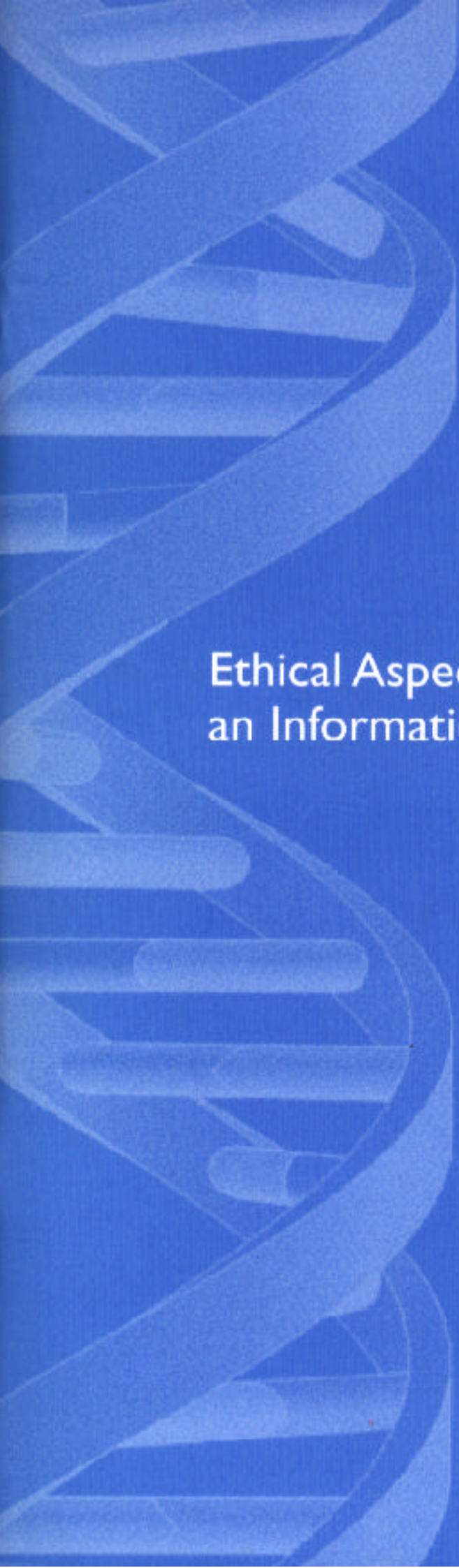

Ethical Aspects of Human Genetic Testing: an Information Paper

NHMRC
National Health and Medical Research Council

Ethical Aspects of Human Genetic Testing: an Information Paper

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CONTENTS

Preamble **5**

Chapter 1 The special nature of genetic information **7**

1.1 Some basic genetics 7

1.2 Genetic disorders 8

1.3 Genetic material, genetic tests and genetic information 9

1.4 The shared nature of genetic information 10

1.5 The uniquely personal and identifying nature of genetic information 10

1.6 The possibility of predicting future disease/health risks 11

1.7 The probabilistic nature of genetic information 12

1.8 The potential for misuse of genetic information 13

1.9 'Geneticisation' 14

Chapter 2 Genetic testing and the storage of genetic material/ information **15**

2.1 Types of genetic test 15

2.2 Other times when tests are performed 17

2.3 The test material 20

2.4 Performance of the test 21

2.5 Test quality 23

2.6 Test cost 23

2.7 Storage of genetic information and genetic material 24

2.8 Equity of access to genetic testing 26

2.9 Commercialisation and direct marketing of genetic tests 26

2.10 Allocation of resources for genetic testing 27

Chapter 3 Consent to genetic testing **29**

3.1 The setting in which genetic testing takes place 29

3.2 Some counselling issues 29

3.3 The information 32

3.4 Consent 39

Chapter 4 Privacy and confidentiality 45

4.1 Introduction 45

4.2 Storage of genetic information 46

4.3 Individual privacy and confidentiality 47

4.4 Individual privacy and the family 48

4.5 The right not to know 51

Chapter 5 Disclosure of genetic information 53

5.1 Stigmatisation and discrimination within society 53

5.2 Possible uses of genetic information which could harm individuals 53

5.3 Psychological difficulties 57

5.4 A possible consequence of concern about discrimination 57

Selected bibliography 59

Glossary 63

Appendix 1

Australian sources of information about genetic testing 73

Appendix 2

Membership of the Genetics Working Party 77

Index 79

PREAMBLE

Research into the structure and function of genes is increasing our understanding of their role in maintaining health and causing disease. The knowledge generated has already created, and will create further, opportunities and sound reasons for genetic testing of humans.

This document discusses ethical issues relating to human genetic testing. It is intended primarily for health professionals and researchers who are involved in the testing process or who refer people for testing. It will also assist others to understand the ethical and practical issues associated with genetic testing and, because a wide audience is expected to read the document, some introductory material on genetic testing has been included as background to the ethical issues.

It deals principally with operational issues related to current practice, such as obtaining consent, counselling, privacy and confidentiality. In general, it does not attempt to discuss broader moral and philosophical issues, although these are recognised as being important. Criteria for developing or prioritising genetic tests, or laboratory standards for delivering tests of high quality, are not addressed.

This information paper is not in the format of NHMRC guidelines and therefore does not prescribe a specific approach. It aims to promote thought about the best way to proceed by identifying issues and options to be considered by health professionals and researchers who are involved with genetic testing and who will frequently need to strike a balance between competing factors.

Some disorders are the result of variations in genes that occur after conception in somatic cells, such as those associated with aging and most cancers. This document is not concerned with this kind of variation. Its focus is on testing for variations in genes that cause, or create susceptibility to, disorders that are potentially heritable, and where the genetic variant is present in germ cells.

There have been many influences on the development of this information paper. They include established codes of medical ethics, the NHMRC *National Statement on Ethical Conduct in Research Involving Humans* and numerous documents prepared by others in recent years regarding ethical issues that have arisen from developments in genetics. The Australian Health Ethics Committee (AHEC) also conducted one round of public consultation during preparation of the information paper so that community views could be considered. An international consensus is developing about some, but not all, of the issues, though with variations which reflect national differences in medical, social, legal and political structure and history.

Some people are concerned that developments in genetics may lead to genetic manipulation of humans with a view to 'genetic enhancement'. While community consideration of this matter is appropriate now, 'genetic enhancement' is not feasible at present and is not addressed here. For decades to come, we shall probably have only the most rudimentary understanding of the genetic contribution

to complex characteristics, knowing already that awareness of an individual's genetic code is likely to allow only the crudest of predictions about those characteristics in a person.

Interested readers are referred to three other NHMRC publications on related themes:

- ***National Statement on Ethical Conduct in Research Involving Humans* (1999), Section 16 Human Genetic Research**

  The Statement identifies the ethical principles and values which should govern research involving humans. Its purpose is to provide a national reference point for ethical consideration relevant to all research involving humans. It provides guidance for researchers, ethics committees, institutions, organisations and the public on how such research should be designed and conducted, so as to conform to those principles and reflect those values. Section 16 addresses ethical issues that may arise in the conduct of human genetic research.

- ***Guidelines for Genetic Registers and Associated Genetic Material* (1999)**

  The purpose of the Guidelines is to provide guidance to those intending to establish a genetic register, Human Research Ethics Committees that are asked to approve the establishment of a genetic register, and institutions and organisations in which a genetic register is to be established. The document identifies matters for ethical consideration that relate to the establishment and operation of a genetic register. These include administrative arrangements, recruitment of registrants, consent, confidentiality and privacy, how family members may be approached, security, amalgamation and winding up, and the collection and storage of genetic material in association with a genetic register.

- ***Guidelines for Ethical Review of Research Proposals for Human Somatic Cell Gene Therapy and Related Therapies* (1999)**

  Human somatic cell gene therapy remains experimental. The purpose of the Guidelines is to provide guidance to Human Research Ethics Committees that are asked to review and approve research proposals involving somatic cell gene therapy, and to assist researchers to prepare their submissions for ethical review. It identifies bodies other than Human Research Ethics Committees from which approval may need to be obtained. An information paper on human somatic cell gene therapy, that provides background information to the Guidelines, is published in conjunction with the Guidelines.

CHAPTER 1

THE SPECIAL NATURE OF GENETIC INFORMATION

1.1 Some basic genetics

Every cell in the human body (with the exception of mature red blood cells) contains a cell nucleus within which are tightly coiled threadlike structures known as chromosomes. Humans normally have 23 pairs of chromosomes, one member of each pair derived from the mother and one from the father. Each chromosome has within it, arranged end-to-end, hundreds or thousands of genes, each with a specific location, consisting of the inherited genetic material, DNA (deoxyribonucleic acid). The DNA of each gene is characterised by a unique sequence of bases (adenine, cytosine, guanine and thymine) which, when arranged in triplets in various orders, represent the 'genetic code'. Each gene has its own unique position on one of the chromosomes. DNA is used as a template to produce RNA (ribonucleic acid) which in turn may either instruct the cell to make a specific protein or participate in the regulation of gene expression. Proteins carry out various functions in the body; some are the basic components of tissues (structural proteins), some carry out chemical reactions (enzymes), some act as messengers (hormones) and some regulate gene expression (transcription factors).

While all humans have the same set of genes, the precise DNA sequence varies in different individuals (by about 0.1–0.2 per cent). This fact explains both our similarities, which are the result of our common inheritance, and individual differences. Sequence variations in DNA can differ in their effect, from those that almost always cause disease (disease-causing variants), through those that have less certain effects on health (susceptibility-creating, or protective, or disease-modifying variants) or that underlie individual differences such as hair colour or height, to those that have no effect on the individual (harmless variants).

The term 'mutation' describes a variation in the base sequence of DNA. Depending on the effect of the mutation on the function of the gene or the protein it makes, a mutation may fall into any of the above three classes of genetic variation, though the term is most often used when referring to a disease-causing variant. The term 'polymorphism' is used to describe the presence, in a proportion of people in a population, of multiple sequence variations at a particular point in a gene. A polymorphism may affect susceptibility or may modify the effect of a disease-causing variant or may have no effect, though the term is most often used as though it refers only to variants that have no effect.

A DNA variant can be present in germ-line DNA or in somatic DNA.

A germ-line DNA variant:

- was present in the ovum or sperm from which the individual developed;
- is present in all the individual's cells;

- may provide information about future health;
- may have been inherited from parents (but not always, as a variant can be the result of mutation which occurred in the ovum or sperm from which the individual developed); and
- can be passed on to children because it is present in the individual's sperm or ova.

A somatic DNA variant:

- was not present in the ovum or sperm from which the individual developed;
- arose in a single cell at some time after conception (that is, during prenatal or postnatal growth and development);
- is limited in its distribution in the body;
- will not be present in parents; and
- will not be passed on to children (unless it involves the sperm or ova as the result of somatic mutation in a cell which was a progenitor of germ-line cells).

This document is concerned with genetic information generated by testing for disease-causing mutations or susceptibility-creating/disease-modifying variants in germ-line DNA but not with those in somatic DNA.

Most variations in DNA are without known effect on gene function and are not associated with disease and are present in large numbers throughout the genome. Individually, they can be used for diagnosis of disorders where the gene mutation responsible for the disorder is near to the variation in the DNA (see Section 2.4.4, linkage tests) and in combination can be used to uniquely identify an individual (DNA 'fingerprinting'/'profiling').

1.2 Genetic disorders

Genetic disorders are usually classified as single gene disorders, polygenic disorders and multifactorial disorders.

- **A single gene (monogenic) disorder** is one where a variation in the DNA sequence of one or both members of a gene pair has such a severe effect on the function of its product that its presence usually results in disease. Examples are cystic fibrosis, thalassaemia and haemophilia.
- **A polygenic disorder** is one where the presence of variants in two or more genes results in disease, increases the risk of developing disease or modifies disease severity. It will often be the case that individually, the variations in these genes will have a smaller functional effect on the gene product and less predictable effects on health; it is their combined effect that is important. Examples include many of the common birth defects, such as cleft lip and palate and congenital heart malformations.

