
MEDICAL, ETHICAL, LEGAL AND SOCIAL ISSUES IN GENETIC TESTING AND GENETIC SCREENING PROGRAMMES

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Dr Denise Goh Li Meng

MBBS(Hon), MMed, MRCP, MD, Dip ABMG, FAMS, FACMG
Consultant, National University Hospital
Assistant Professor, National University of Singapore

Genetic Testing

Introduction

Over the last decade, there has been tremendous, almost exponential, growth in the knowledge we have about the roles genes play in causing disease. It is estimated that the genetic bases of more than 1600 diseases have been identified while even more are being investigated. As a consequence, genetic testing has moved from the realm of the imagination into the world of reality. Twenty years ago, only a handful of genetic tests existed. Today, there are more than 700 different genetic tests available.

Definition of Genetic Tests

There is no universally accepted definition of what constitutes a genetic test.¹ A genetic test can be defined by its objective. Namely, it is any test or procedure performed to identify individuals with or at risk of developing a genetic disorder. This broad definition incorporates history taking, physical examinations, and laboratory tests as examples. If a genetic test is restricted to laboratory techniques that are used to achieve the above aim, then a genetic test is a laboratory test that can be based on protein, RNA, DNA or chromosome analysis. This definition can be further narrowed to tests that only directly analyse DNA, RNA or chromosomes.

There are several main reasons why different definitions of genetic tests exist. First, the impact genetic testing has made in medical practice is not yet comprehensive. Hence, clinical diagnostic criteria are still the main means of diagnosing many genetic conditions (e.g. Neurofibromatosis Type 1, Marfan Syndrome).^{2, 3} Second, a genetic condition can be diagnosed through different types of laboratory tests. For example, Tay Sach's Disease can be diagnosed based on protein or DNA analysis.⁴ Cost and clinical indications drive the choice to use a particular test. Third, with a global push towards regulation of genetic testing, there are concerns that the broader definitions would impinge upon the use of many common laboratory tests. Tests that are not primarily used to detect genetic diseases but can indirectly reveal a genetic disorder particularly represent this threat (e.g. full blood count, blood lipid profile). Given these reasons, there is a trend towards using the narrowest definition when defining a genetic test.

What Are the Reasons for Doing Genetic Testing?

Genetic testing is usually done for the following purposes:

1. to confirm a specific diagnosis in a symptomatic individual (diagnostic testing);
2. to ascertain the risk of having a particular condition in an asymptomatic individual (predictive/susceptibility testing);
3. to ascertain the risk of transmitting a condition (carrier testing);
4. to ascertain if a foetus has a clinically significant genetic disorder (prenatal diagnosis);
5. for identity or forensic testing;
6. for paternity or relationship testing; and
7. for research.

The first four objectives can be grouped under the heading “clinical genetic testing”. Most clinical genetic testing is physician initiated. Doctors tend to offer genetic testing when there is suspicion that a gene contributes to the pathogenesis of the disease, and when such testing is available. The knowledge of the genetic basis of a disease and availability of genetic tests is highly dependent on the type of genetic disorder involved. The current situation is biased towards single gene disorders as these have been the simplest for researchers to decipher. Single gene disorders are one of the three main groups of genetic disorders. The other two are chromosomal and multi-factorial disorders.

1. Single Gene Disorders

A single gene disorder is caused by a change in a single gene. There are many different types of single gene disorders. Individually, they are usually rare but, overall they affect ~2% of the population over a lifetime. If the gene for the disease has been identified, it is likely that genetic testing is available or will be available soon for clinical use.

2. Chromosomal Disorders

Individuals with chromosomal disorders have either a deficiency or excess of a chromosome or of part of one. Problems are caused by such deficiencies or excesses. Down’s syndrome is an example of this disorder type. Chromosomal disorders are relatively common. About 15% of pregnancies end in first trimester miscarriages, half of which are due to chromosomal defects. In addition, ~0.7% of babies born have chromosomal defects. Karyotype and fluorescent *in situ* hybridisation (FISH) are common tests used to identify chromosome defects.

