Updates about ethical, legal and psychological implications of genetic testing in newborns, children and adolescents

Manal M. Thomas

Clinical Genetics Department, Human Genetics and Genome Research Division, National Research Centre, Cairo, Egypt

Correspondence to Manal M. Thomas, MD, PhD, 33rd El-Bohouth Street, Dokki, Giza 12622, Egypt. Fax number: 2024545345
e-mail: nula_m@hotmail.com

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Genetic diseases affect physical and psychological health status and social well-being of patients and their families. For that reason, many organizations in the genetic field have published new guidelines on ethical and legal issues regarding genetic testing in children and adolescents. This review article aims to highlight the guidelines regarding quality standards of genetic testing in children and adolescents stressing on the ethical, legal and psychological implications of genetic testing. Specific guidelines on genetic testing and laws must be designed in Egypt to regulate genetic testing and enhance patients' rights putting specific legislations that comply with our traditions and beliefs. More knowledge and educational programs are recommended for health professionals and the public about measures to prevent diseases and promote health behaviors.

Keywords:
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Introduction

Over the past 60 years, tremendous progress has been made in the field of genetics from unraveling the mystery of DNA double helix to the breakthrough of mapping the human genome. The rapidly growing genetic and genomic knowledge increased the interest of consumers in genetic testing. As a result, statements about genetic testing and screening of children and adolescents need to be updated to consider the ethical, legal and psychological issues that arise with the new technologies and expanded uses of genetic testing and screening. The growing literature on the clinical and psychosocial effects of genetic testing can help inform us about the best practices regarding diagnostic genetic testing, and how to respond to direct-to consumer testing and the potential of genomic profiling. Ethical principles aim at guiding the use of genetic information in ways that balance the interests of individuals and society (Hoge and Appelbaum, 2012; Ross *et al.*, 2013).

Ethical implications of genetic testing

The familial nature of genetic information comprises ethical, legal and psychosocial challenges for proper management (Botkin *et al.*, 2015). The different types of genetic testing methodologies have expanded rapidly over the past decade. The choice of the proper testing method depends on the types of abnormalities (Genetic Alliance, District of Columbia Department of Health, 2010; Botkin *et al.*, 2015).

Types of genetic testing

Diagnostic testing

(1) Newborn screening (NBS): it is done to newborns just after birth to diagnose early-onset treatable genetic diseases such as congenital hypothyroidism and phenylketonuria (Fig. 1) (Friedman *et al.*, 2017)
(2) Predictive testing: it is used to identify gene mutations associated with late-onset monogenic disorders. It could be helpful to the asymptomatic individual with a positive family history for genetic disorders (Ross, 2013)
(3) Carrier testing: its purpose is to detect gene mutations that have no adverse effects on individual health. It is performed with individuals with positive family history of genetic diseases to assess the risk of disease transmission to offsprings. It is also beneficial to individuals in ethnic groups who have high risks of specific genetic disorders (Wade *et al.*, 2010)
(4) Susceptibility testing: this kind of tests is designed to detect markers with high risks in nonaffected persons (Genetic Alliance, District of Columbia Department of Health, 2010)
(5) Preimplantation genetic diagnosis: it detects the genetic change in the embryo created by assisted reproductive techniques like in-vitro fertilization (Genetic Alliance, District of Columbia Department of Health, 2010)
(6) Prenatal diagnosis: it is done for suspecting fetal-specific genetic disorders. It can decrease disease uncertainties and help to decide about continuing pregnancy (Marokakis *et al.*, 2016)

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(7) Premarital screening and counseling: premarital screening is considered as a growing trend all over the world. Couples seek for premarital counseling in their quest for a safe marriage, disease-free life and for a healthy future progeny. Premarital health counseling helps to avoid many health and stress problems. Premarital health counseling provides couples with accurate unbiased information and assistance (Puri *et al.*, 2016).

Nondiagnostic testing

(1) Forensic testing: DNA sequence is used to identify individuals for legal purpose. It is not used to detect pathogenic gene mutation. It is useful in identifying crime victims and suspects. It is also used to confirm biological relationship like disputed paternity (Genetic Alliance, District of Columbia Department of Health, 2010)
(2) Paternity testing: this test uses specific DNA markers to detect similarities in patterns of inheritance among related individuals (Wright, 2009)
(3) Genealogical DNA test: this type of genetic testing is used to identify ancestry or ethnic heritage (Genetic Alliance, District of Columbia Department of Health, 2010)
(4) Research testing: it is done to discover unknown genes and learn their mechanisms. It gives more details about understanding the various genetic disorders (Genetic Alliance, District of Columbia Department of Health, 2010).

