Chapter – I

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From Science Fiction to Ethical Predicament

The Big Bang and the genetic code are probably the two scientific ideas that have most radically altered our view of world in the twentieth century. The Big Bang seeks to explain how the universe was created and how the primordial constituents came to be formed. The genetic code lays down the pattern for the formation of living material and the transmission of inherited character. Interestingly enough, the same man formulated the first serious theories of both these key ideas; the physicist named George Gamow.[1] In 1953, Gamow read the famous Watson and Crick Nature Letter on the structure of DNA and immediately jumped to the conclusion that the DNA molecule could directly serve as a template for protein synthesis.

Almost a decade after Gamow's prediction the English scientist Robert Hooke published a review of some observations he had made while peering down a microscope. Describing the tiny spaces surrounded by walls that he saw in samples of cork, Hooke coined the word 'cell'. Thus it was discovered that nature is the most expert packer. Once it was realised that the molecular waltzes of life take place largely inside cells, it paved the way of new science, what is now popularly known as biotechnology. Now any new development in science when applied to our society inevitably brings some issues of ethical concern; biotechnology is not an exception in this regard. As biotechnology is a vast area, the ethical issues involved with this are not less vast. Hence our effort will be to confine our discussion within one aspect, namely Human Genome Projects and some of its

1. *Nature*, vol. 404, 30 March 2000, p. 437

consequences such as genetic screening, genetic counseling and genetic therapy. Although headlines in journals and newspapers often depict the Human Genome Project as a 1990s phenomenon, the project is actually a continuation of genetic research performed throughout the later half of 20th century.

About the Project

Let us first see what sort of research will fall under the rubric of the Human Genome Project (HGP). The Human Genome Project is an ambitious plan to map and sequence all 100,000 or so genes found in human DNA. It is a task that has occupied hundreds of scientists in labs around the world since 1986. Part of the motivation to sequence the entire genome (i.e., all the genes present in a complete set of chromosome) was the desire to learn more about the genetic roots of disease and to discover more genes that might be used in gene therapy. The ability to map genes was boosted by the development of recombinant DNA technology[2] in particular the use of restriction enzymes to cut DNA molecules into small fragments with known endpoints. The restriction enzyme cutting sites act as easily identified markers that let scientists compare different fragments for the presence or absence of particular genes. Bit by bit, they build up collections of fragments that overlap each other in known order until they have eventually spanned the entire length of chromosome. Adjacent fragments from ordered chromosome libraries that help researchers locate particular genes. Mapping the location of genes on a chromosome is, however, only the first step. The ultimate aim is to know the sequence of bases in each gene. This is an even lengthier task, since there are about three billion base pairs in a set of 23 human chromosomes.

2. DNA molecules that have been assembled by splicing together fragments from the same or different species with the use of restriction enzymes.

Many scientists found the launch of this huge research program stimulating. Reviewing the genome project in 1989, James Trefil, professor of physics at George Mason University, wrote: "It presents nothing less than the ultimate scientific response to the Socratic dictum 'Know Thyself'.[3] Our scientists were less enthusiastic, seeing much of the exercise as a colossal waste of time, money and human resources. Critics say that for medical purpose, the simpler identification of genes responsible for disease is all that is needed. They say that most of the genome is not, in fact, made up of genes that encode protein production, such as turning genes on and off, or helping cells duplicate genes during division. Other regions may simply be evolutionary baggage with not useful function, like the human appendix.

Another concern, shared by people at large, was that full knowledge of the human genome was a scary sort of power, evoking the story of Frankenstein. Putting things in a different perspectives, Joseph Gall wrote in a issue of American Scientist in 1988: "(Genetic Maps) will like having a whole history of the world written in a language you can't read". What Gall was pointing out that mapping and even sequencing genes is only a beginning That knowledge alone won't tell us the genes' functions.

Because of the potential misuse of HGP information, almost in every country certain percent of the projects' annual budget is earmarked to explore ethical, legal and social implications of the result. Will people identified as the 'healthy ill' — those who harbour genes that are likely to one day make them sick — experience discrimination, will negative eugenics resurge? Concerns about stigmatisation following the revelation of one genotype have already frightened

3. *Biotechnology Unzipped*. Universities Press, 1998.

people away from taking certain genetic tests.

Since the dawn of humanity, people have probably noted inherited traits among themselves, from height of the body and body build, to hair and eye colour, to special abilities, behavioural quirks, and illness. Genetics provides the variety that makes life interesting. Today, genetics is rapidly becoming a medical field in its own right, and in the future it will affect our lives in various ways. The list of genetics applications is long and ever expanding. We should keep ourselves prepared to deal personally with the avalanche of genetic information that will arrive with the new century.

Genetic Screening

Genetic screening is a search for defective genes, identifies featuses, children, and adults whose genotypes may cause disease in themselves or in their descendents. Genetic screening, in some cases, may provide an early warning for the later appearance of a disease and allow time for life-style modifications. All techniques of genetic screening are attempts to gain information about the foetus. This is done by viewing the foetus using X-radiation, ultrasonography, or fetoscopy. Information gained from prenatal tests and shared with prospective parents allows parents to decide on whether to abort or to continue the pregnancy. Before prenatal testing procedures were available, families at risk for a genetic disorder were counselled only on statistical odds and, because of the fact, may pregnant females opted for abortion of normal foetuses. Since the mid 1970s, through the use of ultrasound and prenatal testing procedures that allow for chromosome analysis and biochemical or metabolic screens of foetal cells and amniotic fluid, it is possible in some cases, to lower the overall calculated risk for particular birth defects or say with great

certainty that a given birth defect will be present and discuss various implications of their situation with prospective parents.

Prior to the development of the prenatal screening, genetic screening was performed primarily on the newborn. Newborn screening consisted mostly blood biochemistry.