- **A multifactorial disorder** is one where the presence of variants in one or more genes, together with environmental factors and chance events, results in disease, increases the risk of developing disease or modifies disease severity. Examples are many congenital malformations, diabetes, cancer and psychiatric disorders.

These concepts are useful but have had to be modified as understanding of the genetic basis of disease has improved. It is now accepted that the causation of most disease is multifactorial, with varying contributions from genes, environment and chance. The associated complexity means that predictions about future health or disease, based solely on a person's genetic information, are necessarily imprecise.

1.3 Genetic material, genetic tests and genetic information

Genetic material is any source of DNA or RNA which can be tested to obtain genetic information. It thus includes cells, whether as single cells or as part of tissues, and extracted DNA and RNA.

A genetic test is one that reveals genetic information. It may be performed on DNA, RNA or protein (the 'gene product'), or involve measurement of a substance that indirectly reflects gene function. Examples of the latter two groups are haemoglobin electrophoresis to diagnose carriers of beta-thalassaemia and measurement of blood cholesterol to diagnose familial hypercholesterolaemia in a child whose parent has the disorder.

Genetic information

(a) Genetic information includes both DNA sequence information and inferences that can be made from knowledge of the sequence. It thus includes, for example, both the presence in a person of the abnormal DNA sequence associated with Huntington disease and the fact that a person with that genetic abnormality will almost certainly one day develop Huntington disease.

(b) Genetic information also includes information that allows inferences to be made about DNA sequence. Such information may be revealed by:

- Study of entire chromosomes, RNA, proteins, substances in blood or tissues in certain circumstances, and medical imaging techniques.
- Diagnosis of a genetic disorder by clinical examination.
- Study of a person's family tree if that allows inferences to be made about the DNA of family members.

(c) Genetic information can relate to a condition that is clinically apparent (such as when a genetic test is performed to confirm a diagnosis in someone who has symptoms of a particular disorder) or latent (such as when a genetic test is done on someone who is free of a disorder now, to determine the likelihood that he/she will develop the disorder in the future).

(d) Genetic information can be about individuals, families or groups of people with common ancestry. General inferences may be possible about the genetic information of an individual who belongs to such a group if information is known about other members of the group. This document focuses on genetic information about an individual derived from tests on that person's genetic material.

1.4 The shared nature of genetic information

Genetic information is not only about ourselves but may tell us something about close blood relatives, in both succeeding and preceding generations. For example, diagnosing familial adenomatous polyposis in a person implies that each of their children has a 50 per cent chance of developing the disorder as well. Showing that someone is a carrier of cystic fibrosis implies that one of his/her parents is also a carrier.

It can have an impact on how an individual relates to other members of the family, or they to him/her, potentially strengthening some relationships and weakening others, and potentially creating new, or removing existing, obligations felt towards family members.

It can require an individual to balance the loss of personal privacy involved in disclosing the genetic information derived from a test, against the benefit to a relative from informing him/her that he/she might have inherited a genetic predisposition to a significant health problem.

1.5 The uniquely personal and identifying nature of genetic information

Each of us has a unique DNA sequence that is a major contributor to our individuality. By birth, even the sequences of identical twins have differences.

- Information about that sequence, and the inferences which can be drawn from it, can have a great impact on an individual in terms of perceptions of health and body image and perceptions of worth as an individual, family member and member of society.
- The influence of information about that sequence can extend over the lifetime of the individual.
- The ability to perform tests to reveal that sequence can create the need to make decisions, sometimes of great significance and novelty, for example:
  - deciding whether to find out if symptoms of a family illness are likely to appear at a future time; or
  - choosing among reproductive options and techniques, such as prenatal diagnosis, which may subsequently require a decision about whether or not to continue a pregnancy if the foetus has inherited a disease-causing gene; or

- pre-implantation diagnosis and the consequential non-use of embryos which have inherited a disease-related mutation.

- A single DNA sample contains all of an individual's genes. It can thus be used to identify an individual or be stored and re-tested over time, with the progressive accumulation of information about the individual.

1.6 The possibility of predicting future disease/health risks

Until recently, assessment of an individual's susceptibility to genetic disorders was based on his/her family history and any recognised exposure to environmental or lifestyle factors known to be potentially harmful, and was usually a rough approximation.

Currently, for those with a family history of one of a number of uncommon adult-onset disorders resulting from mutations in just one gene (monogenic disorders), it is possible to make much more accurate predictions if the family's mutation has been identified. If the mutated gene has been inherited, testing can sometimes be followed by implementation of strategies to prevent the disorder. Alternatively, knowledge that one has not inherited the mutated gene can alleviate anxiety and make burdensome and expensive surveillance or prevention strategies unnecessary. The number of such monogenic disorders for which testing is readily available remains relatively small and the number for which prevention strategies are available is even smaller. In Australia, as elsewhere, guidelines have been developed for the delivery of these genetic tests, especially those which are highly predictive of future health, and such services are being provided eg for Huntington disease or familial adenomatous polyposis.

Testing for monogenic adult-onset disorders can also be performed during pregnancy to determine whether the foetus will, after a healthy childhood and early adult life, develop the disorder in question in mid–late adult life. For some families, the burden of growing up and living one's early adult life in the knowledge that the disorder may appear later in life, of seeing one's parent develop the disorder, and of the disorder itself once symptoms start, is sufficient reason to consider prenatal diagnosis. Information gained from predictive and prenatal tests can prompt profound questions about what constitutes a worthwhile human life, which in turn can lead to discounting of the possibility that effective treatments may be developed in the future.

As genetic testing improves, it may become possible to make more accurate predictions, in the absence of a family history, about the likelihood that individuals will develop the common multifactorial disorders which are caused by interaction of genes with each other and the environment. Such information may make possible specific preventive interventions and health promotion strategies targeted to susceptible individuals.

There are many examples of existing health promotion programs which recommend lifestyle changes to reduce the chance of developing common multifactorial disorders (eg by eating a healthy diet, not smoking, taking regular exercise and drinking alcohol in moderation) or which screen for problems at an early stage

followed by appropriate intervention strategies (eg measurement of weight, blood pressure and blood cholesterol, Pap smears for cervical cancer and mammography for breast cancer).

Key differences between these established practices and genetic susceptibility testing would be that genetic testing (eg for susceptibility to high blood pressure) may, in the future:

- be performed before there is clinically detectable evidence of a problem (eg before blood pressure starts to rise);
- distinguish between those with high or low susceptibility, allowing specific targeting of interventions to those with high susceptibility (eg recommending regular blood pressure checks to susceptible people only, rather than to the whole population, but noting that if lifestyle/environmental factors alone can cause high blood pressure, it would be necessary to continue to recommend blood pressure checks to the whole population); and
- define the cause of susceptibility, leading to specific interventions for different groups of people (eg the use of different anti-hypertensive drugs depending on which genes are creating the susceptibility).

Currently there are no examples of such strategies. For the present, susceptibility testing is limited to monogenic disorders and, in the main, is being delivered to individuals and families rather than to populations. It is imperative that existing health promotion programs, which potentially benefit the entire population, remain in place and are expanded where appropriate.

1.7 The probabilistic nature of genetic information

It would be simplistic and inaccurate to suggest that an individual's health can be specified solely by the sequence of bases in his/her DNA or that genetic susceptibility equates with genetic inevitability ('genetic determinism'). It is clear that an individual's genes are only one of the factors that will determine his/her future health, albeit a substantial factor in many cases. Others are environmental factors, lifestyle, complex interactions between inherited genes, spontaneous gene mutations occurring during life, and chance. While information generated by genetic testing can be very precise eg that a mutation is or is not present, the precision will often prove unhelpful when it comes to predicting future health. Key information for assessment of future health, namely other risk factors such as the environment or other genes, will often be lacking. Thus, genetic information is often about possibilities rather than certainties because only a proportion of those with a particular disease-related mutation or other variant will develop the disorder. For example, a woman with a mutation in the BRCA1 gene, which predisposes to breast cancer, has a lifetime risk of breast cancer which current estimates place at 60–85 per cent, compared to the community risk for women of 7–8 per cent. Thus, at least 15–40 per cent of such women will not develop breast cancer. At present, we do not know which environmental or genetic factors are responsible for triggering breast cancer in some genetically susceptible women or for providing protection

from the disorder in others. These and many other areas of uncertainty can only be resolved by further research.

It is likely that the main benefit of future developments in genetics will be to provide information more accurate and comprehensive than is now available, though often still only probabilistic, and to provide it earlier in life. The possibility of providing information early in life is well exemplified by presymptomatic testing for Huntington disease and familial adenomatous polyposis, where only genetic testing can predict whether an individual will develop the disorder, and can do so with great accuracy decades before symptoms will appear.

However, such tests are often poor at predicting exactly when symptoms of the disorder will develop and may be unable to predict which features of the disorder will occur. For example, an individual with a mutation in MLH1, which causes hereditary non-polyposis colorectal cancer, is at increased risk of colon, endometrial, ovarian and other cancers. But the person may develop none, any one, or any combination of two or more cancers over his/her lifetime. And if cancer does occur, it may do so at any age.

1.8 The potential for misuse of genetic information

There are greater pressures to discover, gain access to and use genetic information than is the case for traditional health information. Its predictive nature makes it of particular interest in situations where information about a person's future, even though imprecise, could be incorporated into decision making eg related to life insurance or employment. Further, opportunities for access to genetic information in the health sector are increased by the multidisciplinary nature of much medical practice and developments in information technology. Its novelty also creates a risk that both the information and its implications will be misunderstood by health professionals, the families of those tested, and others in the community who have access to the information, and as a consequence, that it will be misused. Community and professional education, and the ready availability of information when needed, can minimise misunderstanding of, overreaction to, and misuse of genetic information.

These developments in genetics pose ethical questions for individuals and families, as well as for society. Some arise from the nature of genes and genetic information, which are at the same time both personal and shared with family members and, in many cases, with people outside the family eg with members of an ethnic group. Other questions arise from the fact that until now, individuals and society have not had to deal with predictive information of such quantity and accuracy and there is no considered community view about access to, and use of, predictive genetic information by family members and people or organisations outside the family.

There is concern about the possibility of stigmatisation and unfair discrimination based on genetic information. This is discussed in more detail in Chapter 5.

1.9 'Geneticisation'

'Geneticisation' is a view of human beings as essentially consisting of their genes and describable in the language of genetics. It is associated with 'genetic determinism', a view that human behaviour and health are pre-determined by people's genetic make-up (see also Section 1.7, The probabilistic nature of genetic information, above).

A number of concerns have been raised about naïve forms of these views. Over concentration on research on genes and their health implications could lead to neglect of the effects on human health of other factors, such as the physical, social and economic environments in which people live.

Genetic determinism can undermine personal moral responsibility when it is used as a defence for behaviours that bring community censure. An example would be when an individual excuses his/her outbursts of temper as being genetically determined and unalterable, perhaps inherited from an irritable parent, instead of attempting to curb the outbursts, and pleads 'reduced responsibility' in court when an outburst results in an assault on another person. On the other hand, sometimes an appreciation of the effect of genetic factors might quite properly lead to withdrawal of censure. For example, recognition that conditions such as obesity and depression may be caused, at least in part, by variations in genes, has the potential to make others less ready to blame people for their obesity or depression and more inclined to support them.

Current attitudes of social solidarity could be threatened by 'geneticisation'. An example of loss of solidarity in society would be the expectation that those with genetic susceptibilities, or at risk of having children with a genetic disorder, increasingly take financial responsibility for their own and their affected children's health care. It would be argued by those supporting such a policy that individuals have a duty to prevent illness in themselves and not to have children with genetic disorders. They would also argue that if preventive measures are not taken, society should not have to provide the resources needed for care of those affected. Such attitudes would be an attack on the prevailing view that health care costs should be distributed across the whole community, and would challenge concepts of equality of respect for persons and sense of community.

