

Research Article

Paola Bin, Adelaide Conti, Emanuele Capasso*, Piergiorgio Fedeli, Fabio Policino, Claudia Casella, Paola Delbon, Vincenzo Graziano

Genetic testing: ethical aspects

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Abstract: The aim of this article is to provide an analysis of the main issues related to the application of predictive medicine by analysing the most significant ethical implications.

Genetic medicine is indeed a multidisciplinary matter that covers broad contexts, sometimes transversely. Its extreme complexity, coupled with possible perceived repercussions on an individual's life, involves important issues in the ethical, deontological and legal medical field.

The aspects related to the execution of genetic testing have to be addressed at different levels, starting with the correct information about the “cognitive” meaning they intend (by forcefully disassociating it from the strange “preventive aspect”) to the legal medical issues that can be aroused in the field of forensic pathology, medical responsibility and insurance. There is no doubt that in recent years, from the decoding of the human genome, genetic research has exponentially expanded with an equally exponential increase in its use in clinical practice and the ethical and social evolution of it.

Keywords: Information; Genetic counselling; Protection of privacy

*Corresponding author: **Emanuele Capasso**, Department of Advanced Biomedical Sciences, University of Naples Federico II, Section of Legal Medicine, Via Sergio Pansini 5, 80131, Naples, Italy, E-mail: emanuele.capasso@unina.it

Paola Bin, Adelaide Conti, Paola Delbon, Department of Surgery, Radiology and Public Health, Public Health and Humanities Section, University of Brescia – Centre of Bioethics Research (with the contribution of IRCCS “S. Giovanni di Dio - Fatebenefratelli”), Italy. P.le Spedali Civili, 1, 25123 Brescia, Italy

Fabio Policino, Claudia Casella, Vincenzo Graziano, Department of Advanced Biomedical Sciences, University of Naples “Federico II”. Via Sergio Pansini 5, 80131, Naples, Italy

Piergiorgio Fedeli, SJurisprudence School, University of Camerino, Via A. D’Accorso 16, 62032, Camerino (MC), Italy

1 Informed consent

Informed consent to the medical act constitutes the legitimate assumption of any healthcare provision and is therefore an essential element for the realization of an effective therapeutic alliance between the physician and the patient. The implementation of this principle implies a commitment on the part of the doctor about the type of information to be given and whether or not to inform the patient about his actual health conditions and finally to provide information about the diagnostic and therapeutic activities to be taken in an attempt to restore or improve health conditions. The patient's decision making process as a process based on the availability of adequate and complete information is problematic when genetic tests are the subject of the information [1-3]. The difficulties encountered in the decision-making process derive first of all from the complexity of genetic mechanisms and their interactions, including with environmental factors; such complexity leads to uncertainty about the causes of the mechanisms of genetic diseases and inadequate understanding of the patient's information. The special caution required in the genetic decision-making process also stems from the important choices that the individuals concerned may make regarding the implications for family planning: from the continuation of pregnancy to interruption and prenatal diagnosis [4]. The prescription of a genetic test must therefore be accompanied by all the information necessary to illustrate the possible implications of the obtainable results, from the possible false and false positive results of the concepts of predisposition to the risk factors for disease and the possible options available to the patient. This communicative process is the essential prerequisite for the exercise of a free and conscious choice among the available options. The Italian Code of Medical Deontology [5] (2016) addresses this topic in Articles 45 and 46:

Art. 45 Human Genome Interventions: The doctor prescribes and carries out interventions on the human genome for exclusive prevention of diagnosis and treatment of pathological conditions or these predispositions and to seek new and effective therapies and treatments.

The doctor will provide the patient with appropriate information on the risks associated with the procedures and their Success Stories, acquiring written consent.

Art 46. Predictive Investigations. The doctor prescribes or conducts predictive investigations with the written consent of the person concerned or his legal representative who are the only recipients of the data of the relevant information. The doctor informs the person concerned of the significance of the purpose of the investigation, on the real probability of reliable prediction, the feasibility of available and effective therapeutic interventions and the possibility of adverse consequences on quality of life resulting in knowledge of the results. The doctor does not prescribe performing predictive tests required for products for purely insurance and employment purposes. Pregnancy predictive investigations aimed at protecting the health of the woman are permitted if authorized in writing by the pregnant woman herself, after appropriate information.