The field of genetic screening is moving so rapidly that, in the near future, scientists will be able to develop a screening test for almost any gene. Scientists believe that even now there are certain methods that can in advance predict the presence of certain genes that predispose them certain diseases like cancers, heart diseases, diabetes, etc. Having this knowledge in advance will be most useful because it appears that, for many multifactorial traits, a modification in lifestyle may either stop the expression of the disease or reduce its severity. The problem will no longer be one of being able to find a test for a given gene, but of protecting the patient from potential emotional and economic distress.

Ethical Dilemmas

In September of 1986, two young adults were genetically screened for the presence of the Huntington's disease.[4] Both tested positive. They must now live with the grim certainty of developing this disease. According to a report, about 25,000 individuals in USA alone have a family history of Huntington's disease (HD). About 6% of HD patients commit suicide and about 28% attempted suicide at least once. 21% of at-risk persons said they might commit suicide if their predictive tests were positive. So the question arises: what is going to

4. Huntington's disease is a genetic dominant disease that is generally not manifested until after age thirty. In this disease death is due to progressive degeneration of specific brain tissues.

happen to those who receive an early positive diagnosis? Various studies are underway to determine the psychological care those people will need. How will the knowledge that they will express HD, a death sentence, affect their behaviour over the rest of their lives? How will it affect their families, friends, employers, and insurance companies? In some cases it may not be possible to protect the individual's right to know or to refuse to know his or her diagnosis. For example, if a husband has a positive HD family history, his pregnant wife decides to test the foetus for the presence of HD gene, and foetus tests positive, the at-risk husband knows he is carrying a gene and will demonstrate the disease. The conflict in human rights is obvious. The father has the right not to want to know, but one or both parents have the right to prenatal diagnosis. How does the prospective mother morally abort or deliver the foetus without telling the husband of the risk or lack thereof?

The issues presented in the case of screening for HD applies to most, if not all, genetic disease. It is because of these issues that many see genetic screening perched on the edge of a morass, about to make a headlong rush into a tangle of social, legal, and ethical problems that medicine and society are unprepared to handle

The ability to screen for an increasing number of genetic diseases like HD poses many unanswerable questions. Who should be screened? At what age they should be screened? Can confidentiality be guaranteed? How will an ominous diagnosis affect the psychology of the individual, the family, and friends? What are the employment and insurance options? Who will counsel patients given a grim prognosis? Should geneticists screen for diseases that have no treatment? What are the legal implications? Can one family member sue another for his or her failure to warn siblings about a serious reproductive risk? Will the ability and right to know ultimately become the duty to know? Will

individuals be able to protect their privacy and personal reproductive freedom in an era of almost unlimited genetic knowledge about themselves and their children? These questions far outweigh the answers, and it appears that those questions will grow exponentially as the new genetics opens greater areas of knowledge.

Genetic Counselling

Genetic screening programs must be coupled with genetic counselling that makes it clear to individuals that faulty genes are part and parcel of human biology; that individuals have no say in their inheritance; that, in most cases, they cannot be certain as to which of their genes will enter their offspring or how these genes will perform in a new biological environment; and that, chance, an unguided, uncontrollable event, plays a large part in human reproduction.

For the majority of parents, knowledge of genetic diseases, their heritability, their risks, and recurrent risks is inadequate. Parents need to know the physical manifestations of the disease how the disease is managed, the psychological impact of the disease on the person and family, and the prognosis with respect to prenatal diagnosis. these individuals need to know what will be done, how long the diagnosis will take, where the diagnosis will be conducted, potential complications to the mother, length and type of disability, and potential harm to the foetus. With respect to abortion, parents need to know what will be done, where it will be done, how long the procedure will take, potential complications, effect on future pregnancies, and stage of development of the foetus. Such information can be given by a genetic counsellor. The information may be presented to the counselees in one of the two approaches: nondirective counselling or directive counselling. The nondirective counsellor will present all the facts in an

unbiased manner, placing the responsibility of decision making with the counselee(s). The directive counsellor helps the counselee(s) to make their decision.

The reasons for seeking genetic counselling are at least as numerous as there are genetic defects. Generally, people seek genetic counselling because they have a problem or because there is a medical problem in their family for which a physician refers them for a genetic counselling. Regardless of reason, the counsellor will try to determine if the event is genetic, and what pattern of inheritance and risk is involved.

Genetic screening programme will increase as we have seen, the need for associated counselling. Here what is at issue is control of information. The issue of control of information is related to both informed consent and confidentiality. Informed consent is particularly problematic in genetic counselling. When the problem associated with perceptions of risk are taken into account. To a couple being counselled about a 1 in 4 chance of giving birth to a child suffering from a recessive genetic condition, the numerical probability may be less meaningful than the nature of the condition itself. Further, individuals' of risk can be affected by the way in which information is presented, and by counselees' attitudes to risk generally; whether they are 'risk neutral' 'risk averse' or 'risk-lovers'. The introduction of broad spectrum screening will magnify the complexity of the issues when a number of diseases are at issue at the same time.

There is also a question concerning the extent to which counselling can facilitate autonomous choice. It may be the case that the very existence of genetic screening and counselling encourages a culture which puts pressure on individuals to make particular

reproductive decisions. Counselling, in facilitating counselee decision-making, is thus distinguished from advice. Angus Clarke opines that the very structure of the counselling interview militates against the possibility of non-directiveness, and the fact that, for example, termination of an affected pregnancy is put on the table as an option may somehow suggest to clients that this is an option they ought to take.[5]

The applicability of principles of medical ethics to genetic counselling is further complicated by the fact that the 'client' in this context a normally a couple or family rather than an individual. This raises issues concerning the duty of confidentiality, which are relevant to both screening and counselling. The discovery of non-paternity is an example of a dilemma that might arise; for example, genetic testing of a child and his or her parents might reveal that the male partner is not the genetic father of the child. Does he have a right to this information, or does the mother have a right to confidentiality.

