Genetic Diagnosis—Bioethics

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Abstract: The entire human genome will be completely analyzed very shortly and mankind must resolve the issue of how this knowledge will be applied to general medical care in the 21st century. Due to the progress which has hitherto been achieved in gene analysis technology, genetic testing for carrier detection, pre-implantation diagnosis, prenatal diagnosis, presymptomatic diagnosis, predispositional testing, and other tests has become technically easier to conduct. The progress in gene analysis technology has also made it highly possible for prenatal diagnosis, that presently relies on amniocentesis and CVS, to shift to less invasive methods that utilize maternal-fetal blood. What mankind must resolve is how advanced medical technology will be adequately utilized and how it will be justified from the standpoint of bioethics. If technological progress is pursued without addressing the ethical, legal, and social issues that stem from this technology, it will have difficulty gaining public support. Ethnically original bioethics will not evolve in Japan if the unique culture, customs, and practices that exist in this country are ignored. There is an urgent need to address this issue.

Key words: Genetic testing; Genetic diagnosis; Bioethics

Introduction

The Human Genome Project, which aims to map the entire human genome, has announced that the task will be completed in 2003, two years earlier than 2005, the year originally targeted for the project’s completion. What will subsequently evolve from this project? Undoubtedly, pharmaceutical and various other industries will develop from the information that the project will provide. In addition, if gene analysis methods are simplified due to the facilitated use of the microchip, the issues of cost and labor will be quickly resolved.

One of the foremost issues in medical care in the 21st century is how the knowledge and technology derived from gene analysis will be applied in primary care. Its utilization will undeniably become widespread and prevalent in medical care. However, the fact that gene analysis has made it easier to decode an individual’s genetic information has also engendered a major problem. The progress achieved in the decoding technology will enable genetic information...
to be collected from hair, saliva, nail, and even a single cell, in addition to blood samples.

Recently, pre-implantation diagnosis has come to the fore. The development of the technique of fractionally extracting fetal blood cells from maternal-fetal blood has enabled genetic information of fetuses to be successfully decoded using these cells even in Japan. If the accuracy level of this technique rises, there is the likelihood that it will replace amniocentesis or cervical villus sampling (CVS), the more invasive forms of prenatal diagnosis that are currently utilized.

In other words, decoded human genetic information will become readily accessible. However, there is concern that genetic information may be abused in the areas of employment and insurance not only for tested individuals, but for their family members as well. Genetic information, in some cases, links the members of an entire community. Genetic disorders are often over-represented in ethnic groups and intensive genetic research could be exaggerated in the presence of specific problems. A matter that must be confronted is the therapeutic gap, i.e., the development of diagnostic techniques despite the shortage of available therapy and effective prevention of genetic diseases. Therefore, in view of these circumstances, it is natural that there are critics who disparage the present situation, which brings to mind the development process of the atomic bomb in physics. What lies in wait with the progress in molecular biology? Will modern science (technology) lead to true happiness and prosperity for mankind?

**Genetic Testing**

The process of diagnosing patients based on data obtained from gene analysis is called DNA diagnosis or genetic diagnosis in Japan. Recently, the term, genetic testing, has become prevalent; and it also includes chromosome testing and other tests related to heredity.

In addition to genetic testing of probands, some of the other types of tests are carrier detection, presymptomatic testing (for autosomal dominant disorders such as Huntington disease), susceptibility testing (testing for the BRCA 1 gene linked to the genetic type of breast cancer), prenatal tests, and pre-implantation diagnosis.

There is a strong need to strictly define the term DNA diagnosis because the majority of the tests carried out by many private DNA testing laboratories or genetic testing services are DNA tests and they are not a DNA diagnosis, which should be given in conjunction with the family history and an accurate interpretation of the mutant gene in question. Pretest counseling is indispensable. Subsequently, there is concern that the public will send in their samples unquestioningly to such services or laboratories under the misconception that a DNA diagnosis will be provided. In many cases, it is not easy to determine the type of diagnostic technique that should be used and to read and interpret the data that is obtained.

