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5 Practical Ethics Issues in Gene Therapy and Genetic Testing

5.1 Introduction

The development of biotechnologies, as well as the emergence of genetic engineering and other innovations, promises great benefits, but it could also have a negative impact on the development of the human species and nature. Genetics is an area of research with an impressive history of evolution and significant practical advances that influence human experience. In 1953, Crick and Watson identified the structure of DNA. By the early 1970s, scientists succeeded in isolating genetic material from one species and attaching it to the genetic material of other species, thereby bringing about genetic engineering. In the same decade, the foundation for a program in gene therapy was established via the discovered possibility of identifying the genetic background of different pathologies.

During its development, this field of research gathered supporters and opponents. Supporters point to successful achievements, such as solving the food problem, creating food with a higher medical value, potential development of food vaccines, treatment of genetic mutations, prevention of diseases in children in the prenatal period, extending the human life span, and prevention of diseases using genetic tests. Opponents highlight the risks of genetic defects, limited genetic diversity, increasing inequalities, and emergence of eugenics. This article analyzes some ethical issues that arise in practice from the use of genetic testing, gene therapy, and germ-line therapy, topics that are increasingly discussed in European context.

5.2 Genetic testing

By the early 1980s, scientists envisioned the possibility of mapping all of the human genes, thereby laying the foundation for the Human Genome Project. Genetic testing can be used to precisely identify a disease or to find the faulty gene that increases the probability of a particular disease's onset in a person. Nowadays, it is possible to predict the development of a large range of disorders, such as Huntington's chorea, Alzheimer's disease, muscular dystrophy, hemophilia, multiple sclerosis, and different types of cancer. Genetic testing is used to detect carriers of faulty genes who may show no signs of the disease but can pass it on to their children. For instance, if both parents are carriers of cystic fibrosis, then it passes almost with certainty to their child. Genetic testing is used to identify a fetus with certain

diseases such as Down syndrome, as well as to screen newborns for the same disease. For instance, newborn screening is widely practiced in the case of the hereditary metabolic disorder phenylketonuria (PKU). If the blood test is positive for PKU, a special diet is used to avoid the buildup of an enzyme that causes brain damage (Buchanan et al. 2000, 13).

Despite its therapeutic and preventive advantages, application of genetic testing raises ethical issues in practice, mostly related to technological limitations of genetic testing, ownership of genetic information, and potential for discrimination. The tests cannot always identify the mutation, and even if they did, a faulty gene is not necessarily indicative of future symptoms, such as the severity of the condition or age of onset. Unawareness about the limits of genetic testing can set false expectations and lead to dissatisfaction with medical service or to unmanaged psychological distress.

But widespread application of this new technology faces many social issues. Who should be tested? Why? How much does it cost and who should pay for it? Currently, most doctors accept that only those with a familial risk should be tested for a specific disease. Because this technology is very expensive, it prohibits people from having unnecessary screening and limits access for low-income and marginalized groups.

Further, should parents have the right to choose the traits of their children beyond therapeutic goals? Would it be right for a community to create designer babies because they decide that it is their right to choose what they want, and what would be best for their child? One way to approach this issue is to claim that prenatal genetic screening is morally permissible as long as the risks to the mother and fetus do not outweigh the benefits of the information gained by the test. This kind of testing should be allowed if it is undertaken for the purpose of early intervention.

Another issue is devising effective means of protecting privacy (confidentiality) and developing criteria for a voluntary screening program. Among these criteria are the following: a) the program should involve tests that are highly sensitive and specific and that have high positive predictive value; b) there must be available therapy or other interventions that are more useful if applied before symptomatic disease appears or the knowledge gained must be otherwise valuable to the individual being screened; c) the program can be justified economically in comparison to other ways in which health funds could be used; d) the program must be based on laboratory work whose high quality can be assured; and e) the program must involve adequate counseling before the screening to ensure informed consent as well as adequate counseling about the meaning of the results afterward (Brody 1998, 90-91). According to the principle of confidentiality, access to patient outcomes by a third party is prohibited without the express consent of the patient.