Different types and common methodologies of genetic testing are illustrated in Fig. 1.

Ethical implications in children

Genetic counseling for children is very complex owing to the fact that parents take the decision for their children. Multiple guidelines for minors stress on performing genetic testing only for diagnostic, therapeutic and/or preventive actions (Ross, 2013; Caulfield *et al.*, 2015). A confirmed diagnosis helps with counseling and offering prenatal diagnosis to prevent recurrence in the family. In certain disorders, genetic testing is a medical and social emergency, such as disorders of sexual differentiation, which necessitate performing the testing very early in the neonatal period to establish the diagnosis and initiate the proper management (Phadke and Gowda, 2013).

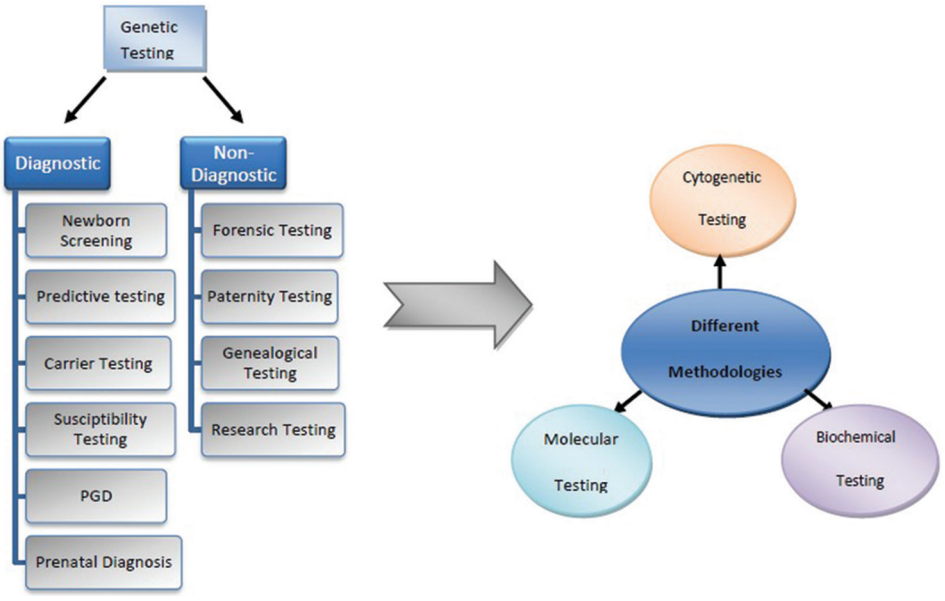
Carrier testing

Routine carrier testing of minors was a matter of debate owing to stigmata and discrimination which occur as a result of confusion between the affected versus the carrier status (Wade *et al.*, 2010). Different genetic disorders have different penetrance rates. They range from complete penetrance, where all or a high percentage of carrier children will develop the disease, to incomplete penetrance, where carrier children risks differ by the type of the inherited genetic disease (Wakefield *et al.*, 2016). Pretest counseling is very important as it provides information about the disease burden and the implications of carrier detection. Carrier testing can prevent the birth of an affected child if the couple decides for abortion (Muthuswamy, 2011).

Factors affecting genetic testing in children

Carrier testing in autosomal recessive or X-linked

Figure 1



Illustrates the different types and methodologies of genetic testing.

recessive disorders has no implications for the child's health, other than its implications for the child's future reproductive choices (Clayton *et al.*, 2014; Botkin *et al.*, 2015). On the contrary, requesting early testing is important in certain diseases with autosomal dominant inheritance like multiple endocrine neoplasia II to test for mutations in RET oncogene in the offsprings. In addition, early testing could be helpful in management like medullary thyroid carcinoma, which was reported in young children. Testing for mutation in the RET gene can help in planning for prophylactic thyroidectomy. Consequently, certain diseases in which early intervention in childhood would lead to a favorable medical outcome, testing can be done without considering the minor's right to decide in the future (Phadke and Gowda, 2013).

