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Genetic Screening of Heredity Diseases

Donia Gamudi and Renald Blundell
Department of Physiology and Biochemistry,
University of Malta, Msida, Malta

Abstract: Clinical Genetics is concerned with the diagnosis and management of the medical, social and psychological aspects of hereditary disease. As in all other areas of medicine, it is essential to make the correct diagnosis and provide appropriate treatment which must include helping the affected person and family members understand and come to terms with the nature and consequences of the disease.

Key words: Clinic genetics, cancer, screening, ethical issues, genetic testing, medicine

INTRODUCTION

When a disorder is susceptible of being heritable, there are other things that need to be taken in consideration; the need to inform other family members of the risk they have to contract the disease as well of the means available that help them to modify these risks. Just as the unique feature of genetic disease is its tendency to recur within families, the unique aspect of genetic counselling is its focus, not only on the original patient, but also on the members of the patient's family, both present and future. Genetic counselling, a core activity in medical genetics is concerned not only with informing the patient and the family but also with providing psychological oriented counselling to help individuals adapt and adjust to the impact and implications of the disorder in the family (Nissbaum *et al*., 2004). The most common indications for genetic counselling are:

- Previous child with multiple congenital anomalies, mental retardation or an isolated birth defect such as neural tube defect, cleft lip and palate etc.
- Family history of a heritable condition such as Fragile X syndrome, cystic fibrosis, thalessemia and Huntington disease
- Consanguinity
- As a follow up for a positive newborn test e.g after testing positive for PKU

Established standards of medical care require that providers of genetic services obtain a history that includes family and ethnic information, advise patients as well as the other family member of the genetic risk, offer genetic testing or prenatal diagnosis when indicated and outline the various treatment or management options for reducing the risk of the disease (Andrews *et al*., 1994).

In some cases patients are not told what decisions to take as regards to the various testing and management options but instead are just provided with information and supportive care. This approach to counselling also known as non directive counselling has been adopted widely as the standard of practice in this field.

CLINICAL APPLICATIONS OF CANCER GENETICS

The ultimate goal of medical genetics is to improve the health and well being of the individuals, their families and society in general. With the information coming from the Human Genome project, it can anticipate that medical genetic technology, especially in the areas of testing and screening for hereditary disorders will have an even greater impact on the health and well being of the population. On the other hand, ethical values and social concerns must help shape the application of genetics so that we maximise the benefits and minimise any harm (Nissbaum *et al*., 2004).

Genetic screening is used to identify persons with certain genotypes known to be associated with a genetic disease or a predisposition to a genetic disease. Genetic screening is an important public health activity that will become more significant as more and better screening tests become available for hereditary disease and for other conditions with an identifiable genetic component (Nissbaum *et al*., 2004).

SCREENING OF NEWBORNS

The best known public health efforts are the government programmes that carry out population screening of all newborns to identify genetic disorders like thalessemia and phenylketonuria, for which early treatment can prevent or at least ameliorate, the consequences.

Corresponding Author: Renald Blundell, Department of Physiology and Biochemistry, University of Malta, Msida, Malta

The validity of the test results is particularly important, false positive results cause unnecessary concern to the parents, whereas false negative results vitiate the whole objective of the programme.

Two heritable conditions clearly satisfy all these criteria, Phenylketonuria (PKU) and galactosaemia. The prototype of such disorder is PKU. Routine neonatal screening for PKU is mandatory by law in all but one of the states in the United States and in almost all developed countries. Galactosaemia screening is less common. A number of other disorders such as sickle cell anaemia, congenital hearing loss, biotinidase deficiency, congenital adrenal hyperplasia ad various abnormalities of amino acid metabolism are less commonly screened for. The reasons for this are that they are not that common and effective treatment is not available (Andrews *et al*., 1994).

Not everyone agrees that screening should be performed only for highly treatable conditions. It has been argued, for example that the newborn screening for cystic fibrosis or severe combined immunodeficiency syndrome would benefit the newborn by allowing the institution of appropriate treatment while the newborn is relatively well, before the onset of malabsorption, failure to thrive and infections. For other conditions, such as Duchenne muscular dystrophy for which treatment is only palliative, early diagnosis might in theory, prompt genetic counselling to help parents in their planning of future pregnancies (Chadwick, 1999).

