge. Genetic testing is simply the availability of knowledge about the genetic constitution of a particular individual. The problems arise from the implications of such knowledge to the individual concerned, to his or her family, to third parties, and to society in general. Who has the right to such knowledge? Who should decide whether genetic information about an individual is to be obtained or not? That is, who is to decide whether a particular individual should be tested or not? Who should decide to whom this knowledge should be made available? Who should decide what actions are to be taken when a gene abnormality is discovered? These problems are the main determining factors that impose moral constraints on the use of genetic testing in the future.

I begin with the implications of genetic testing for the particular individual. Inherited diseases which manifest themselves late in life are the ones in which these implications are most significant, but they can also be used as models for other diseases. Individuals who are afflicted with severe genetic diseases which appear late in life, such as Huntington's disease, experience the normality of life, the hardship of being afflicted with a serious and incapacitating disease, and the sorrow caused by the daunting prospects of transmitting the same disease to their children and to future generations. Huntington's disease appears late in life, usually after the reproductive years, and often after the individual has transmitted the deleterious genes to the next generation. It is possible to know, through genetic testing, whether a particular individual who is at risk is affected or not, and in my view, the individual should be free to make his or her own choice about whether to be tested, whether he or she would prefer the reality of knowledge to the uncertainty of chance. With the former, distressing as it might be, it would be possible for an individual to plan his or her life, including marriage and children. Some individuals, however, prefer not to be tested, to leave everything to chance, and to live with the uncertainty of risk. The decision is expected to vary depending on the individual and his or her family circumstances. One main factor is whether the individual is already married and has children, or whether he or she is considering marriage or having children. The present trend is that young individuals prefer to "face reality" before entering into relationships with other persons, and that marriage partners expect to know the truth about their future spouse.

Because it is essential to respect an individual's freedom of choice, it is generally accepted that the options for genetic testing are not extended to minors, except in situations where outcomes could be of direct and

immediate benefit to a child; as, for example, in a boy with muscular dystrophy or a child with familial intestinal polyposis which requires surveillance for possible malignant growth.

The implications of being tested are serious, and the responsibilities are great, so that the individuals concerned need psychological support and adequate knowledge about the disease itself, the mutant genes and the possible implications, in order to be able to take responsible decisions. In other words, the opportunity for testing brings with it the moral obligation of providing adequate support and counselling services. If these cannot be provided, it seems unethical to carry out genetic testing.

What are the options for preventing the propagation of genetic diseases? One time-honoured option is to voluntarily abstain from having children, a decision which must be entirely free and which should not, in my view, be forced upon prospective parents. Although this approach is usually adopted, couples often do feel the strain of not being able to have children, and typically seek alternatives. The second option is to elect selective abortion following prenatal diagnosis. The third option, which is now becoming more easily available, is pre-implantation diagnosis on a four-\or eight-cell embryo. One of these cells is removed by micro-techniques and its DNA amplified and tested. If it is found to carry the abnormal gene, the remaining embryonic cells are discarded; whereas if the tested cell is found to carry a normal gene, the embryo is implanted. These three methods of inhibiting the propagation of an abnormal gene are all methods of artificial selection against the disease gene.

It is not appropriate to discuss here the moral issues which relate to selective abortion and pre-implantation diagnosis, procedures which some consider morally acceptable but others consider morally unacceptable, and therefore not really options for them. However, irrespective of the acceptability of the procedure itself, one questions whether it is morally right to terminate a pregnancy, whether in the pre- or post- implantation stage, because a disease may appear thirty to sixty years later. Besides, the condition may be treatable. Is it morally justifiable to deny life to an embryo or fetus because it is carrying a gene which predisposes to cancer, manic depressive psychosis or schizophrenia? All of these are undeniably serious diseases, but it should not be concluded that they necessarily make life not worth living. To carry the implications further, is it justifiable to deny life to a fetus because it carries a pre-mutation which does not cause any disease in the individual who carries it, but might manifest itself as a serious disease in future generations, such as may occur in

X-linked mental retardation? These are serious issues which confront us and which require responsible decisions, since they affect future generations.

Besides, the very use of genetic testing and selective termination, rather like weeding a garden of unwanted specimens, is repulsive to many when applied to fellow human beings, and constitutes one of the worst forms of discrimination, imposing therefore one of the most serious moral constraints on the use of genetic testing and subsequent termination of pregnancy .

What are the alternatives? Genetic engineering is expected to provide possible solutions. One of these might be germ-line cell genetic engineering intended to replace the mutant gene with a normal one. Once corrected, the engineered germ-line cell would be expected to ensure that the disease is not transmitted to future generations. However, this approach is replete with uncertainties. Firstly, although a known defective gene may be successfully engineered in a germ-line cell, new mutations still continue to arise so that genetic diseases can only be limited to a certain extent. Secondly, genetics is only beginning to alert us to the fact that genes in germ cells may behave differently from those in somatic cells, and furthermore that they may behave differently in female and in male germ cells. These scientific uncertainties impose a grave moral constraint on the use of such procedures, which should not be employed until there is at least sufficient scientific knowledge about the genetics of germ cells to make germ-line genetic engineering a worthy proposition. Besides, genetic experimentation on germ cells which are subsequently fertilized would pose moral and ethical problems which are in many ways similar to experimentation on embryos. Because of these uncertainties, genetic engineering is, at present, not permissible on human germ cells. Nevertheless, these problems are not unsurmountable, and it is expected that in the future-germ line cell genetic engineering will become feasible and could make important contributions to the prevention of genetic disease.