Guidelines recommended that carrier testing should not be performed in childhood, and testing should be postponed until the child can give proper consent to be tested. Informed consent is defined as 'the willing acceptance of a medical intervention by a patient after adequate disclosure by the healthcare provider of the nature of the intervention with its risks and benefits and of the alternatives with their risks and benefits' (El Shanti *et al.*, 2015). Informed consent to genetic testing is the main hallmark in dealing with children. Young children lack the capacity to make decisions so their parents make these decisions, which are subjective, especially concerning major interventions and dealing with profound disabilities (Botkin *et al.*, 2015). The decision to do genetic testing in children is a joint effort involving a counselor who provides information and a parent or legal guardian who provides consent on behalf of the child. Some parents strongly believe they should have the final say in terms of genetic testing in their children. Opinions concerning who should decide to perform testing in a child varied between the parents and professional counselors depending on the urgency of the studied genetic disease. Informed consent is done to guarantee that the testing procedure is understood and agreed upon including the risks, benefits and tests alternatives (National Society of Genetic Counselors NSGC, 2015; Wakefield *et al.*, 2016). However, there are always questions about the validity owing to lack of maturity or inability to understand future implications. In addition, each child has different capacities at his/her developmental stages to decide and understand the test results and their potential implications. Many studies showed that the decision-making ability is impaired in children younger than 10 years, whereas other studies showed that it was not entirely dependent on age as some children gained this ability by 12 or 14 years of age. As a consequence, it is important to individualize each case and assess the capabilities of the child in concern (Phadke and Gowda, 2013). In Islamic ethics, the challenge of reaching genetic diagnosis and detecting carrier testing is to ensure that it is carried out in accordance with Islamic rules. The consent has to be obtained in accordance with the Islamic ethical and cultural background of the individual through community-based genetic counseling in his or her own language. Principles and components of consent that are generally acceptable in western countries are also applicable to Muslims, although Muslims (depending on their level of education, background and culture) will often want to consult with family members and their own religious scholars before consenting to major procedures. Consent must be obtained in the presence of two witnesses (Al-Aqeel, 2007).

Parents' perception of the long-term implications would be different from their child. In addition, testing at an early age deprives the child from his/her right to decide when reaching adulthood. Genetic counselors play an important role in determining whether genetic testing is offered and how the results will be delivered to patients and their families. Some studies suggested testing on a case-by-case basis, taking into accounts professional opinions and the family desires. Some studies regarding carrier testing in minors found that most parents are interested in having their children tested to feel reassured and relieved from anxiety in case of negative results and to inform and support their children as they grow up in case of positive results (Mackoff *et al.*, 2010; Phadke and Gowda, 2013). National Society of Genetic Counselors recommended involving children in the decision-making process whenever possible (National Society of Genetic Counselors NSGC, 2015).

Predictive genetic testing

There are many problems with the results of late-onset genetic diseases. Individuals wait a long time to find out whether or not they will have the genetic disorder. In addition, uncertainty of diagnosing certain genetic diseases raised many challenges to genetic counseling. This could be owing to variable genetic penetrance, gene-to-gene interactions, different diseases severity and environmental influence. Accurate diagnosis is necessary to predict the prognosis of a genetic disorder, especially if there is genotype–phenotype correlation. For example, the severity of myotonic dystrophy correlates with the number of trinucleotide repeats. In certain diseases like unilateral retinoblastoma in the child, surveillance is important to prevent involvement of the other eye if the child is a germline carrier of RB1 mutation gene. Likewise, unnecessary procedures such as colonoscopies in familial adenomatous polyposis can be avoided if the genetic test result is reported to be negative. In addition, predictive testing could be helpful

for other family members as well, for example, testing younger siblings of an affected child with Duchenne muscular dystrophy could spare the whole family of fear and anxiety in case of negative results. On the contrary, early detection for untreatable late-onset diseases such as Huntington disease is not useful as there is no treatment to change the course of the disease. In addition, living with the possibility that an individual is at risk of developing a disabling genetic disorder with symptomatic treatment only is very devastating. On the contrary, negative test results can be reassuring, so testing minors for adult-onset conditions may be beneficial under certain conditions. This shows the diversity of genetic testing in various situations, which must be assessed from the perspectives of the child, the parents and the geneticists (Phadke and Gowda, 2013).

Chromosomal microarray and incidental findings

Chromosomal microarray (CMA) is considered nowadays as a standard tool to diagnose wide varieties of diseases. CMA led to emerge of enormous amount of genetic data which were not related to the initial reason of the study and the appearance of 'incidental or secondary findings'. Hence, this raised a debate about the ethics to deal with these findings (Hayeems *et al.*, 2016). Secondary findings are 'clinically relevant information not related to the condition for which the test was ordered' (Green *et al.*, 2013). CMA testing raised ethical issues that necessitated having informed consent from the parents of the child. A significant challenge emerged in the difficulty of differentiating pathogenic variants from rare polymorphisms leading to the so-called variants of uncertain significance. Variants of uncertain significance is defined as genetic variants with unclear significance about the accuracy and benefit of the test results. Obstacles were encountered with the interpretation of different variants and copy-number alterations with unknown significance having insufficient information about benefits, risks and costs of disclosing incidental findings to make evidence-based recommendations. This was explained by reduced penetrance or lack of sufficient clinically associated data (Green *et al.*, 2013; Hofmann, 2016). There is a big argument about regulating information regarding the incidental findings and whether or not to routinely look for it. There is a conflict between withholding the results versus maintaining patient autonomy. Autonomy is concerned with 'the respect of the individual's rights and ability to understand information and make decisions that are right for that individual' (Caulfield *et al.*, 2015). Autonomy is a core concept respected and preserved by the National Society of Genetic Counselors' Code of Ethics which states that genetic counselors should 'enable their client to take informed decision, without oppression, through providing necessary facts, and making clear of the alternatives and anticipated consequences'. In case of children who lack autonomy, they should only be genetically tested only for the sake of their best interest and that the parents are responsible for managing the genetic information. On the contrary, there is a debate about how to define and evaluate a meaningful conception of the best interest of the child (National Society of Genetic Counselors NSGC, 2015).