Likewise, the guidelines developed by the Higher Health Care Working Group address the issue of informed consent as a result of a process that should help the subject decide whether to undergo the test or not. Of course, in both situations informed consent arises from a dialogue during which the potential user must receive comprehensive information from the health care provider managing the genetic test regarding all possible implications of the obtainable results [1,6]. The European Society of Human Genetics (ESHG) has worked on some of the documents relating to the application of the spread of genetic tests and the precautions to be taken in this growing practice, stating that genetic testing performance should be based on the self-determination principle of the person concerned and hence on explicit informed consent from the person intending to undergo a genetic test. Along with the right of information, there is a “right not to know” or the right of an individual not to know about genetic information that concerns him. The recognition of the value of this claim is mainly affirmed in cases where therapeutic remedies are lacking for the disease in question and, moreover, during the period between the execution of the test and the availability of the results when it is possible that particular events or reflections will cause the person concerned not to want to be informed on the outcome of the survey [7]. The Convention on Human Rights and Biomedicine stipulates that every person has the right to know any information gathered about their own health. However, a person’s wish to be unaware is to be respected. Affirming the right not to know in the genetic context is related to the possible negative impact that the genetic information about the peculiarities outlined may have on the personal

family life of the subject. If the right to not know has its foundation in the principle of autonomy, it is affirmed as a means of protecting the patient’s psychological integrity. Even the right “not to know” cannot be supposed but requires an explicit manifestation by the person concerned [8]. The information should also cover the management or conservation methods and the possible subsequent use of the biological material taken. The taking of a biological sample must be preceded by an interview during which the information necessary to enable the person concerned to reach informed decisions without pressure or manipulation is easily and comprehensively provided. (Guidelines of the Italian Society of Human Genetics) [9]. The European Human Genetic Society has also been interested in the issue; the need has been highlighted that the individual should express a conscious choice in terms of authorizing the retention and use of his genetic sample for further scientific study, seeking or wants to be informed of possible risks and diagnostic possibilities derived from subsequent research. In light of the continuous evolution of the genetic field, the right not to know is recognized not only as far as knowing the results of a test, but also the news that in the future might affect a person. The patient may choose not to save his sample, which means he does not want any new knowledge generated by the scientific process that may affect his condition [1].

2 Protection of privacy

The most important international documents such as the Convention on Human Rights and the Universal Declaration on the Human Genome and Human Rights guarantee the right to the confidentiality of genetic information, the right to know the test results and the confidentiality of the data obtained. In particular, adopting a number of precautionary measures to ensure the confidentiality of the information, ensuring access to such data and, above all, binding any communication to third parties. It should be noted, however, that genetic tests provide indications of a risk not only for the individuals involved but also their family members, which raises sensitive issues regarding extending the information, regardless of the patient’s will. In this case, any assessment of extending the acquired genetic information to third parties affected thereby must be based on the consideration of three factors: seriousness of the condition under consideration, availability of an effective treatment or preventative measures for the pathology and reliability of diagnosis. It is therefore a balancing act between possible harm to the confidentiality

of the patient and the possibility of third parties exercising their autonomy in relation to the genetic information that interests them even if indirectly [1]. General Authorisation No. 8/2014 for the Processing of Genetic Data In 2014, the Italian Data Protection Authority [10] authorised the processing of genetic data by the entities specified hereinafter in accordance with the requirements set. Before commencing and/or continuing the processing, information systems and software shall be configured by minimising the use of personal and/or identification data so as to rule out their processing if the purposes sought in the individual cases can be achieved by means of anonymous data and/or appropriate arrangements allowing data subjects to be only identified where necessary.

The Italian Data Protection Authority defines “genetic data” as the result of genetic tests and/or any other information that, regardless of its type, identifies an individual’s genotypic characteristics that can be inherited within a related group of individuals, and “genetic test” as the analysis, for clinical purposes, of a specific gene, or of a product and/or function thereof or of other DNA constituents and/or a chromosome, in order to carry out a diagnosis or confirm a clinical suspicion in an individual already affected by disease (diagnostic test), or else in order to detect or rule out a mutation associated with a genetic disease that might develop in a healthy individual (pre-symptomatic test), or in order to assess an individual’s liability to develop multi-factor diseases (predictive or susceptibility test) [10]. The authorisation should be granted to health care practitioners, in particular medical genetics experts, and to public and private health care bodies with regard to data and operations indispensable exclusively for health care purposes in respect of the data subject and/or a third party belonging to the same genetic line as the data subject.