CHAPTER 2

GENETIC TESTING AND STORAGE OF GENETIC MATERIAL/INFORMATION

2.1 Types of genetic test

2.1.1 Tests to make a diagnosis in a person who has features of a genetic disorder.

***Diagnostic test*—a test performed to make or confirm a diagnosis of a specific disorder in a person who already has symptoms and/or signs.** The information is usually used by health professionals to make a diagnosis and provide appropriate management and genetic counselling to the affected person. It is also the starting point for family studies designed to identify and advise family members, if they wish, about their chance of developing the disorder and of ways, if any exist, to prevent the disorder or to minimise its effects. Examples include testing an individual with intellectual disability for fragile X syndrome, or a movement disorder for Huntington disease, or with diabetes mellitus for haemochromatosis, or the chromosomes of a foetus shown on ultrasound to have several malformations.

2.1.2 Tests to determine the presence or absence of a genetic variant, or variants, in a person who has no features of the disorder at the time of testing, in order to use the information to predict the likelihood that the person will develop the disorder in the future.

These tests reveal susceptibility to develop the disorder in question. Several different names have been used for such tests—'presymptomatic test', 'predictive test' and 'susceptibility test'. The choice of name has depended on the magnitude of the susceptibility and whether the disorder has a monogenic or multifactorial basis. In practice, susceptibilities can range from 0 to 100 per cent and it is not meaningful to distinguish between tests on the basis of susceptibility figures, though from the point of view of the person tested, there is a big difference between 10 per cent and 90 per cent, say, or even between 90 per cent and 100 per cent. In addition, the more that is learned about the causes of disease, the more the distinction between monogenic and polygenic/multifactorial disorders becomes blurred. There is a continuum between disorders where a single gene dominates the aetiology and pathogenesis, and disorders where aetiology and pathogenesis are determined by multiple genes and environmental/lifestyle factors. 'Presymptomatic', 'predictive' and 'susceptibility' tests are described below, as the terms are in common usage, but the reader should be aware that in reality, they are all tests which determine susceptibility.

(a) ***Presymptomatic test*—a test performed on a person who has no symptoms of a specific disorder at the time of testing, to determine whether or not he/she has a mutant gene.** Most often it will first be necessary, in an affected family member, to identify the specific mutation present in the family. Then, if the mutant gene is shown to be present, the person is almost certain to develop symptoms of the disorder at some time in

the future, provided he/she lives long enough. Presymptomatic testing for Huntington disease, familial adenomatous polyposis and myotonic dystrophy are examples.

The information may be sought by an individual with a family history of the disorder in question, in order to have a better understanding of what the future holds and to be able to plan for it, to make use of preventive health strategies, to make reproductive choices or to provide information to children and other family members. Parents may wish to know whether their child is likely to develop a disorder in the future, especially if prevention or early diagnosis can alter the outcome for the child. In general, the term is used when testing for disorders caused by a single gene (monogenic disorders) and can be applied to dominant, recessive or X-linked disorders with onset at any age. Currently most presymptomatic tests are performed for adult-onset dominantly inherited disorders. They are also performed in childhood for disorders that have their onset in childhood or adolescence, if testing is of clear benefit to the child eg testing for familial adenomatous polyposis and multiple endocrine neoplasia type 2A.

The screening of newborns for phenylketonuria (PKU) and hypothyroidism represents a special case of presymptomatic testing. Here there is a very short time interval between detection of an abnormal test result, in a newborn with no clinically detectable features, and the subsequent onset of symptoms (see also Section 2.2, Screening test).

(b) ***Predictive test*—a test performed on a person who has no symptoms of a specific disorder at the time of testing, to determine whether or not he/she has a mutant gene.** If the mutant gene is present, the person has a high probability, rather than certainty, of developing symptoms of the disorder at some time in the future, provided he/she lives long enough.

As for presymptomatic testing, predictive testing is usually performed on individuals with a family history of the disorder in question and testing is for disorders where most of the predisposition is caused by a single gene (monogenic disorders). The reasons for requesting predictive testing are similar to those for presymptomatic testing. Examples are predictive testing for mutations in BRCA1 and BRCA2, which are associated with a high risk of breast cancer, and for mutations in MLH1 and MSH2, which are associated with a high risk of colon cancer.

(c) ***Susceptibility test*—a test performed on a person who has no symptoms of a specific disorder at the time of testing, to determine whether or not he/she has a genetic variant or variants which increase the likelihood (the risk increases are often small) that the person will develop symptoms of the disorder in question at some time in the future.** In general, the term is used when testing for disorders where genes and environment interact to result in the disorder (polygenic/multifactorial disorders). A susceptibility test may be performed because of a family history of the disorder or as part of population screening.

2.1.3 Tests performed to determine the presence or absence of a genetic variant which will not cause a disorder but which, if transmitted, may be associated with the disorder in offspring.

***Carrier test*—a test performed on a person to determine whether or not he/she has a mutated gene or chromosome abnormality which will not affect the person's health, but increases his/her chance of having children with the disorder in question.** The term carrier is used with respect to autosomal recessive and X-linked genes and balanced chromosome rearrangements. For a carrier of an autosomal recessive disorder (who may be male or female) one of a pair of autosomal genes has the mutation while the other is normal. For a carrier of an X-linked recessive disorder (the term refers to females only) one of a pair of genes on the X chromosome has the mutation while the other is normal. In the case of autosomal recessive disorders, a carrier can only have a child with the disorder if his/her partner is also a carrier. For X-linked disorders, the risk to children is determined solely by the fact that the mother is a carrier. A carrier test may be performed because of a family history of the disorder, for example haemochromatosis or fragile X syndrome, or as part of population screening, which has been performed for example, for beta-thalassaemia, cystic fibrosis or Tay-Sachs disease in particular populations.

It should be noted that when referring to a mutant dominant gene, the term 'carrier' is often used in its literal English sense to mean that the person 'has' or 'possesses' the particular mutant gene. Thus a person may be described as a 'carrier' of 'the Huntington disease gene' or of 'the adult polycystic kidney disease gene'. Such usage is imprecise from a scientific genetic viewpoint.

2.2 Other times when tests are performed

***Prenatal test*—a test, usually diagnostic or presymptomatic, carried out on a developing foetus.** A prenatal test may be performed because it is known that the foetus is at increased risk of having a particular disorder, as for example when the parents have had an affected child previously, or are both known to be carriers of a recessive disorder or when a woman is older and at increased risk of conceiving a child with Down syndrome. The procedures used to obtain foetal cells for testing are chorionic villus sampling (CVS), amniocentesis and occasionally foetal blood sampling (cordocentesis); couples should be informed that they are associated with a small procedure-related risk of miscarriage.

Prenatal tests may also be performed as a population screening test such as when all pregnant women are offered maternal serum screening to determine if their foetus is at increased risk of having spina bifida or Down syndrome, or ultrasound screening for malformations in the foetus.

A couple's decision to have a prenatal test, or intentions expressed about what they might do if the test result is abnormal, must not bind them to a particular course of action once the test result is known. They may face decisions about termination of pregnancy in the event that the foetus is shown to have a significant abnormality and it should not be presumed or expected that they will decide to act in a

particular way. (See Section 3.2 for a discussion of some relevant counselling issues.)

***Preimplantation test*—a form of presymptomatic test carried out on early embryos in the laboratory, with a view to transferring to the mother's uterus only those which will not develop the disorder in question.** It is also possible in some circumstances to perform testing on egg cells (oocytes, ova) before conception, so called polar body testing.

***Screening test*—A screening test is one that is performed on individuals not known to be at increased risk of a particular disorder that is, those with no family history, symptoms or other reason to suggest an increased risk.**

The following test types can be used in screening mode, and individuals, groups within populations and entire populations can be screened:

- diagnostic tests eg using CVS or amniocentesis to check the chromosomes of foetuses of older mothers for Down syndrome;
- carrier tests eg for cystic fibrosis carriers;
- presymptomatic tests eg for PKU in newborns or for haemochromatosis in adults; and
- susceptibility tests eg maternal serum screening of pregnancies to identify foetuses at increased risk of Down syndrome; there is no current example of a test suitable for postnatal susceptibility screening.

Many screening tests are not diagnostic and simply provide an indication of increased or decreased chance of abnormality. It is essential that before testing, people are informed that:

- the test cannot detect all those with the disorder in question. Other ways of describing this are that the 'sensitivity' of the test is less than 100 per cent or that the test has a 'false negative' rate;
- some of those with an abnormal test result will be shown not to have the disorder after further testing. Other ways of describing this are that the 'specificity' of the test is less than 100 per cent or that the test has a 'false positive' rate; and
- some of those with an abnormal test result may have a disorder which was not being sought.

For example, maternal serum screening for Down syndrome may identify only 60–70 per cent of affected pregnancies, may identify 4–5 per cent of all pregnancies as abnormal (although only 2–3 per cent of these will be shown to be affected after further testing), and may by chance identify pregnancies with chromosome abnormalities other than Down syndrome.

When performed prenatally, screening tests may identify foetal abnormalities. For example, ultrasound may identify serious malformations such as anencephaly; a

small number of abnormalities that can be treated before birth such as foetal heart block, accumulation of fluid in the skin and body cavities resulting from anaemia, and evidence of certain types of infection; or abnormalities that may be better managed by early delivery such as certain urinary tract malformations. Screening tests can also identify pregnancies with an increased chance of foetal abnormality eg maternal serum screening for Down syndrome, and provide some reassurance when no abnormality is found eg a normal prenatal ultrasound scan or a maternal serum screen showing the pregnancy to be 'not at increased risk'.

When performed postnatally, the goal of genetic testing will usually be to identify individuals at increased risk of developing symptoms of a disorder in the future, with a view to offering an intervention to reduce risk eg newborn screening for phenylketonuria and hypothyroidism where the aim is to identify affected newborns before symptoms appear and to provide treatment which will prevent the brain damage which begins soon after birth. Alternatively, in regard to carrier screening eg for cystic fibrosis or beta-thalassaemia, the aim is to identify couples who are at high risk of having affected children.

Those undergoing a screening test will often have little understanding of the disorder in question, as they may have never met an affected person or had the opportunity to learn about the condition. Further, there is a relatively small chance that the test result will be abnormal, and if the test result is abnormal, the chance that they will develop the disorder may be only a little or moderately increased. Their information and counselling needs are different from those of people who have had experience of a disorder in their own families and who have a large chance of an abnormal result because of their close relationship to an affected person.

Testing as part of research —The NHMRC's *National Statement on Ethical Conduct in Research Involving Humans* (1999) provides guidelines for genetic testing when performed as part of a research study. In some research settings participants should be treated in the same way as when the test is performed in clinical practice. In others, there are considerable differences. Some of the key concepts are highlighted below:

- **Genetic research which addresses disorders caused by rare high-risk mutant genes and is designed in a way which may reveal genetic information of significance to the future health of participants and their families.** Perhaps 2 per cent of human disorders can be attributed to disorders of this type. An example would be a research project which aims to identify cancer-predisposing mutations in specific families with breast cancer. At the time of obtaining consent for such research, and prior to testing, detailed counselling about the possible consequences of testing must be provided to participants. The research will need to use identified or potentially identifiable (coded) genetic information and material so that relevant research findings can be given to individual participants. Therefore particular care needs to be taken to ensure the confidentiality of participants. Providing pre-test counselling and test results requires counsellors with appropriate qualifications, experience and skill. Appropriate health

professionals may be members of the research team but if not, health professionals collaborating with the researchers should provide these services.

- **Genetic research which addresses disorders caused by high-risk mutant genes, but which will not reveal new genetic information of significance to the future health of participants.** An example would be a study which compares the histology (appearance under the microscope) of breast cancers caused by mutations in BRCA1 and BRCA2 with that of common breast cancers. For such a study, the information provided to participants would not need to be accompanied by detailed counselling. The research could be conducted using de-identified genetic material and information. And, if it is intended to inform participants about the outcome of the research, the feedback would take the form of a written report containing grouped data.