According to the UNESCO Declaration on the Human Genome, the right of every individual to decide whether or not to be informed of the results of genetic examination and the resulting consequences should be respected. The American College of Medical Genetics (ACMG) recommended that incidental findings should be reported if the tested individual chose to receive the result. In addition, ACMG recommended reporting only for diseases associated with phenotypes for which preventive measures and/or treatments are available with clinical benefits for a child or his/her relatives. Likewise, ACMG recommended reporting the incidental findings in case of genetic diseases in which the individual with a pathogenic mutation may be asymptomatic for a long period of time. The debate was on whether or not the information was accurate and actionable, that is, whether the information provided was helpful or nonvalidated and confusing. ACMG recommendations have stated specific sets of genes for which known pathogenic or likely pathogenic alterations (thus excluding variants of uncertain significance) need to be investigated and reported by genetic testing laboratories. This was determined according to the clinical action ability of the pathogenic mutation in these genes. The initial guidelines recommended that these alterations should be universally reported. ACMG guidelines state that patients have the choice to refuse the analysis of clinically actionable genes (American College of Medical Genetics ACMG Board of Directors, 2015). The parents have the authority in making decisions for their children, but this could be ignored by the counselor if the parents decided not to receive information regarding secondary findings especially with serious implications of secondary finding or if the clinical response to secondary findings would prevent serious morbidity or mortality for the child. There is an ongoing debate between the clinicians and the researchers about how and when to test for secondary findings as both have different perspectives. Although the clinician looks for the best interest of the child, the researcher's concern is more to study in details all findings even if not relevant or significant. The American Society of Human Genetics (ASHG) recommended that it is ethically accepted, but not mandatory, to search for secondary findings that are

not relevant to the clinical or research indication for sequencing (Botkin *et al.*, 2015).

Newborn screening

NBS is considered to be a very influential public health program. It is important to implement a good legislative system and provide education for the public, medical professionals and legislators. It is also important to establish an integrated infrastructure system with financial and legislative support before establishing nationwide NBS (Al-Aqeel, 2017). ASHG, American Academy of Pediatrics and ACMG support NBS mandatory offering for all children. NBS programs can help the affected child to receive a fast and accurate diagnosis and provide proper healthcare as well (American Academy of Pediatrics AAP Committee on Bioethics, AAP Committee on Genetics, American College of Medical Genetics and Genomics Social, Ethical, and Legal Issues Committee, 2013). It can be beneficial to the families of the newborns by acknowledging parents to the reproductive risks for future pregnancy. NBS could also be beneficial to societies by offering understanding of diseases. In addition, the information related to the reproductive risk can be provided by the carrier status results. However, this may raise challenges about information availability without informed consent, which is not always available for the minor (Miller *et al.*, 2009). There is an ethical debate about the dried blood spot (DBS) used in NBS on whether to retain it for further research purposes or not and whether or not to obtain parental consent. Previously, no consent was required by federal laws to use DBS for research purposes as DBS was not considered as a human subject. Nowadays, consent is mandatory in most states in the USA for federally funded researches and for easier identification of participants for returning their results. The State Department of Health is the one responsible for returning the results. However, some studies showed that returning the results depends on whether or not the screened disease was severe and treatable. Many arguments were made between respecting personal rights privacy and confidentiality versus the advantages for the public when used for medical research and biobanking. However, there are concerns regarding the potential negative effects of NBS programs as well as budget limitations and governmental restrictions. Recommendations were made to provide parents with adequate education on DBS storage and uses and to increase the parent's awareness and responsibilities about biobanking (Lewis and Goldenberg, 2015). One of the disadvantages of DBS is that it takes between 1 week and 1 month, which is too long to presymptomatically treat the case. This is specifically a big problem in emergency departments that necessitate rapid intervention. This has ethical and prognostic implications. Poor legislative recall system might miss retesting of more than 50% of positive cases. It is essential to report how many proven positive cases were managed and what is the long-term follow-up and prognosis. On the contrary, it is beneficial to know what second-tier testing was used to confirm positive cases like molecular testing and what further management and family counseling measures were used for further preventive reproductive options (Al-Aqeel, 2017).