Presently, genetic testing services have begun to conduct cancer linked gene analyses and tests for delayed nervous diseases. There are many cases where such tests are complacently conducted and the testing services are faced with the difficulty of informing the client of the discovery of mutated cancer linked genes and providing adequate answers and appropriate counseling. Subsequently, the testing services are forced to recruit the services of a medical geneticist in order to address the needs of the client.

**Principle of Bioethics**

What standards of assessment and reasoning should be employed in the debate on bioethics? How should bioethics be interpreted? In the past, nations have sanctioned ethical standards and perspectives that are collectively adopted by the entire global community, in addition to standards that are compatible with the culture and religious mores of that particular country.
Willer has recently compiled the Christian concepts of the Lutheran church on genetic testing. On the topic of prenatal diagnosis, he has written, “The ability to know prenatally whether or not a child will have a birth defect may raise difficult questions for some Christians. If a baby is born with a chromosomal abnormality, most people feel obligated to love and take care of the child. Should that belief change when a fetus is prenatally diagnosed with chromosome abnormality? Perhaps the parents feel that preventing the birth of the child is the most loving decision. On the other hand, the couple may decide to continue the pregnancy, believing God will provide the strength required to take care of such a child. What they believe about God can shed light on such choice”.

However, what ethical standards do those who are not religious or defer to religious precepts rely on? Naturally, it is difficult to pin-point one ethical perspective or standard that is deferred to in a diverse society. In his debate on bioethics with regard to genetics, Burugio has written the following thought-provoking comment. “In the 18th century, philosophers taught us that all humans are born equal and after birth they are made unequal by men. Perhaps today, with our knowledge of genetics, we might say that the contrary is true: in other words, all men are born unequal and there is the danger that humans will make them equal. The answer is that both hypotheses are wrong; we are all equal in some ways and unequal in others, and any intervention, whether medical or political, which increase equality in one dimension will likely lead to decrease in another dimension.” In a nutshell, a one-dimensional ethical perspective does not offer a realistic solution.

The pillars supporting bioethics are said to be the philosophies of James Mill’s utilitarianism, Immanuel Kant’s theory of duty, natural law, and Rawls’s theory of justice. A though a detailed explanation of these concepts will not be delineated here, the philosophy of Mill, which expounds the virtue of providing the greatest benefit to the vast majority with the least amount of risk, and the philosophy of Kant, which advocates the protection of individual rights, irrespective of whether those rights are in the minority, are at the extreme poles of the spectrum of thought.

The principles of bioethics that are presently endorsed by the majority of theorists and health care personnel are an amalgamation of such contrasting philosophies. Specifically, the four principles of Beecham and Childs exemplify this integration as listed below.

1. Respect for the individual and the right to self-determination (autonomy).
2. Avoid injurious or harmful acts (non-maleficence)
3. Pursue the best interests or welfare of the individual (beneficence).
4. Strive for equity at all times, i.e., a comparison of risk versus benefit, cost versus effect, etc. (justice).

Genetic Testing, Genetic Diagnosis

1. Prior to undergoing genetic testing

The objective of genetic testing is to acquire the genetic data of a client. Its significance greatly differs from that of a liver function test since the genetic information that is obtained is a future assessment of the health of both the client and other blood relations. Therefore, counseling is essential for the client before genetic testing is conducted in view of the gravity of the information that is collected, as well as the fact that it is fundamentally a test to pin-point genetic diseases. The frequency of the disease in question, its natural history, the recurrence rate (genetic prognosis), and other factors should be explained in layman’s terms to gain the client’s understanding (in conjunction with principle 1 above).

A detailed explanation of the genetic testing process should include the objective, method, content (the benefits and the disadvantages that will be derived), accuracy, especially the unavoidable limitations of the diagnosis, possible risks that
may accompany the testing, and other information that should be accurately relayed to the client (in accordance with principles 2 and 3). A signed informed consent document is required in order to conduct the tests. The client has rights of which he or she is unaware of, as well as the “right to know”. Therefore, after the client has been fully informed about the diagnosis, he or she has the right to refuse the test; and it is the client who must make the final decision to undergo the test (in accordance with principle 1). It is critically important that the client is not exposed to any potential undue influence at this time and to take measures to ensure that the client is not inadvertently exposed to any disadvantages if the test is refused (in accordance with principles 1 and 2).