Such genetic data may be processed and such biological samples may be used as are closely relevant to the purposes mentioned, where these purposes may not be achieved, on a case by case basis, by processing either anonymous data / samples or non-genetic personal data:

a. health care, with particular regard to genetic diseases and protection of the data subject’s genetic identity, with the data subject’s consent, except for the provisions made in sections 26 and 82 of the Code for the case where a data subject is unable to provide his/her consent because he/ she is legally incapable, physically impaired, or mentally disabled;

b. health care, with particular regard to genetic diseases and protection of the genetic identity of a third party belonging to the same genetic line as the data subject, with the data subject’s consent; where consent has not

been or may not be provided because of legal incapacity and/or physical impairment or mental disability, or else because the data subject is nowhere to be found, the processing in question may be performed by having regard to such genetic data as are available if this is indispensable to allow the third party in question to make informed reproductive choices or if it is justified by the need for said third party to undergo preventive care and/or treatment. Where the data subject has deceased, the processing may also include genetic data retrieved from the analysis of the deceased individual’s biological samples, providing this is indispensable to enable the third party in question to make informed reproductive choices or if it is justified by the need for said third party to undergo preventive care and/or treatment;

c. scientific and statistical research with a view to protecting the data subject’s, third parties’ and/or the community’s health in the medical, biomedical and epidemiological sectors, including clinical drug trials, or scientific research aimed at developing genetic analysis techniques (providing the availability of exclusively anonymous data on population samples does not allow the research purposes to be achieved), whereby said research shall be carried out with the data subject’s consent except for the statistical surveys and/or scientific researches provided for by law.

Within the framework of the purposes mentioned, this authorisation shall also be granted exclusively for the purpose of allowing the authorised entities to fulfil specific obligations and/or ensure that such obligations are fulfilled, or to discharge specific tasks set out in Community legislation, laws and/or regulations with particular regard to public health and hygiene, prevention of occupational diseases, diagnosis and treatment including blood and organ transfusions, tissue and hematopoietic stem cells transplantation, rehabilitation from physical and mental disability and/or impairment, protection of mental health, and pharmaceutical assistance pursuant to the law. The processing operations may also concern the filling out of health records, certifications and other health care documents.

Processing of genetic data and use of biological samples to perform pre-symptomatic and susceptibility tests are only permitted in order to achieve health care purposes, including informed reproductive choices and health care-related research purposes.

The authorisation shall also be granted if the processing of genetic data is indispensable also by the agency of alternates, technical experts and/or authorised private detectives, or else to establish or defend a judicial claim, whether related to a third party or not, also without the

data subject's consent – except where the processing requires the performance of genetic tests. The foregoing provisions shall apply on condition the claim to be established or defended is not overridden by the data subject's, or if it consists in a personal right or another fundamental, inviolable right or freedom, and if the data are only processed for those purposes and for no longer than is absolutely necessary to achieve such purposes. The processing must be carried out in compliance with the general authorisations issued by the Guarantor for the processing of sensitive data by self-employed professionals and private detectives. The processing may also concern the information related to the data subject's medical history and/or family members.

The authorisation shall also be granted if the processing of genetic data is indispensable to fulfil specific obligations or ensure that specific obligations are fulfilled, or to discharge specific tasks as set forth expressly in EU instruments, laws and/or regulations applying to social security and welfare, occupational and/or population safety and hygiene, also without the data subject's consent, in compliance with the limitations laid down in the Guarantor's general authorisation for the processing of sensitive data in the employment context and without prejudice to the provisions contained in the code of practice referred to in section 111 of the Code. The processing may also concern the information related to medical history and/or the data subject's family members [10]. The authorisation shall also be granted to establish consanguinity with a view to family reunions of non-EU nationals, stateless persons and refugees. In particular, the processing of genetic data shall not be regarded as indispensable if it is carried out in spite of the availability of alternative procedures that do not entail the processing of such data.