ADULT SCREENING

The concept of newborn screening has been extended to include adult screening. One of the first disease that was screened for was haemochromatosis. This is a relatively common autosomal recessive disorder, in which there is an overload of iron. This can lead to permanent liver, pancreatic and cardiac damage. Screening could be performed either by direct detection of the muatant alleles or by measuring a biochemical parameter, such as transferrin levels depending on which test proves to be the most cost effective. Treatment by repeated venesection to remove the red blood cells or rather the iron they contain is highly effective in preventing organ damage if initiated before symptoms develop. Thus, population screening could identify asymptomatic homozygotes, early enough to prevent serious morbidity and mortality (Chadwick, 1999).

HETEROZYGOTE SCREENING

In contrast to screening for genetic disease in newborns and adults, screening for carriers has as its main purpose, the identification of individuals who are themselves healthy but are at risk of having children with a severe autosomal recessive or X linked illness (Harper, 1997).

Current heterozygous screening programmes have focused on particular ethnic groups in which the frequency of a disorder is high enough to justify screening. Heterozygote screening has so far been used routinely for Tay Sachs disease and Canavan disease, both in the Ashkenzaic Jewish population, sickle cell anaemia in the African American population of North America and β-thalessemia in high incidence areas especially in Cyprus and Sardinia. Heterozygote screening is voluntary and focuses on individuals who identify themselves as being members of a particular high risk ethnic group (Hudson *et al*., 1995).

The impact of carrier screening in lowering the incidence of a genetic disease can be dramatic. Screening the Ashkenzaic Jewish population for Tay-Sachs, followed by prenatal diagnosis has lowered the incidence of Tay Sachs by 65-85% in this ethic group. Prevention of β thalessemia by carrier detection and prenatal diagnosis has brought about a similar drop in the incidence of disease in Cyprus and Sardinia. In contrast, attempts to screen for carriers of sickle cell anaemia in the US African American community have been less effective and have had little effect so far (Hudson *et al*., 1995).

ETHICAL ISSUES IN MEDICAL GENETICS

The successes of medical genetics have been accompanied by a parallel increase in ethical dilemmas and controversies. The new knowledge on screening and diagnosis of genetic disorders is to be used judiciously for the benefit and not to the detriment, of individuals, their families and society as a whole. With the initiation of the Human Genome project in the united states, the U.S. Congress recognised the ethical dilemmas and the potential for serious societal harm from the misuse of this vastly expanded knowledge of human genetics. The congress responded by mandating that a portion of the U.S. Human Genome Project budget is to be used to support Ethical, Legal and Social Implications (ELSI) of the project (Hudson *et al*., 1995).

In any discussion on ethical issues in medicine, three cardinal principles are frequently cited: beneficence (doing good for the patient) respect for individual autonomy (safeguarding an individual's rights to control his or he medical care and be free of coercion) and justice (ensuring that all individuals are treated equally and fairly). Complex ethical issues arise when these three cardinal principles are perceived to be in conflict with one another (Lapham *et al*., 1996).

ETHICAL DILEMMAS IN PRENATAL GENETIC TESTING

Geneticists are frequently asked to help couples use prenatal diagnosis or assisted reproductive technology to avoid having offspring with a serious hereditary disorder. It should be recognised that for some hereditary disorders, prenatal diagnosis remains controversial, especially when the diagnosis leads to a decision to abort the pregnancy for a disease that is untreatable. The dilemma is even more acute when a couple makes a similar request for pregnancy that is not at risk for a serious disease or disability. The motivation for seeking prenatal diagnosis might include avoiding recurrence of a disorder associated with a mild or a cosmetic defect or for selection of sex. The issue of sex selection for reasons other than reducing the risk for sex limited or X linked disease is a very contentious one.

In the future particular alleles and genes that contribute to complex traits such as intelligence, personality, stature and other physical characteristics may possibly be identified during the course of the human genome project. Will such non medical criteria be viewed as a justifiable basis for prenatal diagnosis ? some might argue that parents are to varying extents, already expending tremendous effort and resources on improving the environmental factors that contribute to healthy successful children. They might therefore ask why not improve the genetic factors as well? Others consider prenatal selection for particular desirable genes as a dehumanizing step that treats children simply as commodities fashioned for their parents' benefit (Lapham *et al*., 1996).

Does the health professional have on the one hand a responsibility and on the other hand, the right to decide for a couple when a disorder is not serious enough to warrant prenatal diagnosis and abortion or assisted reproduction? The debate continues about where or even whether one can draw the line in deciding what constitutes a serious enough trait to warrant the application of prenatal testing technology (Lapham *et al*., 1996).