3. Multi-factorial Disorders

This group of diseases arises due to the interplay of multiple factors that can include both genetic and environmental factors. Multi-factorial disorders encompass many diseases ranging from birth defects in babies to common disorders in adults (e.g. heart disease, diabetes mellitus). It is estimated that this group of disorders affects

more than 60% of the population. Genetic testing is currently not available for most of these diseases because the contribution of genetic variation to the disease process is not yet fully understood.

Who Has Access to Genetic Testing?

Access to clinical genetic testing is mainly through physicians. This is reinforced by the fact that most laboratories require a physician to countersign the order forms as well as provide documentation that informed consent was obtained. Identity or forensic testing is used mainly by law enforcement and legal services. Paternity or relationship testing is the one form of genetic testing that the public can freely access.

Access to research genetic testing is a more complex matter. It is largely determined by whether an individual meets a researcher's requirements and whether the individual gives informed consent. The individual must be willing to undergo tests to advance scientific and medical knowledge. There is usually no direct benefit to the individual participating in the research study. Oversight of ethical concerns in research is administered by Institutional Review Boards (IRBs).

What is the Process of Clinical Genetic Testing Like?

If a doctor determines that it is appropriate to offer a patient genetic testing for clinical purposes, he must obtain informed consent prior to testing. Informed consent is the process by which a person is made fully aware of his options and participates in his choices about health care. In genetic testing, this process is also called genetic counselling. Issues that should be discussed include the following:

1. Genetic testing is voluntary and consent is required to proceed;
2. Time should be taken to ask all questions needed to make an independent personal decision. After consent is given, withdrawal of consent can be done at any time or the disclosure of the results postponed;
3. The major medical facts of the disorder (diagnosis, prognosis, treatments available, inheritance pattern, and risks of recurrence in the family);
4. The implications of genetic testing (implications to other family members, detection of non-paternity, and possibility of psychological stress);
5. Sample required and possible side effects of the sample taking procedure;
6. Test procedure and expected turnaround time;
7. Accuracy of test results;
8. Confidentiality of results; and
9. Alternatives to gene testing.

The result of genetic testing is almost never released directly by the laboratory to the patient. As the interpretation of test results are complex, a follow-up visit is usually arranged so that a qualified person can explain the results and implications to the individual in simple layman language. The individual's reaction, expectations and questions will have to be addressed and follow up treatment instituted if indicated.

What is the Current Situation in Singapore?

In Singapore, there are many clinical genetic tests locally available. For tests that are only available abroad, it is usually quite simple for the physician to send a sample there for testing. Clinical genetic testing is mainly physician initiated. Patients initiate a small proportion of genetic testing, and usually request carrier, prenatal or presymptomatic diagnoses. Direct test requisition by the public is very limited as most genetic testing centres require the intermediation of a qualified healthcare professional (e.g. signature of a referral physician stating that the appropriate matters were explained and counselled). The exception is paternity and relatedness testing, where direct access by the customer is possible.

Genetic Counselling

Genetic counselling refers to the process of helping individuals understand their risks of having a genetic disorder, the risks of passing on a genetic disorder to the next generation and/or choices available to them. It enables a person to make an informed decision about the options available to them.

There are two main groups of individuals who benefit from genetic counselling: (1) individuals at risk for passing on a genetic disorder; and (2) individuals participating in a screening programme.

Individuals at risk of passing on a genetic disorder are usually identified because there is:

1. a previous affected child or family history of birth defects such as cleft lip/palate, neural tube defects, club foot and congenital heart disease;
2. a previous affected child or family history of mental retardation or developmental delays;
3. a previous affected child or family history of a known or suspected genetic disorder;
4. a known chromosomal abnormality in the family;
5. a history of multiple miscarriages or still births; or
6. the individual is a female above the age of 35.

Special Considerations in Genetic Counselling

Except for cases with children, the process of genetic counselling is quite standard. In children's cases where the prognosis or implications are grave, it is sometimes prudent not to have the child present. This will enable full disclosure to the parents and for the parents to ask questions freely without inhibition. In addition, it will reduce the risks of the child misunderstanding the complicated and complex matters that are likely to be raised and discussed.