NBS could give rise to other crucial ethical issues. For example, detection of an affected child can disrupt the relationship between the parents and the newborn. Parents may feel guilty at transmitting a genetic disorder to their child. In addition, they might develop social stigmata especially if a reliable carrier screening test was available before pregnancy or child birth. Some NBS tests like testing for sickle cell anemia reveal both the carrier status and the disease status of the newborn. Ethical issues arise from whether or not to reveal genetic information about the carrier status of the newborn to the parents. Yet, the benefit to parents is to give them information that could help them plan their reproductive future. An additional problem may be raised when a newborn is diagnosed with an autosomal recessive disorder, with parents' tested results revealing misattributed paternity. In that case there are recommendations to counsel the mother separately (Hofmann, 2016). Difficulties in collecting data on long-term outcomes of the screened disease compromise limitations to the NBS as the affected newborn should be followed till the reproductive period. Furthermore, data may be lost before the newborn is old enough to use it, or it may be unfavorable data. For that reason, the ASHG recommended longitudinal studies and made certain regulations to assess long-term outcomes and evaluate supporting systems for the affected newborns and their families. Electronic medical records are useful tools to keep genetic data for a long time. In addition, most parents and primary care physicians have poor knowledge on dealing with the positively screened results. Hence, education for the parents, primary care physicians and the public about NBS programs is very essential (Botkin *et al.*, 2015).

Ethical implications in adolescents

Adolescence is a complex period of development. Genetic counseling of adolescents plays a crucial role in presenting information and support about genetic disorders. The occurrence of a genetic disease to adolescents who are already undergoing many life changes can make the period of adolescence more stressing. In genetic counseling of adolescents, assessment

of competence to consent is crucial while making sure that it is without oppression. The genetic counselor plays an important role in helping the adolescent to make an informed decision regarding genetic testing. However, counseling adolescents can provide particular challenges for healthcare professionals. Counseling techniques that are used with adults may not be often suitable to adolescents owing to their unique needs and the challenges of the developmental period of adolescence. Adolescents encounter many physical, emotional and social changes, which should be taken into consideration while counseling. Adolescents may not yet have the full emotional and cognitive ability to process complex medical information, risks and benefits. In addition, counseling is influenced by the developmental tasks of puberty which include family separation, establishment of meaningful peer relationships, identity formation, ability for abstract reasoning, development of confidence and self-esteem and establishment of autonomy and personal beliefs. All these factors could affect the adolescents' response to counseling and turn them to be defensive towards the healthcare professional and reluctant to engage in the counseling process. Likewise, if the adolescent did not achieve family separation, then the decision to have genetic counseling may be influenced by parents and other family members (Pichini *et al.*, 2016). Many studies were published on the debate about whether or not to offer genetic testing to minors. Wehbe *et al.* (2009) suggested that genetic counseling and testing for adolescents should be tailored to individual needs. On the contrary, few studies were done about the counseling process itself and proper techniques that should be applied when counseling adolescents (Gaff *et al.*, 2006). Difficulties in counseling adolescents were reported in the literature. Implications of testing should be presented as a series of short-term steps, as adolescents may have difficulties in comprehending long-term consequences. Additionally, the use of written vignettes and visual aids may be helpful when counseling adolescents. It may be difficult for adolescents to take the decision that confers with their values and interests. However, this ability matures over time, and that we must respect that adolescents may develop these abilities at different ages, stages and within different contexts (Goodlander and Breg, 2011). Referral to a genetic counselor and mental-health professional is advised if the clinician and family need additional support for decision making or in assessing the psychosocial dynamics (Botkin *et al.*, 2015). Adolescents may feel unable to discuss their concerns in front of parents, so giving them some privacy with the counselor with confidentiality reassurance could be more helpful. Yet, parents should be involved in to support any final decision for testing. Other counseling considerations include patience, empathy, nonjudgments and use of open-ended questions that utilize adolescent concerns for peer approval (Griswold *et al.*, 2011). Genetic testing of adolescents for certain diseases could help surveillance and planning for preventive measures such as colon and breast cancer (Phadke and Gowda, 2013). However, in certain diseases like juvenile-onset huntington disease (HD), there is a debate to determine minors' competence to consent to predictive testing. According to the General Medical Council Guidelines, it is the clinician's duty to make judgments about a child's level of understanding and maturity and to act accordingly. The geneticist then has discretion as to the particular time when information should be disclosed, and many studies advocate that psychiatric and psychological assessment should be undertaken to determine the patient's readiness to proceed with predictive testing. Hearing about how an adolescent coped with being informed about HD in the family and his/her personal at risk status may be an important predictor of his/her coping skills to deal with a predictive test result (Elger and Harding, 2006).