Ownership of genetic information is extremely difficult to determine. On the one hand, information belongs to whoever underwent the test, but on the other hand, genetic information is about family and consequently is relevant beyond the tested individual. A physician thus faces the moral dilemma of how to balance individual

privacy and the responsibility of preventing harm to other family members. The decision to inform family members vary according to what moral theory is used (Fulda and Lykens 2006). According to the utilitarian theory, the decision to communicate genetic test results to a third person should be based on a cost–benefit analysis. The benefits for the family must prevail over the benefits of the tested person because the moral principle of the utilitarian theory is to ensure maximum happiness. Not only the family, but also other members of the society, will be able to minimize the risk of developing a disease in the future. Thus, an important task is the assessment of risks and benefits of disclosure according to the complexity of the situation. On the other hand, the most important value of libertarians is moral autonomy: informed decision-making is a vital right of each person. Individuals also have the right to confidentiality, or to choose whether they want to inform their family members. Tested subjects have the right to keep the medical results secret because, over time, they can develop a fear of being discriminated against, if relatives find out that in the future they will develop a certain disease. From a duty-based perspective, we have to respect the command of beneficence for society (or family) and to disclose the result of the test, but at the same time, a physician could break the duty of nonmaleficence for the tested person. Thus, for each case, we have to take into account a risk–benefit ratio for the tested person.

Genetic information has a high potential for discriminating usage, such as discrimination in insurance, discrimination in employment, racial discrimination, and determination of paternity. Knowing that the purpose of a company is making profit, it is plausible to assume that companies that have access to genetic information would be incentivized to prefer healthy employees rather than potentially ill employees. Genetic testing could be used in an inappropriate manner for determining paternity without the informed consent of all parties involved or solely for deciding whether to terminate pregnancy because of gender. Take, for instance, the chilling discrepancy in sex ratios in China, South Korea, and parts of India, where boys outnumber girls by up to 30% (Eberstadt 2002). For example, in 2001, in China were missing 34–41 million females, in India 27–39 millions, and in South Korea 0.2–0.3 million females (Hesketh 2006).

Thus, genetic screening has many benefits, but it also has downsides when we consider its application in practice. To list just a few benefits: early detection of any type of disease or disorder is usually less expensive to treat; genetic screening helps people know whether a heritable disease runs in their family; paternity testing is helpful for single mothers. To list the highlighted downsides: health coverage is limited because of high costs; ensuring confidentiality is difficult; and genetic screening could increase abortion rates.

We also could add that voluntary choice should be the basis for genetic testing. For example, The World Medical Association Declaration on the Human Genome Project declares that “One should respect the will of persons screened and their right to decide about their participation and about the use of the information obtained”.

Thus, to ensure the genetic health of the population, the European Commission has established recommendations on genetic testing to explore the conditions for maximizing benefits and minimizing harms from the increasing capability to use genetic testing. Here are the recommendations that address the ethical issues discussed so far:

R.9 – In the context of healthcare, genetic testing be accompanied by the provision of key information and, where appropriate, by the offer of individualised counselling and medical advice (in the case of highly predictive genetic tests for serious disorders, the offer of specific counselling should be mandatory, and patients should be strongly encouraged to take advantage of it).

R.10 – Genetic data of importance in a clinical and/or family context should receive the same level of protection as other comparably sensitive medical data; b. the relevance for other family members has to be addressed;

R.11 – Data derived from genetic sources should not be used in ways that disadvantage or discriminate unfairly against individuals, families or groups in either clinical or non-clinical contexts, including employment, insurance, access to social integration, and opportunities for general well-being;

C – Timely access to genetic testing should be based on need and appropriately resourced with no discrimination based on gender, ethnic origin, social or economic status. (United Nations Educational, Scientific and Cultural Organization [UNESCO] 2004)

Accordingly, the European Commission suggests that the responsibility of dissemination of genetic test results should be assigned to the family, highlighting the necessity of detailed discussion both prior to testing and even after it, as well as recommending the avoidance of discriminatory use of genetic data. However, further oversight should be put in place to see how these recommendations are respected in practice.