3 Genetic counselling

Genetic diagnosis implies a process requiring at least three phases: information/preparation, laboratory and psychological interpretation and support. Work in the genetic field does not end run with the laboratory, as it entails a relational process between physician and patient, starting from the test execution proposal and ending in the communication of the results of the investigation carried out and providing the patient with genetic counselling. Genetic counselling is therefore the basis of the assurance of diagnosis in the context of adequate information about the nature of the proposed genetic test, the nature of the disease, investigation timing and methods, the valence

and significance to be attributed to the results and how to gain access to the collected data.

The National Committee for Bioethics [6] defines genetic counselling as a geneticist's communication process aimed at helping affected or at risk individuals of hereditary illness, enabling them to understand the nature of the disease and the management of the disease. Such advice therefore requires ethical and psychological technical expertise aimed at allowing free responsive choices and ensuring non-directivity by the consultant. Counselling is proposed as a complex intervention for acquiring consensus by communicating the purpose, type and reliability of the examination, the hypothetical risks, the understanding of the results and the psychophysical repercussions.

It is important to remember that with the spread of genetic tests we are going to need to outline a new category of users who are not sick but are responsible for a genetic anomaly that poses a greater risk for a particular disease and which falls back however, in the field of medicine [11]. There is therefore an "unpatient" that is unborn but still destined for diagnostic actions of prevention and who could however develop symptoms of a psychosomatic nature. The importance of counselling offered in a non-directive way should be emphasized, avoiding assessments that may affect the patient's decisions regarding the test and his life choices after hearing the results. The delineated decision making peculiarities in the genetic field require adequate preparation by the genetic counsellor. The need to ensure competence through specific training programs and exchange of experiences and through the establishment of specific qualifications has been felt even at the European level. The need to consider the psychological implications makes it opportune for operators with appropriate psychological and ethical competences to work with the counsellor physician in genetic counselling [1]. In contrast to the principles outlined above is the practice of offering genetic tests through the internet, where the performance under consideration is offered in packages like any commercial product. It is obvious that this form of genetic testing offer openly violates the principles of informed consent, freedom of choice and protection of personal data.

4 The issue of minors

Performing genetic tests on minors requires adequate caution; it is essential to postpone to an age where the individual is able to fully understand the scope of the test

and thus express an informed consent. The only exception could be the execution of diagnostic tests when they are actually necessary for the health of the individual or if the information is truly indispensable and not replaceable in order to detect the presence of genetic disorders in other members of the family [1,12,13]. The essence of evaluating the probability of performing genetic testing is even more important when the patient is a minor as well as underlined in the main documents addressing the issue of genetic testing on minors. (Guidelines for genetic testing of the ISS Working Group) [14]. Performing a test on a minor in reference to a particular disease for which there is no effective healing preventive action would not have the child's health as its purpose. Moreover, a decision on this would lead to a breach of the right of the person concerned to decide upon reaching the right age for genetic investigation. The choice of undergoing an examination would also have significant psychological implications linked to the alteration of family relationships and social discrimination, such as in school [12,13]. Minors may be subjected to genetic testing with the prior informed consent of their legal representative if there are effective therapeutic interventions or preventive measures to be implemented prior to reaching the right age for the examination. Even in this case, however, the decision must follow as much as possible the minor's opinion and never stray from considering his interests. A careful evaluation is necessary of the relationship between potential harm and benefits of a medical, psycho-social and reproductive order. Genetic counselling is particularly important in the genetic testing on minors; from the point of view of content, such a communication process will have to take into account the negative repercussions that the test can have on the child and thus evaluate the possible harm and benefits. Genetic counselling will have to involve the minor in order to ensure the availability of the tools needed to evaluate and address the results of the examination in the case of testing. Overall, any choice regarding the execution of the tests as well as any other diagnostic and therapeutic performance must be carried out for the interests of the minor or be directed to the promotion and protection of his well-being. In the case of pre-adolescent and adolescent children having the necessary capacity to freely and consciously make informed choices in relation to their state of health, there is a general tendency on the part of the doctrine to encourage respect for the will expressed by minors, compatible with age and degree of maturity achieved. This is also based on the statements contained in declarations of principles in supranational documents such as the European Charter of Fundamental Rights of the European Union adopted in 2000, which

establishes that children can freely express their point of views. This is taken into account in the issues that will affect their maturity depending on their age. In the same document, it is emphasized that in all child-related acts, the child's interest must prevail [1,13]. Also the Code of Medical Deontology, Article 35 states that the doctor must take due account of the views expressed by the child in all decision-making processes concerning him [5].