Genetic Therapy

The purpose of genetic screening is the early defection of a genetic disease or the early detection of its potential. The purpose of genetic counselling is to provide information with which individuals can make informed decisions. Therapy, by definition, is the treatment of an individual. Therefore, the term genetic therapy is used to mean any procedure that has as its purpose the prevention, reduction, or cure of a genetic disease. A good diagnosis and discussion of available therapy will at least eliminate the agony that parents go through while looking for answers to what is it and can it be treated?

5. Clarke, A., 'Is non-directive genetic counselling possible', *The Lancet*, 338, 1991, pp. 998-1001.

The prospect of gene therapy emerged in 1928 when Griffith transformed a species of bacteria from non-virulent to virulent. He brought about a permanent genetic change in these bacterial cells. Since then methods for gene exchanges have been intensely investigated. In 1980, the first attempt, using rec DNA[6], was made to correct beta thalassemia in two defective women.

The future of gene therapy and the cure of genetic diseases appear very promising. The possibility of genetic engineering, i.e., not to correct defects, but to add desirable characteristics, is not a distant hope. It is expected that within next few years the entire human genome will be defined. Genetic check up will, then, become part of a regular physical check up.

Ethical Implications

Optimists take the view that genetic knowledge will facilitate treatments for genetic diseases in the form of gene therapy. However, gene therapy has proved controversial, because it involves actual alteration of an individual at the genetic level. An analogy is frequently drawn, however, between gene therapy and organ transplants—receiving a foreign gene is analogous to receiving a foreign kidney—and thus it is argued that it should be regarded in the same way as other forms of medical treatment. While this argument may hold for somatic therapy,[7] germ-line therapy is more problematic. Many commentators see a moral difference between those two, and suggest that while somatic therapy is morally acceptable; germ-line therapy is

6. RecDNA means recombinant DNA, i.e., DNA molecules that have been assembled by splicing together fragments from the same or different species with the use of restriction enzymes.

7. Somatic gene therapy is the treatment of the body cells of an individual; the genetic alteration will not be passed on to descendents of that individual. Germ-Line therapy, however, will involve changes that directly affect subsequent generations. The 'directly' is an important qualification.

not.[8] The arguments for this position are first, that whereas the individual undergoing somatic therapy has the opportunity to consent or refuse therapy, those affected by germ-line therapy will be as yet unborn generations, who cannot express a choice in the matter. This raises the general philosophical and ethical question about whether we have obligation to future generations.

The issue is made more complicated by the fact that there is at present insufficient knowledge to justify taking risks that may be irrevocable. At the extreme the irrevocable intervention might be action taken to eliminate a particular gene from the gene pool altogether. Just as we have eliminated smallpox, we might decide to eradicate a particular gene thought undesirable, only to discover too late that it had some hidden advantage, thus losing valuable genetic diversity.

Third, there is an argument to the effect that individuals have a right to a genetic inheritance that has not been tampered with, though this is sometimes modified to express the view there is a right to a genetic inheritance that has not been tampered with except to remove pathology.[9] A further moral problem associated with germ-line therapy is connected with the means of carrying it out. Such therapy has either to be able to target the germ cells of an adult or be carried out at the embryonic stage. Its development will therefore involve research on human embryos and give rise to the ethical issues associated with embryo research.

On the other hand there are arguments to suggest that there is a positive obligation to develop germ-line therapy. First, there is the

8. Clothier, C. M., *Report of the Committee on the Ethics of gene therapy*, London, HMSO, 1992.
9. DE Watcher, M., *Experimental (Somatic) Gene Therapy : Ethical Concerns and Control*, Maastricht, Institute for Bioethics, 1993

general obligation to relieve suffering where we can in this case by seeking treatments for genetic disease. Second, there is the argument from scientific freedom, though this argument is largely connected with a view that classifies gene therapy as research. Third, there is an argument from reproductive autonomy. Germ-line therapy might be, for some couples, the only way they can achieve what Marcus Pembrey has called a 'winning combination' of genes.[10] There is an argument that if a woman can consent to somatic therapy on her child, why cannot she ensure that all her descendents should be free of a certain condition. For example, given the availability of gene therapy, if the mother had discovered prior to having children that she carried the gene for the disease from which she suffered, why should she not ensure that none of her children had to face it, rather than simply having somatic therapy on herself?

The potential use of the techniques of gene therapy for 'enhancement' raises further issues. The debate over the distinction between therapy and enhancement raises the question of what should be the goals of medicine. Worries are often expressed in media about the designer babies, but a beneficial use of enhancement could be a kind of preventive genetic vaccination to protect against certain diseases. Soren Holm has pointed out that this could be particularly effective in developing countries, but that a consideration of political and social realities suggests that the techniques will be used to increase rather than reducing existing inequalities.[11] This point makes clear the importance of examining the technologies within social context.

10. Pembrey, M., 'Embryo therapy : is there a clinical need?' in D.R. Bromhem, M. E. Dalton and J. Jackson (eds) *Ethics in Reproductive Medicine*. London, Springer-Verlag, 1992.
11. Holm, S., 'Genetic engineering and the north-south divide', in A. Dyson and J. Harris (eds.), *Ethics and Biotechnology*. London, Routledge, 1994.

Underlying many of the concerns about genetic screening, genetic counseling with the option of termination of affected foetus, and gene therapy, is an anxiety about eugenics, the attempt to improve the human gene pool. This anxiety arises because of historical precedents, which show the potential abuse. The question arises as to the extent to which it is possible to advocate steps to improve genetic public health without the associations of discredited genetic eugenic policies. It is sometimes said that the important factor here is not the attempt to improve genetic quality per se, but the political arrangements that are in place, that it is totalitarian use of these techniques that we have to fear, but not their use in democracy. While this point may be true to a large extent, it ignores the subtle influences of paradigm shifts in relation to both images of human beings and values.