Personnel who are familiar with the conditions, testing and interpretation of the results should carry out genetic counselling. This includes individuals such as physicians,

geneticists, genetic counsellors and nurse clinicians. Average doctors and nurses with no experience or training in genetic conditions are likely unable to provide adequate counsel.

The need for genetic counselling, especially in population based screening programs, will create manpower problems in light of the large numbers involved. For common screening tests where the indications, procedures and outcomes are relatively standard, this can be overcome (1) by having non-medical practitioners such as genetic counsellors and nurse clinicians to take the lead and front line, and (2) by disseminating information through written material. There should still be a physician/geneticist involved in the event of an unusual circumstance or result. For less common conditions, the physician/geneticist should be the primary person involved.

In several foreign countries, a genetic counsellor has a master's degree in genetic counselling and has passed a certification examination. In addition, many belong to professional organisations that recommend professional standards for genetic counsellors. These organisations include:

1. The American Board of Genetic Counselling
2. The National Society of Genetic Counsellors
3. The American Board of Medical Genetics
4. The American College of Medical Genetics
5. Australian Society of Genetic Counsellors
6. Canadian Association of Genetic Counsellors
7. European Society of Human Genetics

Genetic counselling will probably reduce ethical, legal or social concerns arising from genetic screening or testing. Hence, it is important to ensure that it occurs and is of an acceptable standard.

Medical Issues in Clinical Genetic Testing

One of the biggest medical challenges in clinical genetic testing is accurate interpretation of test results. This requires expert knowledge about the patient, disease and accuracy of the tests. Accuracy of the test is dependent on two main factors: 1) integrity of the diagnostic chain (i.e. ensuring no sample switch, contamination etc.) and 2) advantages and limitations of each particular test. The two examples below illustrate the complexity involved in clinical genetic testing.

Example 1: Genetic testing for diagnostic purposes. A positive test result is relatively straightforward and interpretation is uncomplicated. A positive test confirms the clinical diagnosis, may give a prediction of the course of illness, can lead to a better choice in treatment and can be used to identify at-risk family members. The interpretation of a negative test result is less intuitive. If an affected person tests negative, the clinical diagnosis is not necessarily wrong. This negative test result may have arisen because (1) a mutation is present but the test could not find it or (2) another gene is causing the disease. What it does mean is that the individual's outlook and

treatment is not tailored, and at-risk family members are not likely to benefit from predictive testing.

Example 2: Genetic testing for predictive purposes (i.e. a test used to determine if an asymptomatic person is at risk of developing a genetic disorder). The utility of predictive testing hinges on (1) whether we know the mutation in the family and (2) the extent of the gene's contribution to the disease process.

- (1) Assuming we have identified the mutation in the family, the genetic tests serve to answer the question "Does this individual have the family's mutation?" If this person tests negative, then he/she is unlikely to develop that disease. If this person tests positive, then he/she has a risk of developing that disease. However, this risk may be complicated to quantify because (1) the certainty of having disease may not be 100% (non-penetrance), (2) lack of genotype-phenotype correlation.
- (2) If we don't know the mutation in the family, the genetic tests serve to answer the question "Is there a significant mutation present in this gene?" If this person tests positive, then he/she has a risk of developing that disease. Similar to the above situation, this risk may be difficult to quantify because (1) the certainty of having disease may not be 100% (non-penetrance) or (2) a lack of genotype-phenotype correlation exists. If the person tests negative, this does not exclude the possibility of still being at risk because (1) a mutation may be present but a test could not find it, or (2) another gene is causing the disease.

Legal, Social and Ethical Issues in Clinical Genetic Testing

Clinical genetic testing and population genetic screening programs are already a part of medical practice, and it is likely that more tests and programs will be established as the knowledge of the roles genes play in the disease process grows. Apart from medical implications, there are also many legal, ethical and social implications. Examples include access to genetic tests, the use of genetic tests in subgroups that are potentially vulnerable to being abused, risks for psychological stress and risks for discrimination.