- **Genetic research that addresses disorders associated with susceptibility genes.** These are common low-risk mutant genes that do not cause a particular disorder on their own, though they may combine with other susceptibility genes and specific environmental factors to cause the disorder in some people. Perhaps 98 per cent of all human disorders, where genes contribute to causation, are caused by genes of this type and most future genetic research will focus on these genes and disorders. An example would be a research project which aims to compare DNA sequence variation, or variations in gene expression patterns, between a large group of individuals with asthma and a large group of individuals without asthma. Here the aim is to understand the factors that contribute to the cause of the disorder in asthmatics as a group, not in individual asthmatics. For such a study, the information provided to participants would not need to be accompanied by detailed counselling. The research would often be conducted using de-identified genetic material and information. This would ensure the confidentiality of participants. De-identification implies that it would be impossible to go back to participants or their records for further information, but this would not affect the value of such research. And, if it is intended to inform participants about the outcome of the research, the feedback would take the form of a written report containing grouped data.

Testing in contexts that go beyond health care and research —Genetic information may also be sought:

- for determining paternity;
- for forensic or legal purposes; or
- when persons apply for life insurance or employment. (see Chapter 5)

2.3 The test material

Genetic testing will most often be performed on DNA, but can also use RNA, chromosomes or other types of test material. Tests using other materials include measurement of blood cholesterol to diagnose familial hypercholesterolaemia,

haemoglobin electrophoresis for the diagnosis of carriers of beta-thalassaemia, and abdominal ultrasound to detect polycystic kidney disease. When DNA is to be the starting material, it will usually be obtained from cells in a blood or mouthwash sample but can also be extracted from fresh or stored tissue collected during surgery, cultured cells, hair roots and other sources. Tests that use DNA will often be more accurate than tests that rely on indirect measures eg the microscopic appearance of red blood cells as a test for thalassaemia, or which are used in settings where the test abnormality being sought can appear at any time in life and may not be present at the time of testing eg measurement of blood iron levels in teenagers as a test for haemochromatosis.

2.4 Performance of the test

2.4.1 The starting point

As with other diagnostic medical testing, clinical assessment of the affected individual, and documentation of the pedigree (family history), are usually the starting points for diagnostic genetic testing as they will define which gene or genes the laboratory should study. Identifying the mutation causing the disorder will be straightforward if only one gene can cause the disorder, if that gene has been identified and if only one or a small number of mutations in that gene cause the disorder.

2.4.2 Possible complexities

However, testing is much more complex if:

- **Multiple mutations occur in the gene that causes the disorder.**

  For a given genetic disorder, there may be different mutations in different families. It is unusual for a single mutation or even a small number of mutations, or a single mutational mechanism, to account for all mutations in affected individuals. An example of the situation in which a gene has numerous mutations is the CFTR gene associated with cystic fibrosis, with more than 700 different known mutations scattered along the length of the gene, although one mutation, DF_{508}, accounts for about 70 per cent of all mutations in the Australian population. Thus, while demonstrating that an individual does not have the DF_{508} mutation does not exclude carrier status, it does reduce the risk. Examples of situations in which a disorder is strongly associated with a single mutational mechanism are sickle cell anaemia and fragile X mental retardation where everyone with the disorder has the identical mutation, and haemochromatosis where one specific mutation is present in over 90 per cent of affected persons.

- **Multiple genes can cause the disorder and multiple mutations can occur in each.**

  Even more challenging is the testing situation where multiple genes are capable of causing the disorder and there are different mutations in the genes in different families. For example, familial breast cancer can be caused by

many mutations in BRCA1, BRCA2 and other yet to be discovered BRCAs, and hereditary non-polyposis colorectal cancer can be caused by mutations in at least five different genes.

- **The disorder can be caused by multiple mutational mechanisms.**

  In general there will be multiple mutational mechanisms underlying each disorder (deletions, duplications, inversions, base substitutions, regulatory mutations) and for each mechanism, multiple different mutations which can occur anywhere in the gene. For example, about 65 per cent of boys with Duchenne muscular dystrophy will have a deletion in the dystrophin gene. Laboratories can use a screening strategy to detect deletions but may be unable to screen for other mutations when no deletion is found.

2.4.3 The need to screen for mutations

The result of this complexity is that laboratories must screen genes for mutations, or test a small number of known common mutations, rather than being able to offer a single test for each disorder. There are many methods available for screening genes for mutations, each with its strengths and weaknesses eg gene sequencing, chemical/enzyme cleavage methods, protein truncation tests, denaturing gel gradient electrophoresis, single strand conformation polymorphism analysis, heteroduplex analysis and Southern blotting. The reader is referred to relevant texts for details of these technologies.

2.4.4 Additional matters to be considered when performing presymptomatic, predictive, susceptibility and carrier genetic testing

- **There is a need to identify the mutation in an affected family member.**

  The starting point for presymptomatic, predictive, susceptibility and carrier genetic testing is to identify the mutation responsible for the disorder in an affected family member, who may be a symptomatic individual or a carrier. Having done so, it becomes possible to test relatives to determine whether or not they have inherited the abnormal gene. Testing relatives is a much simpler process as the family's specific mutation is now known and a specific test can be developed to identify it. If testing proceeds without prior knowledge of the specific mutation responsible for the disorder in the family, it is of little value to the person tested to demonstrate that he/she has no identifiable mutation in the tested gene. The laboratory may have tested a gene that is not responsible for the disorder in the family eg BRCA1 when there is a mutation in BRCA2, or used a method which does not detect all mutations and may have missed the specific mutation present in the family.

- **It may not be possible to find the mutation and an indirect testing method may be necessary.**

  Sometimes it is not possible to identify the specific mutation responsible for a disorder that has been diagnosed clinically in a family eg because the gene has not yet been identified though its chromosomal location is known, or

because available technology fails to detect the mutation, or because resources are insufficient to screen the entire gene for mutations. However, it may still be possible to infer the presence or absence of the mutant gene in relatives using a testing method called 'genetic linkage'. This uses genetic markers with variable sequences, within or close to the mutant gene of interest, to track it within the family. Examples of such markers are variable number of tandem repeat markers (VNTRs), one class of which are the dinucleotide repeat sequences (microsatellites), and restriction fragment length polymorphisms (RFLPs). This type of testing requires DNA from multiple family members, usually including at least one affected family member, and families of sufficient size. The result of a 'genetic linkage' test takes the form of a probability and therefore, is less accurate than a test that relies on detecting a known mutation. Again, the reader is referred to relevant texts for details of linkage methods.

2.5 Test quality

As for other forms of laboratory testing, clinical genetic testing (as opposed to genetic testing in a research setting) should only be performed by accredited laboratories.

Laboratories need to be particularly sensitive to the possibility of error, both in the performance of the test and in their interpretation of the test result. This is especially so when performing presymptomatic, predictive and susceptibility tests, as the consequences of error or providing misleading information can be serious. As a worst case scenario, to report a harmless sequence variant in BRCA1 as a mutation associated with a high risk of breast and ovary cancer, could lead to prophylactic mastectomy/oophorectomy in the person tested and in female relatives shown to have the same variant. In addition, there may be anxiety about the cancer risk of offspring, and perhaps an inability for all those with the variant to obtain life insurance. In relation to prenatal genetic diagnosis for a particular disorder, errors can result in termination of the pregnancy of a foetus without the suspected disorder or continuation of the pregnancy of a foetus with the suspected disorder.

It is also vital that laboratories report test results in a way which can be understood by health professionals. Most doctors in practice today have not had formal training in genetics and are not familiar with genetic technology and terminology, or with the difficulties that can arise in interpreting results. Each report should ideally contain an interpretation of the test result in light of the relevant clinical and family information supplied by the doctor at the time of referral of the test sample. At times, it may be necessary to communicate with the doctor who ordered the test before releasing the test report. Laboratories can play an important role in educating health professionals about genetic tests.

2.6 Test cost

It should be noted that the cost of genetic tests is relatively small, and comparable to other medical tests, when one or a small number of mutations is the cause of a disorder in all those affected eg fragile X syndrome, achondroplasia and sickle cell

anaemia. The cost is also small once the family-specific mutation has been identified in a family with a disorder where many mutations, in one or more genes, occur eg haemophilia A, familial adenomatous polyposis and beta-thalassaemia. The cost of identifying the family-specific mutation in an individual or family is much greater if it is necessary to screen one or more genes to identify the mutation, as is necessary when many mutations, in one or more genes, can cause the disorder.

2.7 Storage of genetic information and genetic material

Genetic tests are now a routine part of the diagnostic process for many disorders eg fragile X mental retardation, cystic fibrosis, thalassaemia, Huntington disease and haemochromatosis. Routine neonatal screening for phenylketonuria, hypothyroidism and cystic fibrosis is performed in Australia. Prenatal screening eg for Down syndrome and carrier detection eg for cystic fibrosis and haemochromatosis are further examples of routine genetic tests. Genetic tests are conducted on small samples of tissue that, together with the results of the tests, can be theoretically stored indefinitely. This has resulted in the need to consider whether, how and for how long, residual test samples and the information generated by testing are to be stored (See Chapter 3.3.2.17).

2.7.1 Genetic information

Once a clinical genetic test has been completed and the result reported to the requesting doctor, the test result and accompanying clinical details (usually the clinical diagnosis and other information written on the test request form) will be stored indefinitely by the testing laboratory. This is in accordance with good laboratory practice and is required for laboratory accreditation (*Retention of laboratory records and diagnostic material*, 1998).

Individuals having predictive, presymptomatic, susceptibility and carrier tests should be informed that the test result will be retained by the testing laboratory. Those tested and their families need to know where the information can be found if it is needed for their future care. Consideration should be given to providing those tested with a copy of the laboratory report of the test result. This can be kept in their personal medical file and provided to health professionals when necessary.

When testing is performed in a research setting, the test result will be stored for a period in accordance with good research practice and then disposed of. For research that was known at the outset to have the potential to produce test results of significance to the health of research participants, a process will have been put in place to provide research participants with their test results, usually through their doctors. Once this has been done, retention of the information will be the responsibility of the individual participants and their doctors.

There are particular issues with regard to the privacy/confidentiality of such genetic information, and these are discussed in Chapter 4.

2.7.2 Genetic material

Laboratories may receive genetic material for the diagnosis of symptomatic individuals, for presymptomatic, predictive, susceptibility or carrier testing, for research or for purposes unrelated to health care or research such as for paternity testing. Such material should be stored in accordance with accepted laboratory standards until tested, in order to ensure its integrity.

In general, laboratories performing clinical genetic testing will store genetic material for a defined period after initial testing, subject to the availability of appropriate storage facilities. Genetic material may be stored because testing is incomplete, in order to substantiate results if required, for quality assurance purposes, for research, as a legal requirement, or as a requirement of laboratory accreditation. The material may be in a variety of forms including Guthrie cards (newborn screening blood spots), frozen or embedded tissue samples, frozen DNA or RNA, frozen whole blood or frozen cell cultures. Subsequently, the material may be disposed of, and this will usually be the case when the laboratory has completed the test it was asked to perform, if there is no expectation on the part of the person tested that there will be longer term storage of the material, and provided that all legal and laboratory accreditation requirements have been met. Recent guidelines published by the National Pathology Accreditation Advisory Council (*Retention of laboratory records and diagnostic material*, 1998) recommend indefinite storage of DNA and tissue samples, and storage of dried blood spots for 50 years. Individuals undergoing genetic testing should assume that their genetic material will be disposed of at a time determined by standard laboratory practices or legislative requirements.

It is particularly important that an individual is aware that his/her genetic material has been stored as he/she or his/her family may wish to access the material in the future. Depending on the circumstances under which genetic material was collected, laboratories wishing to dispose of it may need to seek the views of the individuals concerned, if it is practicable to do so.

Genetic material is often stored because it is a potential resource for future research. It may have been collected initially for a specified research study, or for clinical testing.