Thus it has become clear that genetic information will allow us to choose to have healthy children, or at least to avoid the birth of unhealthy ones, to choose therapy for ourselves and possibly our descendents; to make informed choices as to whether or not we want to be tested. When new developments are presented in terms of increasing choice, it is difficult to argue against them, it seems almost churlish to do so. That is why it is important to look at the context in which choices are made. The context, in this case, depends on prevailing modes of thought. Developments in Genetics have brought with them new paradigms which themselves represent challenges for ethics, particularly bioethics. These new paradigms concern our understanding of human beings and of the concept of health.

The Legal and Ethical issues raised by the Human Genome Project

There are three levels of issues that Human Genome Project

raises: (1) individual/ family, (2) society, and (3) species. Almost all of our work on genetics to date has involved the individual/ family level, where questions of genetic screening and counselling have centre stage. Negligence in failing to offer or to properly perform these tests has resulted in lawsuits for wrongful birth and wrongful life, and standards for genetic screening and counselling have been set by professional organisations.

Issues at the second level implicate society more directly. In the HGP there are three societal issues: population-based genetic screening, resource allocation and commercialisation, and eugenics. More specifically: To what uses should the fruits of the project be put in screening groups of people, such as applicants for the military, government workers, immigrants, and others, what priority should the genome project have for state funding, and what role should patenting laws play. should we attempt to use the new genetics to improve our citizens, either by trying to eliminate specific genetic diseases or by enhancing desirable traits?

Issues at third level are somewhat more speculative and involve how a genetic view of ourselves could change the way we think about ourselves. This level raises recurrent philosophical questions involving determinism, reductionism, normalcy, and the meaning of health and disease.

This brief cataloguing of the major issues raised on each level suggests that there probably are no unique issues raised by the HGP. On the other hand, this project raises all of the issues in a much more focused manner and the fact that all of these issues are implicated in the genome project may itself make the project societally unique.

Individual/ Family Issues

Although we have not solved any of the major issues raised by past genetic screening and counselling cases, we have been able to identify the major factors to be considered before initiating a screening programme: (1) the frequency and severity of the condition, (2) the availability of treatment of documented efficacy, (3) the extent to which detection by screening improves the outcome, (4) the validity and safety of the screening test, (5) the adequacy of resources to ensure effective screening and counselling follow-up,(6) the cost of the program, and (7) the acceptance of the screening program by the community including both physicians and the public.

This list primarily relates to the scientific validity and a cost / benefit analysis of the testing procedure. In addition, two major legal issues are implicit in all genetic screening programs: autonomy and confidentiality. Autonomy requires that all screening programs be voluntary, and that consent to them is sought only after full information concerning the implications of a positive finding is disclosed and understood. Confidentiality requires that the finding not be disclosed to anyone else without the individual's consent. While not a genetic disease, HIV infection has provided us with an opportunity to see how widespread discrimination against individuals with a particular condition demands that testing be voluntary and that results be kept confidential to protect the rights of individuals.

Provided that testing remains voluntary, and that the results are only disclosed with the individual's permission, genetic testing based on one's genome raises questions only of degree rather than kind. Perhaps even more important, we may find that certain genes predispose a person to specific illness, such as breast cancer or Alzheimer disease. This information may be very troubling to

individuals, but it will be of great interest to health insurance companies and employers.

In the employment setting, for example, it has already been suggested that five principles should guide legislators, regulators, and professional groups in setting guidelines for medical screening: (1) medical inquiries of employees should be limited to job related information, (2) only tests that are safe and of proven efficacy should be used, (3) applicants and employees should be informed of all medical tests in advance, given the results, and told when any employment decision will be based on test results; (4) intracompany and extracompany disclosure of medical records must be controlled and confidentiality assured; and (5) comprehensive, consistent, and predictable handicap discrimination legislation should be enacted. These worthy principles should be supplemented with three others directed at employers: (1) ethical issues involving screening should be fully explored before a screening program commences;(2) screening should only be done on an individual with the individual's informed consent, and (3) counselling should be available both before and after screening, and the resources for any reasonable intervention that can benefit the individuals screened should be in place and available to him or her before screening is offered.

We have so far managed to develop genetic screening and counselling as tools that we have permitted individuals and families to use or not use as they see fit. This has followed the medical model of benefit doctor-patient relationship: a model mutuality in which decisions are made for the benefit of the patient. This model has served us well to date in expanding the reproductive options of individuals. Level two concerns move us away from concern with the individual to concern with society itself.

Societal Issues

Social issues involved in the genome cluster in three areas: population-based screening, resources allocation and commercialisation, and eugenics.

Population-based screening can be aimed at the attempted elimination of genetic condition, at simply identifying the incidence of a genetic condition in a population, or at identifying the presence of a genetic condition in an applicant for a particular benefit (such as employment, insurance, and immigration). As previously discussed, autonomy and confidentiality are the major legal issues involved, and this type of screening becomes problematic primarily when it is mandatory and the results are made known to others without consent. The other two areas are more uniquely social.

The issue of resources allocation itself has its own three aspects. The first is the obvious one what percentage of nation's research budget should be devoted to the Human Genome Project?

The second aspect involves making the fruits of the genome project available to all those who want them. This involves at least two questions. The first is the issue of commercialism, and who 'owns' and can patent the products that are produced by the genome project. Should the fact that much of this research is funded by the government mean that its fruits should be in the public domain. Or should individual companies and scientists be able to patent or copyright maps and sequences of specific areas of the human Genome in order to encourage them to become involved in mapping research? Patent issues have proven the most controversial at the outset of the project, and an international agreement on patenting (or not patenting) genes and gene fragments (cDNA) may be a prerequisite to effective

international cooperation. The third issue is that should the genetic tests and their follow-up procedures should have universal access or should they only be available to those who can pay for them privately? This, of course, is also not a question unique to the genome project, but one that society must confront with every new medical technology.