Access to Genetic Tests

Currently, access to direct testing by the public is very limited as most genetic testing laboratories require the mediation of a qualified healthcare professional (e.g. signature of a referral physician stating that the appropriate matters were explained and counselled). If genetic testing is directly available to the public, the potential consequences may include:

1. more privacy and confidentiality if anonymous testing is allowed;
2. greater ease in using genetic tests;
3. unethical use of genetic tests (e.g. vulnerable individuals may be tested for the benefits of others) or unethical motivations (e.g. eugenics); and

4. the tested individual may not be fully aware of the implications of testing and suffers untoward consequences (e.g. misinterpretation of results leading to unnecessary medical/social interventions).

To minimise the potential harm to the individual being tested, it is probably prudent to continue to limit direct access to genetic testing. In reality, however, this may be difficult to achieve as genetic tests are likely to be available in other countries. If the local authorities limit local direct access, the motivated individual may still be able to have access to direct testing by travelling to another country, for example, or by requesting testing via the internet. One can only hope that genetic testing laboratories will shoulder the onus of maintaining good standards of practice. Even then, one wonders if the public would be able to discern and understand the significance of such measures.

Genetic Tests and Vulnerable Groups

There are certain subgroups of the population that may be more likely to be harmed by genetic testing. These individuals are usually considered to be vulnerable either because (1) the person being tested is unable or incapable for providing consent (e.g. minors or mentally incompetent individuals); or (2) there are concerns about the validity of the consent (e.g. less educated persons, language issues, prisoners or students).

Minors with genetic diseases tend to fall into one of these groups:

1. Symptomatic at diagnosis;
2. Asymptomatic at evaluation, at risk of developing disease childhood/adulthood, availability of intervention or treatment during childhood;
3. Asymptomatic at evaluation, at risk of developing disease adulthood, availability of intervention or treatment only during adulthood; and
4. Asymptomatic at evaluation, at risk of developing disease, no intervention or treatment available.

The issue of testing minors in groups (1) and (2) is quite clear; it is generally accepted that these individuals can be tested because test results are likely to directly benefit them. The issue of genetic testing in minors in groups (3) and (4) is more controversial. The concern is that the person giving consent may have a vested interest in the outcome of the genetic tests, and this interest may not be in the best interest of the child. Moreover, one should also consider protecting the child's right to make his/her own decision when he/she is an adult. The counter argument is that science is rapidly advancing and intervention or treatment in childhood may become available, and to maximally benefit from such advancement, a person must know whether he has the disease. This issue has been widely debated and it is generally felt that genetic testing should not be performed in minors in groups (3) and (4). Every effort must be made to protect the privacy of the child and his right "not to know" his genetic risk.^{5,6}

There are also other vulnerable groups that pose challenges to the medical community. Mentally incompetent individuals are one such group. The physician needs to determine that the legal guardian providing consent does not benefit more from the

results than the affected individual. Non-educated persons and individuals with language issues are another vulnerable group as they may not be able to comprehend and give truly informed consent. These situations involve less educated persons and individuals with language issues. Prisoners and students are also vulnerable as they may feel coerced into giving consent to participate in genetic tests. In such cases, precautions should be taken to ensure that free and informed consent is possible (e.g. having an independent review committee). As mentally incompetent persons are unable to provide informed consent for genetic testing, genetic testing may only be allowed if there are direct benefits for the mentally incompetent individual.

Risks for Psychological Stress

The process of genetic testing may put an individual under a lot of psychological stress (e.g. guilt, anxiety, self-doubt, fear and despair) because no treatment is available. To reduce the amount of stress, doctors should ensure patients that there is an acceptable turnaround time for genetic tests and that counselling can be provided to help them cope.

Risks for Discrimination

There are concerns that genetic testing results may lead to discrimination due to misinterpretation of test result implications. In particular, there is great concern that there will be discrimination by employers, insurance providers and society. Will insurance company understand and correctly comprehend such complex results? Will they take the conservative view and err on the side of caution and discriminate against such at risk individuals? Will employers do likewise? Will these individuals be socially stigmatised? Some of these scenarios have yet to be played out in reality, while others have occurred (e.g. job discrimination in sickle cell trait carriers as a consequence of poor public understanding of the condition).⁷

To maximise the health benefits of genetic testing, it is important to address these concerns. One means of safeguarding against discrimination is to address the confidentiality of genetic testing. Under current practices, genetic results along with other non-genetic results are released whenever a standard medical report is requested. We should continue to allow medical personnel easy access to such results, as access will enhance management of the patient. We may want to consider restricting access by non-medical persons (e.g. insurers and employers) as they may not be able to understand or correctly comprehend such complex results.