Direct-to-consumer testing

Direct-to-consumer genetic testing (DTC GT) is defined as genetic testing that bypasses the role of healthcare provider and deals directly with the consumer. DTC GT is targeted to the consumer mainly through the internet (Koeller *et al.*, 2017). The most famous companies in this field include deCODEme, 23andMe, Navigenics, and Pathway Genomics (Nordgren, 2014). Table 1 summarizes the advantages and disadvantages of DTC GT.

Many countries have put legislations that regulate DTC GT (Borry *et al.*, 2012). DTC GT affects children greatly because many tests aim at identifying the risks for adult-onset disorders, for example, breast cancers, ovarian cancers and Huntington disease (Howard *et al.*, 2011). There are no genetic testing consent regulations concerned with the results given by DTC GT websites. There is no monitoring of samples origin or the sample provider identity, which enables testing of a third party such as a minor (Howard and Borry, 2008). DTC GT websites might provide unbalanced information concerning the tests risks and benefits like uncertain test results, misinterpretations with potential emotional and psychological effects. The development of consumer genomics industry made international debate about the implications of widespread, medically unsupervised access to the genetic information (Goldsmith *et al.*, 2012).

Legal implications of genetic testing

The code of ethics of National Society of Genetic

Table 1 Advantages and disadvantages of direct-to-consumer genetic testing

Advantages of DTC GT	Disadvantages of DTC GT
It can provide information about disease predisposition and carrier status and give individuals health information based on their genetic testing results (Nordgren, 2014)	The deficiency of experienced pretest and posttest counseling, besides clinical interpretations of the result (Skirton *et al*., 2012)
It is relatively affordable and harmless to the consumer (Nordgren, 2014)	The consumer may take misguided healthcare decisions without any interpretive guidance from a licensed healthcare professional (Skirton *et al*., 2012)
Quicker and easier access to information (Wasson, 2008)	The test results might not satisfy the consumers' expectations and jeopardize their safety (Skirton *et al*., 2012)
It could prevent genetic discrimination as the genetic information would be accessed by individuals at home, in private, remaining outside the medical and employment records (Wasson, 2008)	A conflict of interest might develop when the healthcare professional, involved in the counseling, is employed by or linked to the companies selling the test. This could jeopardize the counseling process (Wasson, 2008)
It improves the education and awareness concerning genetics and genetic testing (Hawkins and Ho, 2012)	Deficient counseling would make consumers to take their test results to their primary care provider to help with interpretations. This leads to more burden on the physician and increases the cost for the healthcare system (Caulfield *et al*., 2010)

DTC GT, direct-to-consumer genetic testing.

Counselors states that the genetic counselor must respect the client beliefs, cultural traditions, circumstances and feelings. Justice in the context of genetic testing must be achieved on individual and societal levels. For individuals, it requires respect for individual rights, promotion of freedom of choice, and balancing optimal care practices against containment of testing costs to provide equitable care to all. At the societal level, justice is linked to public health initiatives and governmental rules to properly balance the benefits and burdens of genetic testing (Balcom *et al*., 2016). If every rule is part of code of ethics, exceptions could occur according to certain cases. So it is better to be under the supervisions of professional ethical committees (Conti, 2016). Biochemical genetic testing performed in different laboratories must submit to the Clinical Laboratory Improvement Amendment regulation. This is done to meet the general quality systems and individual requirement for complex tests (Centers for Disease Control and Prevention CDC, 2012). In the USA, three federal agencies participate in the regulations of genetic testing. These are as follows: Centers for Medicare and Medicaid Services, Food and Drug Administration (FDA) and the Federal Trade Commission (Centers for Medicare and Medicaid Services, 2007; U.S. Federal Trade Commission, 2009; U.S. Food and Drug Administration, 2010). Medicare and Medicaid Services are responsible for the regulations of all the clinical laboratories that perform genetic testing to ensure their compliances with the Clinical Laboratory Improvement Amendment of 1988 (U.S. Department of Health and Human Services, 2014). FDA has the highest authority regarding the regulations of safety and effectiveness of genetic testing. It has the authority to regulate commercial laboratory tests as devices if they are used in the diagnosis of disease or other conditions or in the cure, mitigation, treatment, or prevention of disease. Finally, Federal Trade Commission is concerned with the regulations of the genetic tests advertising to make sure that they are not misleading (El Shanti *et al*., 2015).