The third aspect of the resource allocation issue is probably the most intrinsically interesting. It involves determining the balance of resource priorities between how much we should spend on identifying and treating genetic diseases, as opposed to how much we should spend on other conditions that cause disease, such as poverty, drug and alcohol addition, lack of housing, poor education, and lack of access to reasonable medical care. In a country like the India, it is ethical or rational to develop medical technologies that large segments of the population would not have access today, if they were available, or to develop technologies that even if universally available, would only be useful to a few individuals?

What is the social impact of putting the spotlight on an endeavour like the Human Genome Project? Could the fact that we are vigorously pursuing this project lead us to downplay environmental pollution, worksite hazards, and other major social problems that cause disease based on the hope that we will someday find a 'genetic fix' to permit humans to 'cape' with these unhealthy conditions? It has been unpersuasively and bizarrely suggested, for example, that the fruits of the HGP may help solve society's homelessness problem on the basis that many of the homeless are mentally ill, and their condition may be genetically determined and genetically treatable. Finely, what role does or should international economic competition play in deciding how much federal funding should go to the genome project?

The third societal issue, and the most important one, is the issue of eugenics. This issue is perhaps the most difficult to address because of the highly emotional reaction many individuals have to even mentioning the racist genocide of the Nazis, which was based on a eugenic program founded on a theory of racial hygiene: Although repugnant, the Nazi experience and legacy demands careful study to determine what led to it, why scientists and physicians supported it and collaborated on developing its theory and making possible its execution, and how it was implemented by a totalitarian state. In this regard our own natural experience with racism, sterilisation, and immigration quotes will have to be recommended. In so doing, we are likely to rediscover the powerful role of economics in driving our views of evolution and who should propagate.

The U.S. Supreme Court, for example, wrote in 1927, with clear reference to World War I, that eugenics by involuntary sterilisation of mentally retarded was constituently acceptable based on utilitarianism Again in 1988 the U.S. Congress's office of Technology Assessment in discussing the 'social and Ethical Considerations' raised by the HGP, developed a similar theme:

Human mating that proceeds without the use of genetic data about the risk of transmitting diseases will produce greater mortality and medical costs than it carries of potentially deleterious genes are altered to their status and encouraged to mate with noncarriers or to use artificial insemination or other reproductive strategies.

The likely primary reproductive strategy, mentioned only in passing in the report, will be genetic screening of human embryos, already technically feasible, but no nearby to the extent possible once the genome is understood. Such screening need not be

governmentally-imposed, people will want it, even insist on it as their right. New technologies for identifying traits and altering genes make it possible for eugenic goals to achieve through technological as opposed to social control. Huxley's Brave New World, rather than George Orwell's 1984, seems to be in our future.

It is necessary to decide whether or not to use genetics to improve the species, and to articulate the philosophical and moral concerns that a change in the direction of genetics from prevention and treatment to enhancement and improvement would entail. So far most writers have insisted that it is at least premature to follow the example of Moreau and try to improve upon the species, either by enhancing certain genetic characteristics, such as height, or by altering sex cells so that characteristics modified in an individual can be to future generations.

Species Issues

Species issues relate to the fact that powerful new technologies do not just change what human beings can do, they change the way we think, especially about ourselves. In this respect, maps may become particularly powerful thought transformers. Maps model reality to help us understand it.

Columbus changed the shape of the world's map forever—from flat chart to a spherical globe. Monsters could no longer either prowl or guard the edge of the world because there was no edge of the world. Copernicus and Vesalius published their great works in the same year, 1543.

Vesalius' 'maps' of the human anatomy may have been even more important metaphors for us, for the dissecting the human body,

Vesalius insisted that human beings could nonetheless only be understood as whole beings: human beings rather than as parts that can be fitted together to manufacture life forms. For Vesalius, who shows twenty-one of seventy-three drawings in Fabrica as full-figured humans, and ten of twelve drawings in his epitome as full-figured humans, the emphasis is firmly on the person, even though the treaties is concerned with the person's body parts. This is in stark contrast to the bar graph illustrations used by contemporary geneticists in mapping the genome, which are totally devoid of human reference, almost life without life. A similar lifeless reductionist phenomena can be seen in the 'maps' of areas of the human brain, which are said to correspond to various human emotions and the ability to think and to conceptualise. Does this reconceptualization of the human via a new map encourage us to travel into areas that could lead us to simultaneously misunderstood and demean what it is to be human?

What new human perspectives, or what new perspectives on humans, will a sequential map of the 3 billion base pairs of the human genome bring? The most obvious is that breaking 'human beings' down into 6 billion 'parts' is the ultimate in reductionism. James Watson himself has used such reductionist language in promoting the HGP. In his word it is understanding ourselves at the molecular level. Watson continues: 'How can we not do it? We used to think our fate is in our stars. Now we know, in large measure, our fate is in our genes'. Seeing our fate in our genes, of course, resonates with level two concerns: if genes determine our fate, then we can alter our fate by altering our genes. May be we really will come to believe the unlikely prospect that we can look forward to the day that mental illness, and therefore at least some homelessness, can be prevented by genetic manipulation. Such a view suggest most of the species concerns.

The first is the consequence of viewing humans as an assemblage of molecules, arranged in a certain way. The almost inevitable tendency in such a view is that expressed in Brave New World. People could view themselves and each other as products that can be manufactured, and thus subject to quality control measures. People could be 'made to measure', both literally and figuratively. If people are so seen, we might not only try to manipulate them as embryos and foetuses, but we might also see the resulting children as products themselves. This raises the current stakes in the debates about frozen embryos and surrogate mothers to a new height: if children are seen as products, the purchase and sale of resulting children themselves, not only embryos, may be seen as reasonable.