Another means is to ensure that genetic tests are conducted with accuracy and offer a comprehensible interpretation of results. Ensuring accuracy of the test itself is fairly easy as there are acceptable laboratory standards available. Ensuring accurate interpretation by other health professionals and clear communication of that piece of information to the patient is much more difficult. We may need to restrict the interpretation of such results to appropriately qualified persons and may need to standardise certain aspects of test result reporting. However, if we choose to regulate

genetic testing services, we must ensure that our regulations keep up to date with the rapidly changing technology. If not, we will do more harm by hindering medical care.

Population Genetic Screening Programmes

Definition and Aim of a Population Genetic Screening Programme

Most genetic tests are performed on individuals for reasons that are particular to that patient's condition. When a test is used to test large numbers of persons to determine their status with regards to a genetic condition, this test usually becomes part of a population genetic screening programme whose aim is to reduce the morbidity and mortality in the general population. While many of the issues previously raised do apply, there are additional special considerations to bear in mind.

In a population genetic screening programme, history taking, physical examination and/or tests are used to presumptively identify persons who may have a genetic disease, who may be at risk of developing a genetic disease or who are predisposed to having children with a genetic disease. The persons identified by such means are then referred for diagnostic/ confirmatory tests. This approach is usually chosen when the diagnostic/confirmatory test is not the ideal tool for use on the general population (e.g. it is riskier, more expensive, more time consuming etc.).

How Do We Decide If a Genetic Screening Programme is Worthwhile?

As a population genetic screening programme may touch the lives of many persons, it is important that its benefits must outweigh its costs or disadvantages. This is usually ascertained by determining if a screening programme

- Targets a suitable disease;
- Uses a suitable screening test;
- Uses a suitable diagnostic test; and
- Administers a suitable screening process.

A suitable disease is one that has significant morbidity and mortality, occurs at significant frequency in the population, has a period where one can intervene, and where intervention has been shown to be effective. A suitable screening test is one that has a high test accuracy and reliability and is relatively cheap, free from risk and acceptable to the population. A suitable diagnostic test is one that can accurately identify people with the disease or at risk for it. A suitable screening process is one that has a reasonable turnaround time, is capable of recalling persons and is carried out in a socially and ethically accepted manner.

What is the Process of Genetic Screening Like?

If a person fulfils the criteria for having a screening test, the individual will be counselled on relevant issues that are similar to those discussed in clinical genetic testing (see above). The one exception is the implication of test results. Individuals who

test positive on a screening test are only at risk of having the disease and may not necessarily have the disease. These individuals are then referred for further diagnostic testing to ascertain if they truly have the condition.

An analogy of this process can be found in the airport. A gun on an airplane is a condition that can potentially lead to increased morbidity and mortality. If one is able to detect it prior to it being on the airplane, one can reduce morbidity and mortality. A gate-type metal detector is a suitable screening test. It is relatively cheap, does not harm the passengers, can be done efficiently and has an acceptable rate of accuracy and reliability. Hence, it is acceptable to most passengers. If a passenger “tests positive” on the screening, this does not necessarily mean that the passenger has a gun. The passenger is then referred to a diagnostic test (e.g. a hand wand metal detector or a check by a law enforcer) to determine if the passenger truly has a gun. To be effective, these elements must be part of a reliable screening process. In other words, the system must be used to screen all passengers and administered in a reasonable time frame so as to avoid delaying air travel etc.

Are Population Genetic Screening Programmes Subject to Medical Research?

The primary aim of a genetic screening programme remains the safeguard or promotion of immediate well being of the screened subject. At certain points, the performance of the screening program will be and should be audited. Indices such as sensitivity, specificity and cost effectiveness may be derived with the intention of assessing the utility and safety of the program. One of the consequences of this primary aim may be the publication of the assessment in a research journal.