In the USA, although there are regulations provided by many states, the locations of genomic scanning facilities and online marketing services have allowed manufacturers to cross borders and bypass local laws. Moreover, online customers are recruited from all over the globe and ship tissue samples from outside which weakens state regulations (Hogarth *et al*., 2008). Secretary's Advisory Committee on Heritable Diseases in Newborns and Children was established in 2004 through federal legislation. It is responsible for regulating neonatal screening programs through a uniform screening panel (Kemper *et al*., 2014). There are certain rules defining the genetic legislations in the European Union (EU). Genetic data related to health are treated as sensitive data under the EU data protection directive and is therefore treated with confidentiality. In addition, discriminations based on genetics are forbidden in the EU member states. The first law concerning genetic testing was authorized in France in 1994. After that, legislations were validated in Norway, Spain, Italy, Germany, Austria, Portugal, Sweden and Switzerland (El Shanti *et al*., 2015). There are diversities among European countries regarding classifications of and access to genetic testing. Some European countries believe that genetic testing diagnosis or prediction is more important (Organization for Economic Co-Operation and Development OECD, 2007). The UK Genetic Testing Network developed a Gene Dossier to evaluate genetic testing and determine which tests should be used by the National Health System (Hogarth *et al*., 2007). The EU in-vitro diagnostic directive was designed in the year 2000 legislations to improve individuals' levels of health protection of the EU members. In Australia, Medicare regulates the

provision of pathology services through the department of health and aging administration of funding schemes for public health. For the Commonwealth government, the national association of testing authorities is responsible for regulating genetic testing. It is the only national accreditation authority to assess laboratory competency. The national pathology accreditation advisory council made guidelines to assess genetic testing through Medicare (El Shanti *et al.*, 2015). China started its own regulations on March 2014 through China food and drug administration. China food and drug administration is responsible for supervision on medical institutions and other providers of clinical genetic testing. On the international scale, owing to the deficient premarket approval for genetic testing, the FDA and the European Medicines Agency designed guidelines on Voluntary Genomic Data Submission in 2006 to regulate the outcome of genetic testing. On the contrary, data are not consistently collected because submissions are voluntary (Orr *et al.*, 2007).

In the Arab world, there are many challenges for genetic testing because it must be applied within the context of religions and cultures according to Islamic ethical and cultural backgrounds of individuals. In Islam, ethical decision making is carried out within a framework of values derived from revelations and tradition. It is intimately linked to the broad ethical teachings of the Holy Qur'an and the hadiths (statements) and sunna (traditions) of the Prophet Mohammed and thus to the interpretation of shariai'ha (Islamic law). Islamic ethics emphasizes prevention and teaches that the patient must be treated with respect and compassion and that the physical, mental and spiritual dimensions of the illness experience should be taken into account (Al-Aqeel, 2007). Where appropriate, consideration is also given to public interest and local customary precedent. Islamic law is in spirit dynamic and flexible, exemplified by the idea that 'necessity renders the prohibited permissible' (Al-Aqeel, 2005). Islamic teachings offer a great deal related to the prevention and care of genetic diseases and birth defects. Abortion is allowed before the 120th day of gestation if the fetus has a fatal condition. Abortion because of a serious fatal congenital disorder is carried out in some Muslim countries, legally in Tunisia and Iran. However, according to the fourth fatwa of the Islamic Jurisprudence Council of the Islamic World League, abortion is allowed after 120 days if there is a danger to maternal life, regardless of whether the fetus is normal or abnormal. In this case, termination of pregnancy goes against religious well-being, but it is done for the sake of the mother's health (Al-Aqeel, 2007). More difficulties are encountered with the community-based counseling in everyone language owing to limited knowledge, expertise, resources and technologies. Yet the availability of certain research centers and international collaborations made it more applicable for genetic testing and counseling, though there is a shortage of established networks of referral centers in the Arab world (El Shanti *et al.*, 2015). There are no laws to regulate genetic testing in Egypt. According to a survey from the UNESCO, only Lebanon has authorized a law that was specifically designed to regulate genetic testing. Regulations of genetic testing were not totally addressed for the rest of Arab countries. In particular, Egypt, Tunisia, UAE, Saudi Arabia, Palestine, Bahrain, Kuwait, Oman, Jordan and Algeria refer to genetic tests regarding premarital screening, reproductive medicine, forensic medicine and biobanking. They also referred to international guidelines and regulations which are accepted worldwide. Morocco and Syria have many laboratories for genetic testing, although they lack certain legislations (UNESCO Cairo Office, 2011).