The second concern is that, to the extent that genes are seen as more important than environment our actions may be viewed as genetically determined, rather than as a result of free will. We have already witnessed an early example with this type of reasoning in the use of the 'XYY defense'. Those possessing the 47, XYY karyotype was thought to be more prone to commit crime. Individuals accused of crime who also had an extra Y chromosome consequently argued that their genetic composition predisposed them to crime and therefore they should not be held criminally reasponsable for their actions. This defense was generally rejected. Of course, since it is impossible to remove the extra Y chromosome from any cell, let alone every cell, in one's body, a cure is not possible.

Such genetic predispositions are likely to be used in education, and perhaps job placement and military assignments. For example, if intelligence in mathematics is found to be genetic, should schools use this information to track, grade, and promote the genetically gifted in the math classes?

Finally, we know that most diseases and abnormalities are social constructs, not facts of nature. Myopia, for example, is well accepted, whereas obesity is not. We won't discover a 'normal' or 'standard' human genome, but we may invent one. If we do not, what variation will society view as permissible before an individual's genome is labelled substandard or abnormal? And what impact will such a construct of genetic normalcy have on society and on substandard individuals? For example, what variation in a foetus should prompt a couple to opt for abortion, or a genetic counsellor to suggest abortion? What variation should prompt a counsellor to suggest sterilisation? What interventions will society deem acceptable in an individual's life based on his or her genetic composition? Should health care insurance companies, for example, be able to disclaim financial responsibility for the medical needs of a child whose parents knew prior to conception or birth that the child would be born with a serious abnormal genome? Should employers be able to screen out workers on the basis of their genomes? These and many other similar issues exist today based on screening for single genes. But the magnitude of the screening possibilities that may result from analysis of the map of the human genome will almost inevitably change the way we think about ourselves and what it means to be human.

By now it has become clear that there is tension between scientific advancement and ethical concerns. English literature provides us with a rich backdrop from which to begin our consideration, but actual examples of successful regulatory intervention into either scientific research or technological application are much less plentiful. Nor have scientists and policymakers worked together well in the past. As C.P. Snow has noted: 'Non-scientists tend to think of scientists as

brash and bostful.[12] Non-scientists think that scientists underestimate the danger of their work and vastly overestimate its importance. Scientists, on the other hand, tend to think of social policy and ethics as fields that leg behind science and cannot keep up with scientific progress and advance. It is almost as if they believe that morality is a field of knowledge "in the charge of unidentified, but presumably rather incompetent experts."[13] Experts in both fields have little experience with each other, and they generally meet only in courtrooms. Scientists then often revert to the old slogan, "What's good for General Motors is good for the country", or, more precisely, as James Watson has put it. "Science is good for society".[14] The challenge is to get beyond the literacy archetypes, the stereotypes, and the clitches, and to work together to develop a coherent set of goals against which we can judge scientific priorities and actions. Once these goals are agreed on in an open and public forum, it will be easier to devise methods to attempt to accomplish them. A few such methods merit further discussion because they are the ones most likely to be used: moratoriums and bans, regulatory agencies, advisory groups, and private lawsuits.

Moratoriums and Bans

Science has had almost no experience with moratoriums, but one of the few that has actually been implemented was in the area of genetic research, specifically recombinant DNA (rDNA) research. It occurred in 1974, when, following approximately three years of discussion, a group of prominent genetic researchers called for a voluntary international moratorium on certain types of recombinant DNA research. The moratorium was a rare, perhaps unique event in

12. Snow, C. P. *The Two Culture*. New York : Cambridge U. Press, 1964, p. 5.
13. Roszak, T., *The Making of a Counter-culture*. Garden City, NY : Double-day, 1969, p.273.
14. Quoted in *Science*, 199: 33; 1978.

the history of basic science research. The agreement was honoured internationally from July 1974 to Feb 1975. Then an international meeting of rDNA researchers was convened at Asilomar, California, to consider the future of the moratorium. In that meeting it was agreed upon that most of the work on the construction of recombinant DNA molecules should proceed, but that adequate biological and physical containment measures should be taken to prevent the creation and escape of potentially dangerous newly created organisms.

Many fear that the genome project posed great potential hazards that could open the door to Nazi-like atrocities. To attempt to avoid such results, it is suggested that the conferees agree on a moratorium on genetic manipulation of germ line cells, a ban on gene transfer experiments in early embryos.

It is sometimes apprehended that scientists at their research may come up with a disease that cannot be cured—even a monster. Is this the answer to Dr. Frankenstein's dream? Recombinant DNA research is not, of course, the answer to Frankenstein's dream of animating dead tissue; it is more the answer to Moreau's dream of combining various species into a new, unique creature. Nonetheless, as Lewis Thomas observed, having man don the mantle of creator of life raises the fundamental questions that the Frankenstein myth exemplifies:

The recombinant DNA line of research is upsetting . . because it is disturbing in a fundamental way, to face the fact that the genetic machinery in control of the plant's life can be fooled around with so easily. We do not like the idea that anything so fixed and stable as a species line can be changed. The notion that genes can be taken out of one genome and insisted in another is unnerving.

The Frankenstein myth resonated because of rDNA's ability to create new life forms that the creator could not control, and also because of the public's concern that scientists were doing this work for their own enjoyment rather than society's betterment. As Mayor Vellucci put it: 'I don't think these scientists are thinking about mankind at all. I think that they are getting the thrills and excitement and the passion to dig in and keep digging to see what hell they can do? The Mayor here encompasses not only the driving force behind Frankenstein, but that behind Jekyll and Moreau as well. The President's Commission on Bioethics summarized the 'Frankenstein factor' in rDNA research as follows: "The fear was that for researchers creating a new life form—even a monster— would be an assault on traditional values."