Research as a primary objective is usually confined to the development phase of a genetic screening test or program. The aims of such research are usually (1) to develop a test that will discern between asymptomatic people at an increased risk and asymptomatic people at no increased risk, and (2) to assess the effectiveness and feasibility of the test at a population level. When research is the primary aim, consent and ethical approval are required.

What are the Population Genetic Screening Programmes Available in Singapore?

There are several population genetic screening programmes currently available in Singapore. Their aims remain true to the general philosophy (i.e. testing large numbers of persons in order to determine their status with regards to a genetic condition so as to reduce the morbidity and mortality in the general population). The genetic conditions tested include chromosomal disorders, risk for blood group incompatibility, thalassaemia, foetal abnormalities and certain metabolic disorders.⁸ These are conducted during several key times in a person’s life.

1. Pre-pregnancy:
 - a. Screening for a history of infertility, miscarriages, or abnormal children
 - b. Full blood count (Haemoglobin, mean corpuscular volume)
 - c. ABO/Rh blood grouping

2. Pregnancy
 - a. Maternal: Triple maternal serum screen
 - b. Foetal
 - i. Ultrasound scan for structural abnormalities
 - ii. Amniotic fluid for alpha-foeto-protein
3. Postnatal
 - a. Physical exam at birth
 - b. Congenital hypothyroidism
 - c. Glucose-6-Phosphate Deficiency
 - d. Screening for hearing loss
 - e. Screening for metabolic diseases in certain sub-populations

Most of these screening programmes are carried out after obtaining verbal consent. For mostly historical reasons, written informed consent is not widely used; these programs were established in previous decades when written consent was not practiced. While these programmes have become socially acceptable and even expected, the rapid expansion of genetic knowledge means that more genetic screening programmes are likely to come into existence. Thus, the issue of consent will need to be examined. Should written consent be required for future genetic screening programmes? Should it be an active process i.e. informed consent (opting in) or a passive process i.e. informed dissent (opting out)?

Case illustration: screening programme for Down syndrome

Down syndrome is a genetic disorder of significant occurrence. A significant proportion of the population finds it acceptable to screen for Down syndrome in the antenatal period so as to have the choice to intervene. Ideally, the test used should be highly accurate and reliable. However, tests with such desired accuracy and reliability require obtaining a sample from the foetus. Such a procedure has an estimated 0.5% risk of causing harm to the mother and the foetus. For women 35 years and above, the risk of having a child with Down syndrome is ~0.5%, hence it is ethical to offer these invasive tests as both a screening and diagnostic test since the risk of harm is equal to the risk of having a child with the disorder.

However, for women below 35 years old, it is not ethical to use this as a screening test because their risk of having a child with Down syndrome is much less than the risk of harm from the procedure. Needing a different approach, non-invasive screening tests were developed. These tests involve a combination of blood tests and ultrasound scans of the foetus. Using certain cut-off values, the screening process will pick up about 90% of pregnancies with Down syndrome; however, 5% of normal pregnancies are also flagged (false positive). In order to sort this out, these individuals are then offered the invasive diagnostic test.

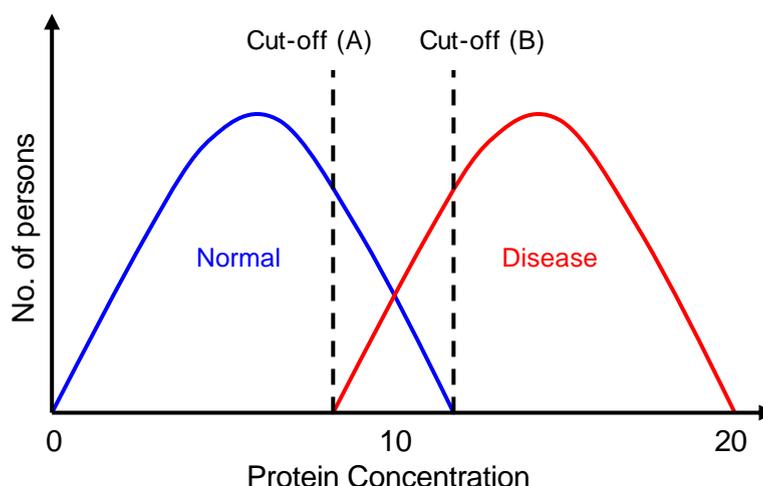
If a couple is not keen to undergo such testing (e.g. it poses a risk to the baby, or they have no intention to terminate the pregnancy) then they should think twice about having such screening tests. As such issues are difficult to anticipate and appreciate

prior to testing, it is essential that genetic counselling be given and consent taken prior to undergoing the screening tests.