Confidentiality

Confidentiality is very essential in preserving clients' autonomy. The potential for genetic testing to predict presymptomatic risks makes genetic information uniquely subjected to inappropriate use and patient discrimination. Confidentiality and patients privacies are therefore particularly critical regarding genetic testing. However, disclosure of genetic information, for example, genetic test results, pedigree analysis and risk assessment, can be very crucial to the patient's relatives. Breaching confidentiality to disclose medical information to relatives raised legal, ethical and psychosocial issues. There is a debate about whether or not the genetic counselor is legally permitted to disclose relevant data to relatives at risk as not all relatives desire to know genetic data. The effect of sharing data about the reproductive future may give rise to emotional and social problems for the family members. This could lead to withholding relevant data from other family members, and thereby not giving them options to perform testing. This conflict forces genetic professionals to balance competing obligations to protect the privacy of their patient against their duty to warn family members of potential risks for genetic disorder (Balcom *et al.*, 2016). In the USA, confidentiality is only broken on rare circumstances like when other lives may be endangered or uncooperative counselees. Regarding the insurance companies, counselors should stress that information is as private as they wish. In the UK, the highest standards of confidentiality are preserved (National Society of Genetic Counselors NSGC, 2015). Obtaining genetic testing insurance authorizations for patients is a complex, timely process and always requires genetic counselors and physician involvements. A sort of

collaboration emerged between genetic counselors, industrial engineers and patient services associates to alleviate this complexity and meet the increasing number of genetic testing insurance authorization requests (Uhlmann *et al.*, 2017). The counselor should suggest that other family members be told of risks of genetic diseases. Some opinions agree with reporting information to the public health authorities without permission of the counselee (American Academy of Pediatrics AAP Committee on Bioethics, AAP Committee on Genetics, American College of Medical Genetics and Genomics Social, Ethical, and Legal Issues Committee, 2013). On the contrary, many opinions refuse reporting information to public health authorities. The Health Insurance Portability and Accountability Act regulates the handling of protected health information. However, disclosure of results to unwanted parties like insurance companies, employers or public health authorities could occur. This shows the sensitive nature of genetic testing (Mackoff *et al.*, 2010).

Psychological implications of genetic testing

Advances in molecular medicine raised the interest in the psychological implications of these technologies. The psychological effect of genetic diseases varies with the severity and treatability and with the different responses of individuals and families. Psychologists could play a critical role in assisting patients and their families (Wakefield *et al.*, 2016). Genetic counseling with positive results of genetic testing may lead to anxiety, worry, guilt and depression (Cameron and Muller, 2009). Genetic testing may also lead to uncertain results, with unclear significance of the genetic alteration. This could have a negative effect on patients' psychology (van Dijk *et al.*, 2008). Additional psychological support should be provided with referral to a psychologist when needed. Children response might be affected when they observe their family's reactions on receiving the tests result. They may also struggle to understand what risks they personally face based on their family members' results which potentially increase anxiety and stress (Wakefield *et al.*, 2016). Psychological distress such as anxiety and depression is encountered when dealing with genetic testing on children. Other negative effects include guilt feeling and self-blame, loss of child's autonomy harming the child identity, especially the harm to self-concept and self-image with impaired quality of life and behavioral problems. There are negative effects on the family including survivor guilt whereby a sibling becomes withdrawn owing to tests outcomes and harms to the parent–child bonds. This could affect the emotional equilibrium of the family. In addition, there are negative effects on the community such as social isolation, stigmatizations or discriminations from a third party in education, employments and insurance (Cacioppo *et al.*, 2016).

The importance of education in genetic counseling

All healthcare providers, clinical geneticists and genetic counselors must have knowledge and skills regarding genetic and genomic testing. They also should excel in basic genetic counseling with interpreting the test results and communicating the results to patients and families. This could be achieved through educational programs about clinical, ethical, legal and psychosocial topics. Nondirective counseling without encouraging a particular course of action is the hallmark in the counseling process with respect of individual autonomy. The counselor should provide information about genetic risks and explain options concerning genetic testing and future managements without giving any specific recommendations. The presence of a psychiatrist could help in counseling to provide the counselee and family psychological support (American Academy of Pediatrics AAP Committee on Bioethics, AAP Committee on Genetics, American College of Medical Genetics and Genomics Social, Ethical, and Legal Issues Committee, 2013). Additionally, there must be a supporting system to integrate genetic information into clinical practice with collaboration among geneticists, governments and society. A well-informed society would take better individual and collective decisions. Likewise, suitable funds must be provided to support the genetic service and educational programs (Hyland *et al.*, 2013; Botkin *et al.*, 2015).

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