- When collected initially for research, the individual concerned should be informed that storage is planned and consent should be obtained for any future uses other than that for which the genetic material was obtained.
- Institutions or organisations wishing to conduct research on genetic material collected for clinical testing should develop and disseminate a general policy which informs patients that such material may be used for future research following HREC approval. Patients of such institutions or organisations should be informed that this policy exists, and that their privacy and confidentiality will be protected. They should be given the opportunity to refuse consent to use of their material for such research.

- Guidelines addressing the research uses of genetic material and information are provided in the NHMRC's *National Statement on Ethical Conduct in Research Involving Humans* (1999).

Laboratories may obtain genetic material from an individual for both a test to assist health care and for research testing. Completion of the clinical test may have to await new knowledge or technology and can sometimes take a long time. Subject to Human Research Ethics Committee (HREC) approval in accordance with the *National Statement on Ethical Conduct in Research Involving Humans*, the genetic material may also be used for research during this time. Laboratories must ensure that sufficient genetic material is always retained to meet any outstanding clinical obligations.

2.8 Equity of access to genetic testing

Access to genetic testing services which have been shown to have potential to provide significant health benefits should not be dependent on where a person lives or on their socio-economic status.

Ensuring equity of access irrespective of place of residence is straightforward in terms of the laboratory aspects of testing, as DNA is stable in blood and samples can be readily transported to a distant laboratory. What cannot be so readily provided in country areas is the skilled counselling needed for many genetic tests. In time it is likely that general practitioners will become familiar with the counselling issues which accompany certain types of genetic test and will be able to do some of the counselling. It is likely that specialist genetic counselling services will continue to be needed, ideally delivered as an outreach service to country areas.

Ensuring equity of access irrespective of socio-economic status may be more difficult to achieve but can be addressed through strategies such as Medicare rebates for genetic tests and block funding of laboratories at a national and/or state level. A national approach that will ensure the availability of testing for uncommon genetic disorders is needed. Some tests for rare disorders may need to be performed by laboratories overseas and a mechanism for purchasing such tests is required.

2.9 Commercialisation and direct marketing of genetic tests

Concerns have been expressed about commercialisation of genetic testing because of doubts about the adequacy of pre-test information and counselling, which are essential for informed consent, and of post-test counselling and support, especially when tests will determine carrier status or susceptibility to a disorder (see Giardiello *et al*). Commercialisation affects private sector laboratories and, increasingly, public sector laboratories. Laboratories may be tempted to rely on health professionals to provide information, counselling and support services at a time when the level of professional knowledge about genetic testing is insufficient, and when there is a shortage of trained counsellors, especially in primary care. There is also unease that economic issues will drive aggressive marketing of tests, determine which tests are

available irrespective of their usefulness for health care, inhibit planning and promote unnecessary duplication.

There has been particular concern about the possibility of direct marketing of genetic tests to the public. The small amount of DNA required for many genetic tests and the stability and transportability of DNA, as in a dried blood spot on a piece of blotting paper, has made possible 'over the counter' genetic tests that could potentially be marketed, ordered and results given by mail or via the Internet. For example, direct marketing of carrier testing for cystic fibrosis is already available in some countries. Such testing is unlikely to provide the level of information, counselling and support that should be provided with genetic tests.

2.10 Allocation of resources for genetic testing

Genetic testing has the potential to improve health but when provided to entire populations, the costs involved can be significant and genetic technologies must compete with other technologies and services for resources. It is therefore vital that genetic testing is provided in the most cost-effective way and without unnecessary duplication and this may entail the establishment of national referral centres for certain tests.

The application of genetic testing technology has the potential to improve health through improved diagnosis and treatment, and through programs to screen for susceptibility to a disorder and early implementation of effective preventive interventions. It can also identify those who do not have susceptibility to certain disorders, thus allowing direction of resources for prevention and surveillance to those with demonstrated genetic susceptibility. The balance of costs and savings is uncertain at the present time, but there appears to be potential for reducing health care costs in childhood and early/mid adult life.

CHAPTER 3

CONSENT TO GENETIC TESTING

This chapter deals primarily with genetic testing performed as a clinical service in a clinical setting. It addresses the setting in which consent to testing takes place, the counselling process that precedes testing and accompanies the obtaining of consent, and the information to be provided at the time of obtaining consent. Some of the guidance it provides will also be relevant to research settings but, as these are very diverse, researchers will need to consider the matters presented here, address (in the information leaflet, consent form and consent process) those which are relevant in the particular research setting, and seek approval from an Human Research Ethics Committee.

The chapter covers most of the matters which may need to be addressed when obtaining consent and, by doing so, runs the risk of appearing to create unnecessary complexity for both health professionals and those undergoing testing. In practice, the details of the consent process will vary according to the circumstances. For example, at one end of the spectrum will be consent to perform simple diagnostic tests such as for factor V Leiden for someone who has just had a venous thrombosis, while at the other end will be consent to perform presymptomatic testing for a disorder for which there is no prevention or treatment such as for Huntington disease.

3.1 The setting in which genetic testing takes place

Genetic testing and the collection of genetic information usually take place in a health care setting. The request for testing will sometimes come from the person to be tested and will sometimes be recommended, or raised as a matter for consideration, by a health professional. There are several aspects related to the setting that may need to be addressed.

- The reasons why the person has come forward at this time to obtain genetic information, and their understanding of what information the test can provide, should be determined.
- A private, comfortable and quiet environment is important.
- An appropriate amount of time, without interruption by phones or other people, needs to be set aside by both the health professional and the person being counselled. The person should be advised of the duration of the appointment at the time it is made.

3.2 Some counselling issues

The counsellor's role is to help individuals, couples and families make decisions which are genuinely their own and appropriate to their personal situation. Counsellors do this by:

- providing relevant information about genetic testing;
- raising issues that may not have been thought of;
- helping people to see the possible consequences of the available choices;
- providing practical help with decision-making eg reviewing technical information about the test, being someone with whom matters can be discussed as people reflect on the decision to be made in light of their personal situation and the available medical information; and
- providing emotional support.

'Provision of information about a genetic test' and 'genetic counselling' are not synonymous. Information giving is primarily an educational process that can utilise printed/audiovisual resources or explanation by a health professional or both. Training as a counsellor is not required for those whose role is limited to information giving. This can be contrasted with genetic counselling, which encompasses both information giving and discussion of the implications for the individual in a contextual framework that is unique for each person. Here specific training and experience in counselling is required.

The provision of information only may be appropriate for diagnostic testing, and prior to genetic carrier testing in populations where the group to be tested has been consulted and supports the program eg for Tay-Sachs disease in the Jewish community or beta-thalassaemia in communities having their origins around the Mediterranean. Genetic counselling is generally required before and after presymptomatic or predictive tests, following a positive genetic carrier test and following an abnormal result on a prenatal diagnostic or screening test.

It should be recognised that the availability of a genetic test, and of certain options which may follow from testing, are not value neutral. The fact that the test and post-test options are available in a community is likely to be perceived by some to imply that the community at large considers these choices to be ethically acceptable, or even desirable, because the law permits them and some health professionals provide them. This is best seen with regard to prenatal testing.

The preferred language of the person or couple should be determined and an interpreter provided if required. He/she should ideally be a trained health interpreter rather than a family member.

The health professional or researcher should be appropriately qualified eg as a medical practitioner or genetic counsellor, knowledgeable about the area in which he or she is counselling, able to communicate effectively, aware of the consequences for individuals and families of genetic test results, and able to deal with emotional responses to stressful information.

There is an imbalance of knowledge and power between the health professional and the person making the decision, and the health professional is in a position of trust. As a result, health professionals must be aware that they can easily and sometimes unknowingly influence decisions. Sometimes, when testing is clinically

indicated eg to make a diagnosis in a symptomatic person or when predictive testing has clear health benefits whatever the test result, it will be their role to recommend genetic testing and to provide information and counselling. At other times, information and counselling should be given in a way which is not, and cannot be perceived to be, directive. This can be difficult and, when considered necessary, it may be appropriate for the health professional to arrange a separate counselling session for the patient with another counsellor. For example, this approach has proved helpful with regard to presymptomatic testing for Huntington disease that usually involves discussion, at separate appointments, with members of a multidisciplinary group. This allows the person to receive information from several people with different backgrounds, attitudes and experience.

The person requesting genetic testing should be encouraged to articulate his/her own reasons for requesting testing. Some people will do what they perceive, accurately or inaccurately, the health professional would want them to do. Infrequently, a person may find it hard to make a decision, and will genuinely want, and will ask for, advice from the health professional. Consideration should be given to the response to such a request. In general, counsellors should assist people to make a decision which is truly their own and should avoid telling them what they should do. Further counselling sessions may help people to come to a decision. However, if it is decided to advise, the health professional will need to inform himself/herself as completely as possible about the circumstances of the person and advise with the best interests of the person uppermost.

There may be circumstances when it is not appropriate for the professional who provides health care to a person, or his/her family, to act as counsellor when it comes to making decisions about genetic testing. For example, a doctor who is treating a child with a serious inherited disorder, may view the disorder as treatable and may find it difficult to avoid indicating what he/she thinks the family should do when the parents ask about the possibility of prenatal diagnosis for the next pregnancy. In addition, some parents will feel uncomfortable about raising this matter with their doctor, as it could appear that they do not value their existing child or the care provided by the doctor. Health professionals who are aware that, or are asked whether, prenatal diagnosis is available but do not wish to discuss it themselves, or feel unable to do so in a dispassionate way, should offer families referral to another appropriate health professional.

Counselling and support should be provided both before and after testing. This will be provided by the health professional but in addition, many people appreciate the opportunity to bring a partner, family member or friend to counselling sessions, particularly the one where the result of a test is given. It is highly desirable for both members of a couple to participate in counselling about reproductive issues, including prenatal testing.

It is essential that the counselling process allow time for discussion and reflection. Multiple information giving/counselling sessions may be needed. An appropriate amount of time should be allowed between the provision of counselling and performance of the test. Once the person has made his/her own decision about how

to proceed, the counsellor can assist the person by helping him/her to see the reasonableness, or otherwise, of the decision.

In situations where a genetic test is available, attending for genetic counselling should not imply that testing will proceed, that testing is recommended, or even that testing will be discussed. It is not uncommon that a person or couple is referred for counselling or testing without a clear understanding of the reason for referral or the issues which might be discussed. Consequently, one of the first tasks for a counsellor is to clarify what the person or couple wishes to discuss and how much they already understand, and to proceed from there. It can be a mistake to assume that someone has come for a test, or even to discuss a test. This is particularly clear with regard to prenatal tests, but also applies to other types of genetic test.

To help build consistency of access and approach to testing throughout Australia, protocols should be developed and used to ensure that all relevant aspects of the counselling and testing process are completed. This is particularly important as different branches of the same family may be seen at different testing centres.

3.3 The information

3.3.1 General matters to consider are:

The person's current level of knowledge and his/her ability to understand the information which will be needed if an informed decision is to be made.

- The information provided and the way in which it is presented should give due regard to age, level of maturity, education, intelligence and emotional state.
- Information should be provided in the person's or couple's preferred language. It should be determined whether an interpreter is required and whether written, audiotaped or videotaped material needs to be translated into another language.

The novelty and complexity of genetic information. Consideration needs to be given to:

- How much information will be provided. It could be confusing to provide a person with everything that is known about a test and its potential consequences, and the challenge for the counsellor is to ensure that the person has all the information which is likely to be of significance to him/her in coming to a decision.
- The form in which information is provided (eg verbally, audiotape, videotape, diagrams, written).
- The content of the information, including the order in which information is presented and the use of simple, clear and concise language.
- Helping the individual to understand the information.

Information should be presented in a culturally appropriate way. This may involve prior consultation with the relevant group and/or participation of a liaison officer from the group in the counselling session.

The health professional should assess whether or not the person has understood the information provided, can apply it to his/her personal circumstances, and make a decision.