There are certain specific areas over which regularly authorities should have controls such as (1) cloning torn-producing genes, (2) introducing drug resistence into an organism, and (3) deliberately releasing genetically engineered organisms into the environment

We should have prior review of all proposed research on genetic modification of human beings.

When it is appropriate to begin human experiments with gene therapy remains controversial. As early as 1980 it was suggested that human trials should not begin until three conditions are met in animal trials: (1) the new gene should be put into target cells and remain their; (2) the new gene should be regulated appropriately; and (3) the presence of the new gene should not harm the cell.

In the early 1980s different group heavily lobbied to transform the different regulatory guidelines into voluntary 'laboratory standards',

but it was refused in many countries. Most scientists would prefer to police themselves and not have non-scientists involved in monitoring or regulating their work. On the other hand, they are often horrified at the notion that they might be held personally responsible for the harm that their research causes others.

The fact is that in most areas, even those heavily regulated, the professionals themselves will have much, if not everything, to say about the standards applied to their work. Under almost any standards, Frankenstein and Moreau would be guilty of gross negligence and cruelty in abandoning their creations and inflicting suffering upon them. Jekyll might properly argue that he was experimenting on himself, but, of course, he would still be criminally responsible for the murders committed by Hyde.

Further lawsuits are likely to be of three kinds. The first will involve the accidental or purposeful release of a dangerous organism into the environment. This is the type of harm Mayor Velluci worried about, and which could give rise to traditional tort suits alleging nuisance, trespass, butlery, and/ or negligent failure to contain the organism. The second kind suit will involve those who apply the new knowledge gained by the genome project to the clinical setting: cases involving wrongful birth (for failure to counsel about existing technology that results in a couple having a child they would not otherwise have had, and who is genetically handicapped) and cases involving wrongful life (suits by a child alleging that it would have been better off not having been born, and would not have been born if the physician had properly counselled its parents or properly performed agreed to screening tests). The third type of lawsuit will be one for the breach of confidentiality leading to a loss on the basis of discrimination. For example, a physician may be sued for improperly disclosing a genetic

diagnosis to an employer who then fires the employee on the basis of the genetic information. As can be seen from this listing, tort suits will be most useful after genetic screening tests have been developed and will likely have little impact on their ultimate development itself.

Where do we go from here?

It seems reasonable to conclude from the various methods that have been employed to review genetic research and the clinical applications of that research that individual/ family concerns (level one) will be dealt with by a combination of oversight committees, regulation, self-regulation, and private lawsuits. Societal concerns (level two) are not readily approached by private lawsuits, and so they will likely require legislative mandated regulation, most likely based on suggestions by advisory committees with broad public input. Species concerns (level three) are not subject to legal regulation at all, except insofar as specific practices, such as the purchase and sale of 'high grade embryos' can be outlawed altogether. But this may be the area that has the most long term impact on us, and the one about which we therefore need most careful and creative thinking.

It is on the species level concerns that the cautionary tales with which this chapter opened focus. Mary Shelley's tale, for example, teaches us a lesson that we find hard to deal with seriously: as difficult as it is to create a monster, it is even more difficult to control it or to restore order after the creation has spawned chaos. In seeking to control our world, we may in fact lessen our control over it. Robert Oppenheimer unwillingly made this point in reference to the Manhatten Project to a Congressional Committee in 1945. He was testifying on the role of science in the development of the atomic bomb:

When you come right down to do it, the reason that we did

this job is because it was an organic necessity. If you are a scientist, you believe that it is good to find out how the world works; that it is good to find what the realities are; that it is good to turn over to mankind at large the greatest possible power to control the world.

The striking thing in Oppenhemier's testimony is his emphasis on the notion that science is unstoppable, with the simultaneous insistence that its goal is control over nature—irreconcilable concepts that seem equally at the heart of the Human Genome Project. Of course, with the atomic bomb, control quickly became illusory. The bomb, which carries with it the promise of the total annihilation of mankind has made the nation state ultimately unstable and put it at the mercy of every other nation with the bomb. Necessity has forced all nuclear powers to move, however slowly, towards a transitional community.

In view of the way scientists have thought about their pursuits and projects in past, it is unformative to review the goals of the HGP set forth above with the list of legal, ethical and social policy issues raised by the project. There is almost no overlap. Scientists are working on an interesting scientific question to gain new knowledge and insight into what genes do, and what we can learn about man's origins and relationship to other species. If we take the scientists at face value, they have given no more thought to the potential social applications of genome mapping and sequencing than Frankenstein had given to the consequences of creating his monster, or than Moreau had given to the consequences of his experiments in modifying life forms. Our own 'brave new world' will not be ruled by scientists, any more than scientists decided whether or not to use the atomic bomb or whether to send a man to the moon. Social policy will ultimately be set by elected politicians and their advisers. It is already past time to begin

to involve the electorate in a national debate about the appropriate uses (and misuses) of the products of the HGP.

In this discussion, the focus should be on two central questions: what does it mean to be human, and how can human life on this planet be enhanced? To even begin to address these issues in the genome context, the public and policy makers need to understand the HGP, and the cartographers of the human genome need to be able to recognize and deal with the real monsters lurking outside their laboratories.