5 Prenatal diagnosis

Nowadays a number of genetic tests are related to reproductive life issues, both in terms of the possibility of early diagnosis in individuals with genetic abnormalities and in relation to the ability to identify individuals at risk of transmitting a genetic disorder, in order to plan the couple's reproductive choices. Prenatal Diagnosis can be defined (ISS Working Group Guidelines) [6] as a set of instrumental and laboratory investigations designed to monitor the health of the conceived throughout pregnancy.

Prenatal Diagnosis allows the identification of previously defined hereditary, infectious, iatrogenic or environmental pathologies. The development and dissemination of prenatal investigations has significantly influenced the reproductive choices of risk pairs, enabling them to know the characteristics of the conceived before birth [15]. Prenatal diagnosis thus has an existential meaning for pregnant women, couples and families. Prenatal diagnostics include non-invasive (fetal ultrasound, biochemical and molecular investigations on maternal blood) and invasive methods (amniocentesis, fetoscopy, etc) as well as genetic diagnosis. There are two characteristics of prenatal genetic diagnosis: the first is that it is not performed on the individual that is applying for the examination but on the conceived; the second is related to the strong implications for the personal and family life of those who require the prenatal diagnosis, so the communication of results must take place in a non-directive counselling process based on respect for the principle of autonomy of the pregnant woman and the couple [1]. The National Bioethics Committee also explained the need for an appropriate pre- and post-diagnosis approach. Prenatal diagnosis would be indicated in cases where the disease of which the foetus can be affected is serious and incurable, or in cases where diagnosis is necessary in order to initiate early or intrauterine therapies on a particular birth. This investigation could affect pregnancy in a way where the procreation risk is predictable as well as pregnancies in which the risk of the foetus is highlighted

during gestation. Some national documents have suggested some elements related to the two situations mentioned above:

Advanced maternal age (older than 35 years), parents with chromosomal pathology, parent with structural rearrangement without phenotypic effect, parents with aneuploidy of sex chromosomes compatible with fertility, foetal anomalies or alteration of the volume of the amniotic fluid, a probability greater than 1/350 that the foetus is affected by Down syndrome based on biochemical screening parameters, and other particular situations are evaluated by specialists in the field [12]. The major criticism of these aspects is related to the introduction of a eugenic perspective. This topic is dealt with by numerous authors. It also emerges several times in the Convention on Human Rights and Biomedicine where it is specified that is not possible to have access for predictive genetic illnesses except in the case of a curative medical treatment subject to an appropriate genetic assessment.

In the same Convention on the specific subject of prenatal diagnosis, it is established that the use of techniques of medical care for procreation is not allowed to choose the sex of the unborn except if intended to avoid serious hereditary diseases related to sex.

The Charter of Fundamental Rights of the European Union also stipulates in the field of medicine and biology the prohibition of eugenic practices, in particular those aiming at the selection of persons [1]. Genetic counselling is important in the light of the ethical implications of genetic testing, and plays a crucial role in prenatal diagnostics and in particular precisely to avoid forms of abuse in the use of tests. Access to prenatal diagnosis should be governed by the principle of proportionality or by applying it only in the presence of a medical indication objectively justifying the use of the diagnosis.

Even in the field of medicinal-assisted procreation, the guidelines issued in 2004 (Law 40/2004) include the possibility of genetic counselling by specialists given the foreseeable risk of transmissible genetic abnormalities. In this regard, Law 40 of 2004 restricts access to medication-assisted procreation techniques to cases of infertility or infertility as a result of established and certified medical records, thus excluding their use by other couples carrying communicable diseases. The same guidelines for medically assisted procreation directly address the issue of pre-implantation by explicitly establishing that any pre-implantation diagnosis for eugenic purposes is forbidden. The law also eliminates possible doubts by limiting an observational health survey. In the case of reversible

anomalies in the development of an embryo highlighted in this survey, a couple may refuse the implant [1].

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