3.3.2 Information to be given

The information to be covered will vary greatly depending on the type of genetic test to be performed and the specific situation and needs of the person requesting information. Sometimes, the amount of information to be provided will be large. Those providing testing may consider it advisable, in the interests of clear communication, to include in the consent form only those pieces of information which are directly and immediately relevant to the testing situation and/or which require specific consent. An information leaflet may be used to cover other matters. It may be necessary to provide the following information:

- That testing is voluntary and it is possible to withdraw from the testing process at any stage, even after the test result is available though not yet given to the person tested. When a person withdraws, he/she should be asked for instructions regarding disposal or subsequent use of the information and genetic material collected for testing.
- That there are alternatives to being tested, such as not taking the test at all, postponing the test, or storing DNA now for later testing by oneself or one's family. The implications of the alternative choices should be explained.
- That counselling and support are available before and after testing. The level of counselling and support needed will vary greatly according to the circumstances of the testing. For example, that which accompanies carrier testing for thalassaemia would be appropriately provided by a general practitioner and could be given at the times the blood is taken and the result given, while presymptomatic testing for Huntington disease requires a multidisciplinary team approach involving several pre-test information/ counselling sessions and follow-up for a significant period after the result is given.
- What will be involved for the person having the test, including a description of any medical procedures and the number, nature and sequence of appointments and the estimated time to obtain a result.
- General information about the disorder being tested for, including:
  - the clinical features and their variability;
  - the range of age of onset;
  - the burden of the disorder, including potential pain and suffering, disability, participation in everyday life, education, employment, marriage and having children, life expectancy and the support given by

society to affected individuals (eg financial assistance, services to address disability, help in the home, respite care and community support groups);

- the pattern of inheritance, and the genetic basis of the disorder in as much as it is known;
- the availability of prevention strategies;
- the availability of treatment; and
- whether prenatal testing is possible.

- Discussion of the consequences for the individual and his or her family of being tested or not being tested, and if testing proceeds, of a test result showing that the gene(s) has/have been inherited or not been inherited. In general, there will be potential advantages and disadvantages of each of the possible test results. The following are some of the matters to discuss if relevant and will be given varying emphasis depending on the type of testing (ie presymptomatic, predictive, carrier, diagnostic, etc.) being considered:
  - What the person to be tested expects from the test.
  - The emotional impact of the test result for the individual and his/her immediate family.
  - The possible consequences of disclosure. Those tested should be advised to consider carefully with whom the test result will be discussed.
  - That there is likely to be an emotional response to the test result and a period of adjustment to the information it provides, and that it is advisable to identify those friends, family members or health professionals who will provide support after the test result is known.
  - How the test result might influence life plans.
  - The potential for the test result to alter relationships between members of the family.
  - The possible consequences of genetic testing, in as much as they are known, for employment, insurance and so on.
  - The implications for future reproduction in terms of risks and reproductive options.
- Explanation that a result showing that the gene(s) has/have been inherited may be of uncertain significance for the person tested. Often the test result will be in the form of a probability eg 'a 60–85 per cent chance of developing breast cancer' rather than a certainty of developing, or not developing, the disorder. A significant proportion of those who inherit the gene may never develop the disorder. In general, the test result will provide no, or only imprecise, information about age of onset, severity or symptoms. It should also be explained that while the information given about the probability of developing the disorder may be the best available at the present time, it may change after further research.

- Information about the existence and contact details of any appropriate lay organisations that provide information and support to families with the disorder in question. Such organisations will often be able to provide additional information about the physical, emotional and social implications of the disorder.
- That if requested, a second opinion can be sought about testing, particularly presymptomatic testing.
- Which gene(s) is/are to be tested and details, as appropriate, of the laboratory aspects of the test.
- The type of sample that will be taken for testing (blood/mouthwash/hair/skin biopsy).
- Any limitations of the test, for example:
  - That only some of the mutations in the gene will be tested. For example it is currently standard practice in Australia to test for only the 4–5 most common CFTR mutations when testing someone who has no family history of cystic fibrosis to determine whether he/she is a carrier.
  - That only some of the genes capable of causing the disorder will be tested. For example, a laboratory may be able to test only BRCA1 and BRCA2 in a situation of familial breast cancer, when genes other than these two could be involved.
  - That the testing technology cannot detect all mutations in the tested gene(s). Certain technologies, such as SSCP (single strand conformation polymorphism) analysis or protein truncation testing, will not detect all mutations in a gene.
  - That testing may not produce any result at all. This may sometimes occur when a test to be done by a linkage (gene tracking) method proves to be uninformative.
  - That the test may produce an unexpected result, as when a sex chromosome abnormality is found at prenatal diagnosis performed for Down syndrome or when chromosomal mosaicism is found in a chorionic villus sample.
  - That the test will not provide information about genes other than the one(s) for which it tests.
- What the result could mean for other family members (especially spouse, existing children, parents, brothers and sisters).
  - Demonstration of a mutant gene in one member of a family means that other family members may have inherited the gene and may need to consider their personal situations with regard to information gathering, risk assessment and testing.
  - Testing an individual may have the potential to show that the gene must be present in certain family members who have not requested

testing. These situations can be anticipated as, for example, when testing the child of an asymptomatic person who has a parent with a dominantly inherited disorder, or when testing one of identical twins. Although the possibility should not override a person's access to testing, it should be considered and discussed in counselling before testing.

- That in certain testing situations, if non-paternity or non-maternity is present, the test might reveal it. For example, it may be revealed when the results of genetic tests performed on multiple family members are collated. However, non-paternity or non-maternity is usually not present and when present will usually not be detected. Therefore it seems unnecessary, and in some cases may be intrusive and upsetting, to discuss the possibility of such an outcome in detail ie. whether the person tested wishes to be told if non-paternity or non-maternity is detected and how he/she would like such information provided if it is found. While the matter may be best not discussed routinely, in situations where testing could reveal non-paternity or non-maternity, it should be mentioned in the consent form or an information leaflet so that the person consenting is aware of the possibility.

  Non-paternity or non-maternity should be disclosed in only the most exceptional circumstances as to do so may cause serious and permanent social and emotional harm to individuals and families. Each group offering genetic testing should have a policy on how to deal with such information when it is found.

  It should be noted that most genetic tests are not capable of determining parentage.

- By whom and in what form the result will be communicated to the person tested. For presymptomatic testing, for example, results should be communicated by the health professional at a consultation and confirmed in writing. By contrast, the result of a carrier test, following detailed pre-test counselling, could be provided by letter unless the health professional perceives that the person tested will require post-test counselling and support.

- Information about the storage of genetic information.

(a) That the test result will be confidential and that the person requesting the test can determine who can have access to it and who can know that the test has been performed.

(b) The person tested should be informed:

  – where the test result will be stored; and

  – the intended duration of storage; and

  – who will have access to the information. In general, they will be those who arranged the testing, the laboratory personnel who performed the testing, those who transmitted the result to the tested individual, those

who were authorised by the tested individual to have access to the test result and those who are responsible for storage of the medical record; and

- who is responsible for retention and integrity of the information, and for its confidentiality and privacy; and
- the procedure for accessing the information; and
- whether he/she can seek correction of the test information if re-tested and an error is detected.
- whether he/she can request that a record of genetic information be deleted.

(c) The following should also be explained as appropriate:

- That it would be prudent to reveal the test result only to persons in whom the tested person wishes to confide and who can be trusted to keep the information confidential.
- Genetic tests may generate information of relevance to the health of other family members. The person to be tested should be advised that if this occurs, their consent will be sought to sharing the information with their family. Most people will show solidarity with their extended family by allowing access to genetic information, though this will not always be the case. Sometimes the person tested will want the information provided to the family but will request anonymity. When this happens, it will often be possible to make relatives aware of the key information ie. the nature of the gene mutation, without revealing the identity of the person tested.
- The laboratory may be approached by other family members for access to the results of genetic testing or to stored genetic material. The circumstances in which the person tested authorises the laboratory to release information should be defined, including what is to happen after his/her death. It may be possible to meet the needs of other family members while preserving the confidentiality of the person tested.
- The person tested should specify which, if any, of his/her medical advisers should be provided with the test result. This applies particularly for presymptomatic, predictive and carrier testing. Diagnostic test results would normally be provided to the health professionals caring for the person tested.
- The person tested should be asked for permission for the result of a presymptomatic or predictive test to be provided to the health professionals caring for him/her if circumstances arise that make it impossible for him/her to give consent eg the onset of symptoms of a dementing disorder for which predictive testing was performed many years earlier. Such information could be important for planning the person's treatment.

– Of any circumstances where a government agency might be able to seek disclosure of the information or where the law may require or authorise disclosure without the person's consent.

- The testing laboratory will not use genetic material for purposes other than those agreed to in the consent form, authorised or required by law, or approved by a Human Research Ethics Committee in accordance with the *National Statement on Ethical Conduct in Research Involving Humans (1999)*.

- Information about the storage of genetic material.

(a) In general, laboratories will store genetic material for a period for substantiation or validation of the result, to comply with accreditation requirements, or as a legal requirement.

(b) If genetic material is to be stored for reasons other than standard laboratory practice or legislative requirement, individuals should be informed that this is proposed or will occur, their consent should be sought if storage is not mandated, and they should be told:

– why the material is to be stored; and

– the nature of the material to be stored; and

– where the material is to be stored; and

– the intended duration of storage. In general, storage should be in accordance with the undertakings given at the time of obtaining the material; and

– who is responsible for retention and integrity of the material, and for its authorised use; and

– that in Australia, for the present, the genetic material tested becomes the property of the testing laboratory from a strictly legal perspective. However, this should not be taken to mean that the person tested is unable to access the material, influence access to it by others or influence its use and/or disposal by the laboratory; and

– that the laboratory will store the material in accordance with current practice but cannot guarantee its viability for future use; and

– who will have a right of access to the material. In general, they will be the individual him/herself and, provided that consent has been given, family members, researchers, laboratory staff and others specified persons; and

– the procedure for gaining access to the material.

(c) Laboratories that intend to store genetic material for reasons other than standard laboratory practice or legislative requirement should inform health professionals who request tests that this is the case. Health professionals can then provide the information in (b) to those being tested.

(d) If stored genetic material is to be re-tested in light of new knowledge or new technology, as an extension of the original laboratory service, there will be an obligation:

- on the person tested to keep the laboratory informed of his/her contact details; and
- on the laboratory to inform the person tested about information arising from the retesting.

(e) Whether the stored genetic material might be used for research. Laboratories using stored clinical samples for research should retain sufficient genetic material to meet the future clinical requirements of the person tested, for example when initial testing is incomplete ie diagnostic testing which fails to identify the mutant gene responsible for the disorder, but which might do so in the future in light of new gene discoveries or new technology.

If it is intended that stored material will be used for research, consent should be obtained from the person in accordance with the NHMRC *National Statement on Ethical Conduct in Research Involving Humans* (1999). (The sections on Use of Human Tissue Samples in Research and Human Genetic Research are particularly relevant.)

Consent forms should be designed so as to allow the maximum research use of the donated genetic material. Thus, for example, a person donating genetic material for a current study involving a search for mutations in BRCA1, may be willing to give consent to the use of the material for future studies on BRCA2, on other as yet undiscovered breast cancer related genes, on breast cancer more generally, and even on broad ranging research on cancer. Obtaining consent for specified types of research at this stage will make the person's wishes clear, and these can be taken into account when an HREC undertakes ethical review of future research which proposes to use the genetic material.

3.4 Consent

The aim of the consent process is to enable persons considering testing to make a decision with the best possible outcome according to them. Both the setting and the information provided need to be considered. Free and informed choice is an essential element of giving consent. Health professionals should avoid counselling in a way that might direct the individual's choice, and must not use deliberate deception or coercion. An example of the former would be to withhold information about choices other than testing and of the latter, would be to make a medical service contingent upon genetic testing, or a prenatal genetic test contingent on acceptance of termination of pregnancy.