With both real and psychological walls crumbling around the world, the time may be at hand for meaningful international dialogue and cooperation on the HGP. It may also be possible, although perhaps this is wishful thinking, to engage the world in a manner that strives to enhance the dignity of all human beings. Playwright, former political prisoner, and former president of Czechoslovakia, Vaclav Havel expressed it well in a 1984 speech on 'Politics and Conscience':

> To me personally the smokestack soiling the haven is ... the symbol of an age which seeks to transcend the boundries of the natural world and its norms and to make the matter merely private concern, a matter of subjective preference and private feeling. The process of anonymisation and depersonlization of power, and its reduction to a mere technology of rule and manipulation, has a thousand masks .... States grow ever more machine-like, men are transformed into casts of extras, as voters, producers, consumers, patients, tourists or soldiers...
>
> The question ... is ... whether we shall, by whatever means, succeed in rehabilitating the personal experience of human beings as the measure of things, placing morality above politics and responsibility above our desires, in making human community meaningful, in

returning content to human speaking, in reconstituting, as the focus of all social activity, the autonomous, integral and dignified human "I", responsible for himself because he is bound to something higher.... If we can defend our humanity, then, perhaps, there is a hope of sorts that we shall also find some more meaningful ways of balancing our natural claims to shared economic control, to dignified social status. ...As long, however, as our humanity remains defenseless, we will not be saved by any better economic functioning, just as no filter on a factory smokestack will prevent general dehumanization. To what purpose a system functions is, after all, more important than how it does so; might it not function quite smoothly, after all, in the service of total destruction?"[15]

Havel's image of the smokestack is striking: the inanimate destroyer has replaced the animate monster in industrial society. Governments grow more machine-like and, in consequence, treat their citizens as interchangeable parts of that machine. The machine-men become alienated even from themselves; and technology cannot save them from artificiality. Only their natural humanness and their ability to distinguish good from evil can save humanity.

Havel obviously did not have the HGP in mind when he wrote his 1984 speech. Nonetheless, his words aptly summarize the challenge we face and he properly insists that we all take personal responsibility for our own actions and the future of our world: "Without a global revolution in the sphere of human consciousness, nothing will change for the better in the sphere of our being".

In 1992, after more than two years as president of Czechoslovakia, Havel reaffirmed his belief in the ability of

15. Havel, V., *Living in Truth*, London: Faber & Faber, 1989, pp. 136, 138, 144 (J. Vladislavrd, tr. 1989)

postmodernist politicians to rediscover the 'soul, individual spirituality, (and) first-hand personal insight into things" and to have "the courage to be himself and go the way his conscience points". Although Havel was speaking specially about the need to fill the void left the death of worldwide communication with a new humanism, his words seem directly applicable to the HGP.

In Havel's vision, and in the visions of the authors we have reviewed, the modern era has been dominated by the culminating belief, expressed in different forms; that the world — and Being as such — is a wholly knowable system governed by a finite number of universal laws that man can grasp and rationally direct for his own benefit. This view, both Havel and history suggest, is well wide the mark, and very survival of our species depends on the adoption of a paradigm based not on further collection of information but on such forces as a natural, unique and unrepeatable experience of the world, an elementary sense of justice, the ability to see things as others do, a sense of transcendental responsibility, archetypal wisdom, good taste, courage, compassion and faith in the importance of particular measures that do not aspire to be a universal key to salvation.

Can new science learn to take its social responsibilities seriously? Can we use our species consequences to help us confront not only the promise but also the perils of the new is still seen as better, and where the future is still seen as limitless.

Public Perception of biotechnology

While biotechnology prevents enormous potential for healthcare and the production, processing, and quality of foods by genetic engineering of crops, fertilizers, pesticides, vaccines and various animal and fish species, the implications of these new

biotechnological process of go well beyond the technical benefits offered. The implementation of the new techniques will be dependent upon their acceptance by consumers. Public perception of biotechnology will have a major influence on the rate and direction of developments and there is growing concern about the genetically modified products. Associated with genetic manipulation are diverse questions of safety, ethics and welfare.

Public debate is essential for new biotechnology to grow up and, undoubtedly for the foreseeable future, biotechnology will be under scrutiny. Public understanding of these new technologies could well hasten public acceptance. However, the low level of scientific literacy, especially in the developing countries, does mean that most people will not be able to draw informed conclusions about this important biotechnology issue. Consequently, it is conceivable, and indeed occurring, that a small number of activities can argue the case against genetic engineering in such emotive and ill-reasoned ways that the public and the politicians are misled. The biotechnology community needs to sit up and take notice of and, work with, the public. Ultimately the benefits of biotechnology will speak for themselves.

The applications of human genetic research

Several thousand genetic disorders of humans would appear to result from a mutation in single genes, while many others have more complex genetic explanations and even possible interactions with environmental factors. Results from the HGP are now considered to offer an increased understanding of these fundamental genetic malfunctions and to give in many cases, some hope for alleviation and perhaps cure of the defect. However, paralleling the scientific mechanisms have come many years of public concern.

Areas of Public Concern on HGP

- ✓ Confidentially of testing and screening results.
- ✓ Scope of genetic testing and screening.
- ✓ Discrimination and stigmatisation.
- ✓ Commercial exploitation of human genome data.
- ✓ Eugenic pressures.
- ✓ Effects of germ-line gene therapies on later generations

The major nations now committed to genome projects are also supporting research into the many ethical, legal and social issues that these studies are uncovering. Numerous committees now foster public debate and understanding of these highly complex issues. Scientific discoveries could on the one hand, bring much relief to millions of sufferers from genetic diseases but on the other they could give rise to questions with mind-blending implications as to the way forward for the human race.

The biotechnology community must aim to inform, not indoctrinate, the public. The consumers and patients of biotechnology products must be given clear and unequivocal information. A recent EV public perception of biotechnology meeting ended with the following message to biotechnology companies. 'Provide the information and listen to the public'.

The progress of biological sciences has been viewed by many as more than spectacular in the dawn of this new millennium. The dominant area in biology continues to be the fundamental understanding of the structure and function cell and gene more at the

molecular level. The last few years have seen a dramatic acceleration of the rate of nucleotide sequencing of the near completion of Human Genome Project and cloning for human welfare. Certainly, the demand has been to demonstrate through excellence and originality the quality of scientific research and its value to society. A periodic look back of what has been happening in field of cytology and genetics and the benefit offered to mankind can be useful in deciding the direction of future research.