Another area of medical genetics in which ethical dilemmas frequently arise involves genetic testing that may have a much later onset in life than when the molecular testing is being performed. A good example of this is the testing done for Huntington disease. In this disease individuals carrying a mutant allele are asymptomatic early on in life but they will develop a devastating illness later on in life for which there is little or no treatment (Lapham *et al*., 1996). For any presymptomatic individual is knowledge of the test result more beneficial than harmful, or vice versa? How does the balance shift when testing for predisposing mutations that predispose to disease but may not inevitably cause disease? For example in autosomal dominant hereditary breast cancer, individuals carrying mutations in the BRCA1 or *BRCA2* have a 50-90% chance of developing breast or ovarian cancer. Identifying heterozygote carriers could have benefits, because individuals at risk could choose to undergo more frequent surveillance or preventive surgery such as mastectomy and oophorectomy. These measures reduce but do not eliminate the increased risk of breast cancer. On being tested for a predisposing gene mutation, these individuals incur the risk of stigmatization in their social lives and discrimination in insurance and employment (Hudson *et al*., 1995).

The ethical decision to be tested or not is an absolute decision made in a vacuum. The patient must take an informed decision using all available information concerning the risk for and severity of the disease, the effectiveness of preventive and therapeutic measures and the potential harm that could arise from testing (Hudson *et al*., 1995).

GENETIC TESTING IN CHILDREN

Additional ethical problems arise when genetic testing involves children. As with adults, testing healthy children for late onset disease is beneficial if interventions that decrease morbidity or increase longevity are available. Genetic testing in children also carries the risk of stigmatisation, psychological damage and insurance and employment discrimination. This needs to be taken into consideration prior to testing. Another ethical principle that needs to be considered is autonomy. Children's autonomy their ability to make decisions for themselves about their own genetic constitution must be balanced with the desire of parents to obtain such information. There are various reasons why parents may wish to have their children tested. Some might argue that even if there are no clear medical interventions, it's the parents duty to inform and prepare their children for the future possibility of developing a serious illness. The parents may also seek this information for their own family planning o to avoid what some parents consider the corrosive effects of keeping important information about their children from them (Hudson *et al*., 1995). The preponderance of opinion among bioethicists is that unless there is a clear benefit to the child, testifying for a late onset disease or a carrier state should only be done when the child is sufficiently mature enough to take informed decisions (Lapham *et al*.,1996).

PRIVACY OF GENETIC INFORMATION AND ITS MISUSE

A third major ethical principle, along with beneficence and respect to autonomy is justice-the requirement that everyone would be able to benefit equally from progress in medical genetics. Is it fair to stigmatize people who without a fault of their own are found to carry a genetic predisposition to a disease?

As regard employment should employers be able to obtain genetic information in making hiring decisions, if that information helps them choose healthy employees with low absenteeism? Some have argued that an employer who funds an employee health care plan should have an access to such information in making hiring decisions so that the employer can refuse to hire individuals at risk of developing a serious illness later in life that could bankrupt the employee health plan (Pokorsi, 1997).

In the area of life insurance, insurers insist that they must have an access to all pertinent genetic information about an individual that the individual himself or herself has. Life insurance companies calculate their premiums based on actuarial tables of age specific survival averaged over the population. Premiums will not cover losses if individuals with private knowledge that they are at a higher risk for disease, conceal this information and buy extra life insurance (Pokorsi, 1997).

As can be seen from the above examples, medical genetics will have a profound impact beyond the narrow confines of medical practice. Integrating this knowledge into sound public policy will require the coordinated efforts of government, employers and the public (Pokorsi, 1997).

CONCLUSION

It should be emphasised that genetic counselling is not limited to the provision of information and calculation of the risk of the disease but it's a communication process. The ability to define and address the complex psychosocial issues associated with a genetic disorder is central to this practice.

In the future as the knowledge base of medical genetics expands, the scope of genetic counselling will increase proportionately. For physicians, the challenge Is to appreciate the importance of genetic counselling in medical practice, to understand its scientific basis and to be aware of the limitations of their knowledge. Sir William Osler wrote in a clinical context but could have been well discussing genetic risk, errors of judgement are bound to occur in the practice of an art that consists largely in balancing probabilities.

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