Special care must be taken when obtaining consent from those with special needs, such as those from non-English speaking backgrounds, those with different cultural backgrounds, young people, those with psychiatric illness or those with intellectual disability. In these situations, it may be appropriate to suggest the involvement of a

supporter to accompany and advise the person during the process of obtaining consent. This could be a family member or friend but in some cases, a more independent person or advocate will be best. An interpreter should be available to assist those who have difficulty with the English language.

In most circumstances, when testing populations with distinct ethnic, cultural or religious background, it will be important to seek approval from the community as well as the individual eg if it is proposed to screen Jewish high school students for carriers of Tay-Sachs disease.

3.4.1 Written, verbal or implicit consent?

Consent for diagnostic genetic testing (individuals who have symptoms and seek diagnosis) is usually given verbally or is implicit in the request for diagnosis and management of the problem, as is the practice when diagnostic medical testing uses other technologies and takes place in the context of the doctor–patient relationship. However, it may be prudent to obtain written consent when testing symptomatic individuals if the test may give an uncertain result, or a certain result with uncertain implications eg testing a woman with breast cancer for inherited mutations in breast cancer genes. The consent form should provide a record of the matters involved and discussed. Consent for carrier testing in families in the context of a known family mutation may be given verbally but, because some of the consequences are more complex and far reaching, written consent is often requested. Genetic material obtained with verbal consent for the above clinical purposes can only be used for research if approved by a Human Research Ethics Committee in accordance with the *National Statement on Ethical Conduct in Research Involving Humans* (see 3.4.4 below).

In general, written consent should be obtained for presymptomatic, susceptibility, prenatal, preimplantation, and screening tests (eg for gene carrier status) and when genetic material is collected for research.

Written consent is also appropriate when it is known at the time of collection of genetic material for a clinical purpose, that the material is to be stored and may be tested for non-clinical purposes in the future, for example as part of a future research study which has been approved by a Human Research Ethics Committee.

3.4.2 Circumstances in which consent may be waived

Consent for the testing of stored genetic material, as part of a research study, may be waived in the circumstances set out in the NHMRC *National Statement on Ethical Conduct in Research Involving Humans*, in the sections on Use of Human Tissue Samples and Human Genetic Research.

There are long established and well-accepted public health screening programmes, notably newborn screening programmes for disorders such as phenylketonuria and hypothyroidism, where the health benefits resulting from detection of affected children are so clear and any potential harms are so minor, that performance of the test has become routine practice. Parents are provided with written information

about the tests and can opt out, but testing proceeds without consent unless they do so.

3.4.3 Some situations where testing raises specific ethical problems

3.4.3.1 Disagreement between a health professional and a legally competent adult regarding the appropriateness of performing a genetic test

Occasionally, a genetic test will be requested by a legally competent adult but the health professional may decline to perform the test for reasons such as the following:

- when the individual might come to harm eg predictive testing of suicidal individuals;
- when it is considered that the individual cannot give fully informed consent because of his/her emotional state, intellectual capacities or apparent coercion;
- when the individual refuses some aspect of an established testing protocol, considered to be an important part of the process, such as pre-test counselling;
- when the health professional considers that testing is not appropriate from a medical perspective eg because the chance of finding an abnormality is very small, and when others have a higher priority for access to scarce resources; or
- when the health professional believes that testing is inappropriate from his/her own ethical perspective eg a request for foetal sexing with a view to termination of the pregnancy of a foetus of the unwanted sex.

In the first three of these situations, the wish of the requester competes with the concern the health professional has for the requester's wellbeing and/or the requester's perceived capacity to understand matters which are important for making the decision about whether or not to be tested. Professional judgement, which acknowledges the requester's choice but gives due emphasis to the health professional's duty of care, is required. On the one hand it would generally be inappropriate to provide testing simply because it is requested, without considering the potential consequences. On the other hand health professionals should think carefully before refusing testing, especially if there is a possibility that their perception of the requester's capacity to make a free and informed choice, or the likelihood of harm as a result of testing, might be incorrect. When a health professional forms the view that a person's capacity to give informed consent is impaired by his/her emotional or mental state, referral to a psychiatrist or other appropriate health professional should be offered and testing postponed. Discussion with colleagues may assist with decision making and in some circumstances, referring the requester for a second opinion will be appropriate.

In the last two situations, the priorities of the requester and health professional differ. In the counselling process it will be important for them to discuss these differences.

3.4.3.2 Predictive and carrier testing of apparently healthy children

The psychosocial consequences of predictive and carrier testing of children are unknown.

With regard to presymptomatic, predictive and susceptibility testing, there is general agreement among those in Australia providing such tests that they should not be performed on children unless testing is clearly in the child's best interests. Thus, presymptomatic testing of children for adult onset disorders for which there is no preventative strategy or treatment, such as Huntington disease, myotonic dystrophy or familial early-onset Alzheimer's disease, is not considered ethical. Such testing would remove from the child the possibility of deciding, on reaching adulthood, whether or not to have the test in question, and the timing of testing. Also, it would not respect his/her privacy with regard to the information revealed by the test. If the child has inherited the mutant gene, he/she will grow up with, and have to cope with, the certain knowledge that the disorder is very likely to develop in the future. Parental perceptions of the child may alter as a consequence of such information, resulting in altered behaviour towards him/her, and the child may suffer diminished self-esteem and difficulties with future interpersonal relationships. There may also be implications for insurance and employment. Testing should be deferred until the child reaches an age at which consent can be given; the age of consent to medical procedures varies in different States/Territories, and the law also provides for consent by mature minors.

Sometimes it will be appropriate for a doctor to recommend presymptomatic or predictive testing to parents. This will be when there is a highly effective intervention for susceptible children that can prevent a serious future health problem that is very likely to occur. An example is multiple endocrine neoplasia type 2A, a dominantly inherited disorder caused by mutations in the RET gene, which creates a high risk of thyroid cancer. The risk commences around 5 years of age. Thyroidectomy can prevent the cancer and is recommended at around this age for children who have inherited a mutant RET gene. Genetic testing is available to determine whether or not the child of an affected parent has inherited the mutant gene. Occasionally, parents may be unwilling to give consent to genetic testing following extensive counselling, or refuse consent for thyroidectomy after testing shows the child to have inherited the mutant gene. If the case for genetic testing is very strong, and the doctor considers that the parents are not acting in the child's best interest, application can be made to displace the parents' authority by legal proceedings, so that a court can decide the matter.

Familial adenomatous polyposis is another example of a disorder where testing of children may be considered. The child of an affected parent has a 50 per cent chance of having inherited the mutant gene and if he/she has done so, will usually develop colonic polyps in his/her teenage years or in early adulthood. Ultimately one of the polyps will develop into a cancer. Between 10 and 15 years of age

(usually closer to 15), such children are offered a surveillance program of yearly or second yearly sigmoidoscopy and, once polyps have appeared, colectomy is offered in order to prevent colon cancer. Presymptomatic testing before surveillance is due to start may show that the mutant gene has been inherited, in which case surveillance is commenced. If the mutant gene has not been inherited, burdensome surveillance can be avoided.

Any request for presymptomatic, predictive or susceptibility testing of a child from a person or persons with parental responsibility should be discussed with experienced health professionals who can assess the family situation, nature of the disorder, possible medical or other benefits and implications of testing for the child and other family members. The vulnerability of children must be recognised, as must a health professional's need to be satisfied that due care has been taken when making decisions on their behalf. Those requesting testing should be encouraged/ assisted to make an honest assessment of their reasons for doing so and to consider carefully how the test might directly or indirectly benefit the child. Relief of parental anxiety (and occasionally a child's anxiety) is considered insufficient reason for proceeding at this time, in the absence of guiding research.

Carrier testing of children for an inherited recessive condition or balanced chromosome rearrangement also impairs the child's autonomy and the possibility of informed choice at an older age. However, the result of carrier testing has no implications for the future health of the child. It provides information about the chance that the child, once an adult, could have children affected by the disorder. Research is required to determine the benefits and harms that might result from such testing. Parent groups see carrier information to be different from information predicting the later onset of a disorder and their views should be given due weight and be respected. They argue that there may be benefit to the child if he/she has the opportunity to learn about, to understand and to come to terms with the information gradually over time, in parallel with other aspects of development and in the context of family discussion and support. While there is general agreement that presymptomatic, predictive and susceptibility testing should not be performed on children unless there is clear benefit to the child, practice varies with regard to carrier testing in the absence of research studies to guide it.

It may be difficult to reconcile the legal and ethical positions when an older child or adolescent requests genetic testing but is not old enough to give legally effective consent. Often however, both the young person and his/her parent(s)/guardian will participate in the counselling process and if the young person decides to go ahead with testing and gives his/her consent, the parent(s)/guardian can give their consent too, and this will be legally effective. If the young person does not wish to involve his/her parent(s)/guardian, it may be advisable to postpone testing until the age at which legally effective consent can be given, provided that in doing so, the health of the young person is not compromised. In a situation where testing is performed with both the young person's and his/her parent(s)/guardian's consent, it will usually be the case that the result will be given in the presence of the young person and the parent(s)/guardian and hence known by all parties. If the young person wishes to keep the result private, it would be appropriate to respect this wish. Health professionals should acquaint themselves with legislation in their State or

Territory that relates to the age of consent to, and definitions of, medical procedures/treatment, and consent by mature minors.

If it is decided to proceed with predictive or carrier testing of a child who is too young to provide an effective consent, mechanisms should be put in place to ensure that the information revealed is passed on to the child when he/she is old enough to understand it and its implications for his/her future. In general, the information would be discussed, in a way that is appropriate to the maturity of the child/adolescent/young adult, on more than one occasion as he/she passes from childhood into adulthood. The information should be conveyed prior to the commencement of sexual activity if the disorder can be passed on to children. Separation of parents and death of parents are events that can lead to the failure to inform children at the appropriate time. Accordingly, parents need to provide mechanisms to ensure that children are advised of their test results should such events occur.

3.4.3.3 Predictive and carrier testing of others with reduced capacity to give informed consent

Special consideration needs to be given to predictive and carrier testing of those with reduced capacity to provide informed consent, for whatever reason. Counsellors should try to ensure that the information presented is understood by the person to be tested and is correctly interpreted. A family member, friend, legal guardian or professional advocate should be present, depending on the nature and degree of disability present and whether the person is legally able to give consent. The motivation for requesting testing should be explored as coercion is perhaps more likely in this setting eg a person who depends on his/her family for basic care may agree to testing because of concerns about withdrawal of that care. Yet the perceived benefit to the family may have to be considered in addition to those for the tested person alone eg when testing is requested to inform decisions about future care needs and to make provision for them.

CHAPTER 4

PRIVACY AND CONFIDENTIALITY

4.1 Introduction

Privacy refers to a person's interest in exerting effective control over the collection of, access to, use of, or disclosure of any personal information that has been collected or could be collected by any other person.

Confidentiality refers to an obligation that arises from a relationship, most often fiduciary or contractual, between two people or entities in which one person has given information to the other. The recipient of information is under an obligation not to use that information for any purpose other than that for which the information was given. Confidentiality is also an integral component of medical codes of ethics.

Legally, confidentiality is protected by the right of the person who provided the information to compel the recipient of the information to comply with their obligation. In Australia, privacy is legally protected within the jurisdiction of the Commonwealth and in some States and Territories, by statutory codes of conduct that must be followed by public authorities in collecting, storing, granting access to, using and disclosing personal information.

Exceptions to obligations of confidentiality and to the statutory codes concerning privacy include when:

- the information provider consents to the release of the information;
- the law authorises or compels release; and/or
- the information is released in the public interest.

The *Privacy Act* 1988 (Cth) and similar statutes and regulations in some States and Territories deal with personal information privacy protection.