In the United States, some private DNA laboratories or testing services will not conduct cancer-related genetic tests if there is no history of cancer patients in the client’s family. Similarly, testing services in Japan will also be required to clearly define the responsibility of the company in the future. A fair equilibrium between costs that are paid and the results that are obtained must be maintained (in accordance with principle 4).

2. Permission by a guardian (DNA testing of children)

The decision to undergo DNA testing for clients who are incapable of making a legally competent decision, as in the case of young children, is made by a parental authority or legal guardian or representative; and the decision that is made in such cases must protect the interests of the client (in accordance with principles 2, 3). Therefore, implementation of the genetic testing in children in case of untreatable or non-preventable genetic diseases, which occur with the onset of adulthood is unethical. Despite the proven existence of a variant gene in the client, if there is no distinct benefit or if a disadvantage is derived from the treatment, it should not be pursued. In such cases, the decision should be made by the client when he or she has reached an age to make a legally competent decision (in accordance with principle 1).

3. In the aftermath of the testing

The diagnoses that are based on the DNA tests should be explained in terms that is understandable to the client (in accordance with principle 1). However, if the client is not well-informed about the disease, the task of providing an adequate explanation will not be facile because the clinical symptoms of a genetic disease will vary if the position of the same variant gene causing the disease differs. Therefore, it is impossible for a physician specializing in genetic diseases to know of the heterogeneity of all diseases. Consequently, in the case of specific diseases, working in tandem with a specialist will be required in order to relay accurate information to the client (in accordance with principle 2).

The next issue which must be addressed is how the client is informed of the existence of a variant gene that has been diagnosed. For example, if a client who has hitherto led a healthy, normal life, is diagnosed with the variant gene for Huntington’s disease (which has a 100 percent penetrance), the issue which must be addressed is how the client will be mentally and emotionally supported after being informed. There are testing companies that will have the client undergo a psychological test to determine whether the client will be able to bear the results of the diagnosis before conducting genetic testing. In view of the tragic circumstances that these diseases produce, it is understandable that the extreme argument has evolved that advocates the establishment of such a system before genetic testing is conducted. Similarly, the period following the diagnoses of cancer-related genetic testing is acutely serious. Although the penetrance for cancer is not 100 percent in such cases, clients are more susceptible to groundless and exaggerated fears. The guidelines published by the Japan Society of Human Genetics states, “counseling following genetic diagnoses is essential...
and counseling should be repeatedly provided as needed.9 (in accordance with principles 2, 3).

Proper management of the genetic data and protecting client confidentiality are also important issues. The data must be protected from life insurance companies, private firms, schools, and other third-party institutions (in accordance with principles 1, 2). It is also important to remember that an individual’s genetic information is also information or data that is shared and owned by blood relatives. Therefore, it is ethically appropriate to provide this data to a blood relative with the aim of preventing the onset of the disease or for use in its treatment.9

In 1998, the WHO advocated the following after confirming the importance of protecting the confidentiality of an individual’s genetic data: “…counselors should inform people that genetic information may be useful to their relatives and may invite individuals to ask the relatives to seek genetic counseling”; and “the provision of genetic information to relatives about the family so as to learn their own genetic risks should be possible, especially when a serious burden can be avoided”9 (in accordance with principle 2).

4. What solutions are needed in Japan?

What solutions are needed to resolve the various issues that have been thus far explained? Firstly, basic knowledge in genetics should be taught not only in the field of medicine and health care, but in primary education as one aspect of the information and knowledge about the human body. This is a vital means of combating unwarranted biases. Secondly, an infrastructure of genetic services, especially a system of genetic counseling should be established. Practical measures such as this are what is needed rather than dramatic advances in genetic research.

REFERENCES