What are the Medical Implications of a Genetic Screening Programme?

One major implication of the demands placed on a justifiable screening programme is its effect on the type of disease the programme can screen. These criteria favour conditions that have significant morbidity and mortality, occur at significant frequency in the population and have a period during which intervention has been shown to reduce morbidity and mortality. Diseases that are rare, not treatable or do not improve with treatment are unlikely to be selected for a population screening programme. Exceptions do occur, but usually involve conditions that are associated with specific sub-populations (e.g. Ashkenazi Jews and Tay Sachs's Disease, Caucasians and Cystic Fibrosis^{7,9,10}).

Another implication is the possibility that a screening programme may miss affected persons and/or falsely alarm unaffected persons. Ideally, the screening test should have high accuracy and reliability, and be capable of completely distinguishing the affected from the unaffected. In reality, however, this may be difficult because the test values in affected and unaffected individuals may overlap (see figure). In such instances, a cut-off value must be chosen for use in differentiating between a "normal" and an "abnormal" test result. If the cut-off point is placed high (B), the test will be very specific and will pick up only those who are truly affected. However, it will miss some of the affected and give these individuals a false sense of security (a false negative result). If the cut-off point is chosen low (A), then the test will be very sensitive and will pick up all who are truly affected, but will also label many normal individuals as "abnormal" (a false positive result). In this scenario, a more definitive diagnostic/confirmatory test is then needed to differentiate between true positives and false positives. If a person tests "abnormal" on the diagnostic test, then they have or are at risk of the disease. If they test "normal", then they are unlikely to have the disease. Thus, the decision as to which cut-off value to use must take into consideration the disease involved, the cost effectiveness, the consequences of missing those with the disease and the amount of anxiety afflicted on those labelled falsely as affected.



The dissemination of accurate and comprehensible information is an important criterion for an effective screening program. However, the objectives, screening process and potential need for further testing are difficult issues for both the public and medical community to anticipate and appreciate. In addition, the interpretation of a screening test result requires a physician who understands the accuracy, reliability and cut-off values of the test as well as the disease involved. Two major challenges therefore arise: (1) how to ensure that the individual is aware of the consequences of their choice to participate; and (2) how to ensure that physicians have the correct knowledge to interpret the tests results.

The first challenge involves the issue of informed consent. How do screening programs ensure that their participants have given informed consent? This is achieved through the process of genetic counselling where a trained professional explains such matters to the individual. Educational pamphlets can also be used to further ensure that an individual is fully informed. The issues that need to be discussed generally include the following:

1. the nature of the condition being screened including diagnosis, prognosis, treatments available, inheritance pattern, risks of recurrence in the family;
2. that participation is voluntary;
3. the sample required and possible side effects of the sample collecting procedure;
4. the screening process;
5. the implications of a positive or negative test, and potential need for further diagnostic testing;
6. the potential to uncover undisclosed non-paternity, if applicable to the test; and
7. the confidentiality of results. Genetic screening results are accorded the same level of confidentiality as regular medical records.

The second challenge concerns the education of medical and paramedical staff. This can be facilitated by using continuing medical education programs that are already in existence in many countries, including Singapore. In addition, educational websites can be set up to provide information for both the public and professional community. Printed educational material can also be distributed through the registry of medical professionals. Finally, the results of screening tests can be issued with the correct test

interpretation to reduce the burden on the individual physician to interpret the test findings.

Conclusion

The influence of genetics in medicine is growing and will continue to grow. While it carries with it much promise for improving the prevention and treatment of diseases, there are potential obstacles and repercussions that may hamper this vision. Some of these issues have been highlighted in this paper. We have a unique opportunity to recommend ways of safeguarding ourselves before a negative incident happens, and we should seize this chance. After all, prevention is the best cure.

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