One output of the human genome project is the accurate identification of individuals who will develop various diseases requiring very expensive treatment. Thus, we must remain vigilant to detect any potential patterns of discrimination against those who are genetically predisposed to various illnesses. The goal of health coverage is to spread risks among large populations regardless of genetic heritage. Similarly, equal opportunity for employment mandates that genetic heritage should not become the basis for employment selection. Even properly validated genetic testing should never be mandated for insurance or employment proposes, and those who are voluntarily tested should have total control over who receives the results. Thus, according to the insurance principle adopted by the Council of Europe, "insurers should not have the right to require genetic testing or to enquire about results of previously performed tests, as a precondition for the conclusion or modification of an insurance contract" (Council of Europe 1992). It is increasingly clear that the principles of autonomy, confidentiality, and nondiscrimination are put to the task of new applications and interpretations in the context of genetic testing,

release of genetic information, and use of genetic information in employment and insurance decisions.

5.3 Gene therapy

Gene therapy aims to treat incurable illnesses – resulting from defective genes – by the insertion of healthy genes into an individual's affected cells and tissues. The technique is tested on viruses because viruses are good at injecting their DNA payload into human cells and reproducing it.

In the initial stages of treating genetic disorders, scientists were confident that gene therapy would curb a vast amount of human suffering due to painful, and sometimes fatal, genetic diseases. But since 1980, when the first experiment using these techniques was conducted, the initial enthusiasm has become tempered, mostly because of increasing side effects. Important media outlets such as the *New York Times* wrote about these cases: "The Arizona patient, Jesse Gelsinger, 18, died four days after doctors at the University of Pennsylvania injected a corrective gene, encased in a deactivated adenovirus, into the hepatic artery, which leads to the liver (...) Leading scientists and government officials said Gelsinger was the only person known to have died as a direct result of receiving gene therapy. Other patients receiving gene therapy have died, but doctors treating them in the trials say their diseases, not the therapy, killed them. What remains unknown is how many patients experienced side effects directly related to gene therapy and what they were" (Stolberg 1999). The lack of expected results leads to the acknowledgment that much more basic research is required, but lack of success did not burn out the optimism for gene therapy.

Genetic engineering, which sometimes is called genetic modification, is the process of altering the DNA in an organism's genome. Usually genetic engineering is used by scientists to enhance or modify the characteristics of an individual organism. Genetically engineered bacteria and other microorganisms are currently used to produce human insulin, human growth hormone, a protein used in blood clotting, and other pharmaceuticals, and this number will only increase in the future.

Enhancing cognitive capacities beyond human limits is still a promise for the future, but the basic argument in favor of doing it is so that it could make life better by improving intelligence, beauty, endurance, certain personality characteristics, and behavioral tendencies. If these traits were found to have a genetic basis, we could enhance people by intervening in the genetic makeup. However, such a technique could be dangerous in discriminating against persons with disabilities. If we lack a robust system of distributive justice for bioenhancement services, then discrimination for those without access to these services is expected (Beauchamp 2013). People with disabilities are often discriminated against by having fewer opportunities than others. By removing genetic disorders, and the resulting impairment, it is true that gene therapy could remove this source of inequality, but

an implicit assumption is that people with genetic disorders need to be treated and made "normal". The objection sees gene therapy as a form of discrimination against impaired and disabled people.

The last point is that human enhancement could lead to a resurgence of eugenics in new forms. In the past, eugenics was used to justify practices including involuntary sterilization and euthanasia. For example, "the eugenic movement in the United States in the early 1900s was based on the use of 'genetic science', which claimed that complex social traits such as alcoholism, criminality, and depression were inherited in a simple fashion. This 'science' was cited as justification for policies that restricted immigration into the U. S., as well as for state law that permitted involuntary sterilization of criminals, mentally disabled individuals, and even unwed mothers. However, eugenics research was ultimately dismissed as significantly flawed, and the movement ceased by 1940" (Norrgard 2008). However, many now defend a new brand of eugenics by which individuals are free to choose whether to use genetic technologies for reproductive purposes (Buchanan et al. 2000; Agar 2004). One has to ask whether reproductive liberty is the absolute value for guiding policy in this context.

Another issue that has sparked the debate is what conditions should be treated by gene therapy. Proposed policies set two limits for gene therapy: a) gene therapy should not be pursued for nontherapeutic aims; b) gene therapy should not involve germ-line therapy.

Proponents for germ-line gene therapy argue that it is morally wrong to allow children to be born with fatal genetic diseases when the capability exists to remove those genes from the population once and for all (Savulescu et al. 2015). They also claim that this kind of therapy is a significant tool to curb human suffering, as well as a practical measure against the high costs of conventional treatment for generations of people afflicted with a given disease.