A feasible alternative to germ-cell engineering is expected to be genetic engineering of the early embryo in its two-\or four-cell stage. Here, one is dealing with somatic cells but the results of the genetic engineering would also include the subsequent germ cells. Genetic engineering in embryos is considered to be a sophisticated and extremely delicate form of surgery intended to correct a defect, and at least prima facie would not appear to present serious moral constraints.

It has already been stated that it is essential to maintain strict privacy in

genetic testing especially for adult-onset disorders which are to be performed following the obtaining of informed consent. However, it is rightly argued that the offspring, siblings, and other close relatives of an affected person have a right to know the results of genetic testing, because they too might be at risk. Pressures are also applied by insurance agencies and employers who claim that they have a right to know of existing genetic risks before entering into a contract with their customers. If these demands are acceded to they could easily amount to compulsory testing. These matters, presently strongly debated, are fundamentally concerned with the question of privacy, of who should decide on whether genetic testing is to be performed, and most importantly, with the issue of discrimination which might take the form of increased premiums, of denial of medical or life insurance, or work. Such considerations are more important in some countries where health services rely on private insurance, but of less significance in countries like Malta where full health services are available to all. A similar problem of privacy arises when a population-wide screening program is proposed for a common genetic disorder. This too might amount to compulsory testing.

As genes for more and more diseases become known, and genetic screening becomes easier to perform, the pressures for indirect compulsory screening are bound to increase, though perhaps surreptitiously. It is imperative that such pressures be resisted, not only to guarantee confidentiality of genetic data but above all to ensure that genetic screening is not misused as a form of discrimination.

In assessing the most recent contributions of human genetics, we see that the most prominent advances have been in the field of medical genetics. This is not fortuitous but stems from the real and genuine appreciation of the need to understand and eventually find remedies for serious genetic illnesses, which have for so long eluded us. Medical care has always been committed to preserving life and curing disease. This is not by any means an exclusive characteristic of medical people but merely a commitment to help others, just as people have committed themselves through their various professions to voluntarily care for the weak, the diseased, the disabled, the oppressed, the socially disadvantaged, and those who have been abused by others. It is true that some people have, on the contrary, committed themselves to greed. Why should we now doubt the good intentions of geneticists and scientists who have worked and are still working to identify the basis of genetic disease and in the process are unravelling the fundamental structures of life? Should

they be mistrusted and treated as though they were irresponsible?

Most of the concern that has been expressed regarding possible misuse of genetics to the detriment of future generations stems from the fact that exploration of the genome is largely exploration of unknown territory, which always brings with it a certain degree of fear and anxiety. However, danger is not really a deterrent but a challenge to proceed with caution. Many fears and concerns had been expressed in the 1970s when the first genes were cloned in bacteria, but scientists cautiously but steadily carried on in their venture while concerned onlookers cried out DANGER! and even warned of impending doom. Scientists and institutions responsible for their funding took the appropriate measures to ensure that scientists were self-critical and self-controlling. There was consensus on this matter at national and international levels. In 1989, at the Council of Europe, ministers of European countries agreed that "throughout the execution of the programme the ethical, social and legal aspects of human genome analysis should be the subject of wide ranging and in-depth discussions, and possible abuses of the results or later developments of the work should be identified. Principles for their utilization and control should be proposed." It is incumbent on scientists, doctors, and others involved in research to ensure that the application of knowledge is for good purposes and that possible abuses are detected and stopped. Who can do this monitoring better than the scientists themselves? Who knows what is going on and who are in the best position to detect abuses?

Now continuation of genetic research is leading to a better understanding of human life, and ourselves. However, people are again expressing fear and mistrust of science and the powerful technology it creates. Again, this stems largely from fear of the unknown and feelings of threat from a powerful technology which is in the hands of scientists. We hear warnings of another impending calamity (due to the misuse of genetic engineering in human germ cells) posing a threat to the human genome of future generations unless action is taken to prevent it. But, we should stop and reflect. Is it realistic to think that scientists and geneticists involved in this tremendous project are so overwhelmed by the momentous discoveries that a "watchdog" is needed to oversee their activities? Is there really any threat to the genome of future generations, or is it time that we take count of the reality of the situation as it is at present?

Organizations dedicated to protecting future generations usually have good intentions: to promote the view that what man has today (whether

this is cultural, environmental, or genetic) should be preserved, and possibly even enriched for future generations. At the moment, we are living up to our responsibilities of preserving the human genome and of passing it on to future generations. We must, however, evaluate the present situation of the human genome, give due recognition to beneficial achievements, and identify deleterious ones, doing all in our power to inhibit them. We must educate the public and dispel undue fears. The future heritage of mankind depends on what we do or fail to do today.

There is no doubt that the most important applications of powerful genetic technology have been in the field of genetic diagnosis, and treatment using genetic engineering is well on the way to new applications. These are the tremendous contributions of medical genetics to the control of human disease. There is no doubt that this ideal leads the list of eugenic priorities. Genetic testing is only one small but essential step toward achieving these priorities. Let us look forward with courage and optimism to achieving additional positive gains which will safeguard and enhance the future of humanity!

Department of Anatomy
University of Malta