By contrast, opponents argue that it is inadvisable at this time because so little is known about gene regulation or the mechanisms of embryological development. They claim that the premature use of such techniques could be even more harmful than the disease they are trying to cure. It is acceptable to change the genome of a mature individual after medical indications or on his/her own desire, from an ethical point of view. But "a different situation occurs when changing the genes of embryonic cells because

1. this action can be described as amoral, due to the fact that the given research is carried out on unborn individuals;
2. an experiment on the human genome resulting in failure cannot be corrected;
3. an improperly constructed genome can be spread (through heredity);
4. the interaction character of 'new' genes with their totality is not yet fully studied, and reorganization of the genome of the embryonic cells can lead to unpredictable consequences" (Melnov 2016, 218).

An additional concern is that not only will diseases be selected out from the population, but also relatively insignificant problems such as myopia, racial variations such as skin color, and normal variations such as height. Opponents generally argue that germ-line therapy is a slippery slope that will push humanity into eugenic practices, thus resulting in a reduction of diversity in the human gene pool, which could increase our collective susceptibility to new diseases.

The International Summit on Human Gene Editing, which took place in Washington in 2015, reached several conclusions about how gene editing should be handled.

5.3.1 Basic and preclinical research

Intensive basic and preclinical research is clearly needed and should proceed, subject to appropriate legal and ethical rules and oversight, on (i) technologies for editing genetic sequences in human cells, (ii) taking into account the potential benefits and risks of proposed clinical uses, and (iii) understanding the biology of human embryos and germ-line cells.

5.3.2 Clinical use: somatic

Many promising and valuable clinical applications of gene editing are directed at altering genetic sequences only in somatic cells – namely, cells whose genomes are not transmitted to the next generation. Because proposed clinical uses are intended to affect only the individual who receives them, they can be appropriately and rigorously evaluated within existing and evolving regulatory frameworks for gene therapy, and regulators can weigh the risks and potential benefits in approving clinical trials and therapies.

5.3.3 Clinical use: germ line

Gene editing might also be used, in principle, to make genetic alterations in gametes or embryos, which will be carried by all of the cells of a resulting child and will be passed on to subsequent generations as part of the human gene pool. Although each country has its legal framework in different areas of biomedical research, in terms of the human genome, it must be regulated similarly in all countries.

It would be irresponsible to proceed with any clinical use germ-line editing unless (i) the relevant safety and efficacy issues have been resolved, based on appropriate understanding and balancing of the risks, potential benefits, and alternatives, and (ii) there is a broad societal consensus about the appropriateness of the proposed

application. Moreover, any clinical use must proceed only under appropriate regulatory oversight. At present, these criteria have not been met for any proposed clinical use: the safety issues have not yet been adequately explored; the cases of most compelling benefit are limited; and many nations have legislative and regulatory bans on germ-line modification. However, as scientific knowledge advances and societal views evolve, the clinical use of germ-line editing should be revisited on a regular basis (International Summit on Human Gene Editing 2015).

Scenarios on the desired futures for human gene editing differ widely. Several participants in the discussion agreed with the idea that no new biomedical technology is safe. Even though the level of acceptable risk is subject to intense disagreement, gene editing will become acceptable when its benefits, both to individuals and to the broader society, exceed its risk. Some have proposed a moratorium on the basic research needed to enable germ-line human gene editing until an international ban on germ-line gene editing for reproductive purposes can be secured through the United Nations and all countries have adequate regulations for such research (International Summit on Human Gene Editing: A Global Discussions 2015).

5.4 Conclusion

In order to protect humanity from the potential danger that may occur from the implementation of emerging technologies such as genetic engineering, both scientists and policymakers have sought some safe and effective models. This objective could be achieved only after the concept of the precautionary principle has been elaborated. This principle enables decision-makers to adopt precautionary measures when scientific evidence about the environment or human health is uncertain and the stakes are high. Thus, the precautionary principle is understood "as the rule that one should never engage in the technological development or application unless it can be shown that this will not lead to large-scale disaster or catastrophes" (Engelhard & Jotterand 2004, 303). Nevertheless, we think that scientists should have the responsibility to reflect on the potential applications of their research against a plurality of values, for minimizing ethical complications in genetics research.[10]

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