In December 1998, the Commonwealth Government announced that it would develop 'light touch' legislation to support and strengthen self-regulatory privacy protection in the private sector. The scheme is to be based on industry Codes and will apply a legislative framework only where approved Codes are not in place. The privacy standards in the proposed legislation will be based on the National Principles for the Fair Handling of Personal Information, which were released by the Privacy Commissioner in February 1998.

The Information Privacy Principles, in Section 14 of the *Privacy Act*, set standards to ensure privacy of personal information. These standards relate to collection of personal information, storage and security, record keeping, access, alteration of records, and use and disclosure of such information. The NHMRC has produced guidelines, *Guidelines Under Section 95 of the Privacy Act 1988* (2000), that reflect the Information Privacy Principles as they relate to medical research. The NHMRC

has also produced *Guidelines for Genetic Registers and Associated Genetic Material* (1999) which address privacy issues in the context of genetic registers.

4.2 Storage of genetic information

Genetic information can be stored in ways that afford different levels of privacy:

Identified —The genetic information or genetic material can be readily linked to a particular individual. The most useful identifier is the person's name but individuals can also be identified in certain circumstances with considerable accuracy using other characteristics such as the combination of address, date of birth and gender. Clinical information is stored in identified form (in the medical record) and clinical samples will usually be tested and stored in this form as it is essential to be able to identify the person from whom the sample originated. Some research samples will be tested and stored in this form too.

Potentially identifiable (coded) —The genetic information or genetic material has had its identifiers (particularly name and address, but also date of birth and gender) removed and replaced with a code, usually a number. In such cases it is possible to use the code to re-identify the individual about whom the information is, or from whom the material came. In other words, the process of removing the identifiers is reversible. Coding may be done in a clinical laboratory setting to ensure the reliable tracking of samples through the testing process and in a research setting, for the same reason or to maintain the privacy of the samples. It is possible to break the code in order to identify the person from whom the sample originated. The code would normally be broken for clinical samples in order to issue the test result and for research samples, the code may be broken in order to obtain additional information about the participant or to feed back information about the results of the research to the participant. Great care must be taken to prevent error at the time of performing coding and at the time of decoding.

De-identified —The genetic information or genetic material cannot be linked to the individual from whom it came. The process of de-identification removes all identifiers (such as name, address, date of birth and gender) permanently. Synonyms are 'anonymous' and 'not re-identifiable'. Thus, once de-identification has been performed, it will be impossible (except in rare circumstances, see below this paragraph) to identify the person from whom the sample or information originated. Samples to be used for clinical purposes are never de-identified, but de-identification is commonly used to protect the privacy of research participants when identifiers are not necessary for the research eg samples provided by blood banks for research. Researchers need to be aware that the rarity of some genetic disorders might allow certain individuals and/or families to be identified by other researchers, and in some cases by members of the community (particularly a small community), even though the information is de-identified. Such information should be treated with the same level of confidentiality as identified information.

Researchers should consider carefully the consequences of storing information and material in de-identified form for a proposed research study, future research and communication of research results to research participants. If information or genetic

material is de-identified, it will not be possible to go back to participants to obtain more information or genetic material, and it will not be possible to provide participants with research results that relate to them as individuals.

4.3 Individual privacy and confidentiality

Diagnostic genetic information about a symptomatic individual obtained in a medical context is but one form of information needed for his/her health care and should be managed in the same way as other identified medical information. This implies that the information is held in the main medical record and is available to those who would have access to that record for the purpose of attending to the individual's health care.

As discussed earlier in this document, special care must be taken when genetic information describes an identified or identifiable individual's susceptibility to a disorder or risk of having children with a genetic disorder. Such information may have no immediate use in the individual's health care and because of its sensitivity, may need to be handled differently from other medical information eg not placed in the individual's main medical record. For example, the fact that a woman is a carrier of the gene for Duchenne muscular dystrophy is of no relevance to her health care unless she is planning a pregnancy, and that a person is destined to develop Alzheimer's disease some decades from now does not need to be known by health professionals unless a preventative strategy exists. If the result of a genetic test is not placed in the medical record, it must nonetheless be retained by the testing laboratory and those tested should be informed that this will be the case.

There is no consensus on whether presymptomatic and predictive genetic test information should be placed in the medical record so that the test result can be obtained if required by the person tested or by those providing health care. The type of information which could potentially be recorded are the fact that the test has been done, the location of the test result and from whom the test result may be requested. There are concerns that presymptomatic and predictive genetic information could be misused in the absence of legislation protecting the privacy and confidentiality of genetic information.

In contrast, some predictive genetic information will be the basis for implementing preventive interventions and will need to be available to health professionals who care for the individual. It would be incorrect practice for a health professional to prescribe a preventative course of action when the test result that indicated its adoption is not available in the individual's main medical record.

Individual health professionals, testing laboratories, health units and other organisations responsible for the storage of genetic information should consider carefully how genetic information is to be stored eg on paper or electronically, and if electronically, whether it will be accessible through a network or on a patient held 'smart card'. Systems will need to be devised which strike an appropriate balance between access to information needed for health care and the protection of privacy and confidentiality. Special care should be taken with the results of prenatal diagnoses, carrier tests and presymptomatic tests. A different approach may be

taken for different types of genetic information eg diagnostic information about symptomatic individuals may be available on a hospital computer network and in the medical record, while the results of prenatal tests may be placed in the medical record and in a data base only accessible by staff of the testing laboratory and not in the main hospital computer network, and presymptomatic test results may only be accessible by staff of the testing laboratory. The need to establish a workable hospital computer system can result in password protection that is insufficient to guarantee adequate confidentiality and privacy. Appropriate back-up systems for computerised information must be in place to ensure that the information will be available for use by family members, including the next generation.

Researchers may release genetic information in accordance with the consent given by the research participant, as detailed in the consent form and written information describing the research. Sometimes, genetic testing will be performed both as a clinical service activity and for research, or for clinical service alone, and the individual will be asked to sign a consent form. Great care should be taken when preparing consent forms and information leaflets so that they cover all foreseeable eventualities/uses of the genetic information and material. Chapter 3.3.2 describes the information that, as appropriate to the circumstances of the research, should be provided to assist those considering consent. Care should also be taken to explain what are often complex documents and concepts to the individual so that the consent is truly informed.

Individuals and organisations with responsibility for the privacy and confidentiality of genetic information should inform themselves about existing legal obligations concerning collection, use, storage, access and correction of personal information and of the potential legal ramifications of unauthorised release of such information.

4.4 Individual privacy and the family

Genetic information is distinguished from other medical information in that it can potentially provide information about people other than the individual concerned. In particular, it can provide information about the individual's family. For example, if an individual is diagnosed to have familial adenomatous polyposis, his/her blood relatives are at risk of developing this disorder, which almost always results in bowel cancer. If the relatives are told that they are at risk they can choose to be tested too, and preventive measures are available to those who have inherited the disorder. It follows that there is potential for tension between the privacy of a person's genetic information and the potential health benefits which could result if the information were known by other family members. It is generally accepted that an individual has responsibilities to his/her family as well as a right to the privacy and confidentiality of his/her genetic information. In family relationships, there is, in Australia, no established legal duty to warn. Most individuals can refuse to pass on information to relatives without breach of law. However, in deciding not to disclose such information to relatives, an individual will need to balance carefully their right to privacy with the fact that disclosure could lead to the avoidance of a substantial chance of harm to a relative.

Blood relatives

The fact that a genetic test may provide information of significance to other family members should be discussed prior to testing, if appropriate. Once the test result is known, an individual (or his/her next of kin) who is asked, will usually give consent for a blood relative to access genetic information or material which may assist in clarifying the blood relative's susceptibility to a disorder or the chance of having affected children. The individual may wish to determine when the information is to be provided.

When genetic information is to be shared with family members, the most appropriate person to make the initial contact is the individual who has undergone the genetic test. There may be difficulties in communication between particular family members, and in these cases involvement of another family member as a go-between may be helpful. If direct communication between family members is not an acceptable option, the health professional should consider taking on the task of informing relatives, with the consent of the person tested. Health professionals can only recommend that information is shared with relatives and are not in a position to ensure that information transfer occurs. They must rely on their patient to carry out the task if he/she has agreed to do so.

Health professionals should be aware that in Australia, there is no established legal requirement to warn their patient's relatives of a genetic risk. Their duty of care is to the patient, not to the relatives. Clearly though, health professionals will wish information to be passed on to relatives if it is of potential significance to their health. This is most appropriately done by asking the patient to inform his/her relatives, and recording the request in the patient's medical record. The health professional may be able to facilitate the process by providing written information or agreeing to phone contact from the relatives.

Relatives who are not blood relatives

The issues are somewhat different with regard to passing genetic information on to current or intended spouses/partners, or other individuals who are family members by marriage. Unlike the blood relatives of someone with a genetic disorder, they are not at increased risk of developing that genetic disorder, but it is appropriate that they should be informed if their present/future children could develop/inherit the disorder. For example, it would be appropriate for an individual who has been shown by testing to have the gene for Huntington disease to inform his/her spouse/partner, both in terms of their own relationship and possibility of having children who inherit the disorder. As with blood relatives, individuals will usually provide the appropriate information to the relevant persons (current or intended spouses/partners, or other individuals who are family members by marriage). Those responsible for genetic information should not release it to relatives who are not blood relatives without the consent of the person to whom the information relates.

Deceased individuals

Genetic information about, or material from, a deceased individual should be handled in accordance with any instructions given by the individual in life. In the absence of instructions, it may be released to family members with the consent of the senior available next of kin. In general, family members will request genetic information because it is of potential significance for their future health and/or that of their children. Some information will not relate to health care eg paternity information (See 3.3.2.15), and caution should be exercised before releasing such information.

Adopted children and children conceived with donated gametes

Occasionally an adopted child will be the first person in his/her biological family to manifest symptoms of a genetic, and potentially inherited, disorder. It will then be appropriate for the adoptive parents to try to inform the biological parents if there is a risk that the disorder could occur in them or in their future children. For example, the biological mother of a boy with Duchenne muscular dystrophy may be a carrier and could have further affected sons. Or the recognition of adult polycystic kidney disease in a young child may mean that one of his/her parents unknowingly has kidney cysts and deteriorating kidney function. The confidentiality provisions of State Adoption Acts are relevant in such situations.

Care to avoid inadvertent release of information

Since genetic disorders affect families rather than individuals, a health professional will often discuss the disorder in a family context. The pedigree may be updated at the time a family member is consulted and, when explaining the disorder to that person, the pedigree or the clinical features of another family member may be used to illustrate a point eg how the disorder is inherited, who might be at risk, etcetera. It is very easy for health professionals to assume falsely that there has been a free flow of genetic information within families. This is often not the case. Sometimes the transfer of information will have been postponed pending a perceived need or an appropriate opportunity. Sometimes there may be communication difficulties and relational problems within the family. Showing previously drawn pedigrees to family members, or talking about family members assuming that it is generally known who is and who is not affected by the disorder, can result in inadvertent breaches of privacy/confidentiality and care should be taken in this regard.

Reluctance to give consent to release of information to family members

Sometimes an individual or the next of kin of a deceased individual will be reluctant to give consent to release of genetic information or material, but may do so following explanation and discussion with the health professional.

Rarely, an individual will refuse consent to release the information or material. If this happens, the health professional should ensure that the individual understands the potential consequences of such a decision for the health of family members and, indirectly, for the individual him/herself in terms of relationships within the family

if a preventable adverse health outcome occurs. Involving the individual's general practitioner or other health professional as a trusted counsellor may be appropriate. Ultimately, the individual's decision should bind the health professional. However, there may be rare circumstances in which a health professional considers that the risk to the health of relatives is sufficiently large, serious, imminent and potentially preventable that consideration should be given to breaching the individual's confidentiality. Before doing so, the health professional should consider the potential for professional censure or legal action if confidentiality is breached.

Sometimes, the whereabouts of an individual whose consent should be sought will be unknown. Again, the health professional will need to decide whether or not to breach confidentiality.

Discussion with colleagues may be helpful when a health professional is faced with either of these two scenarios.

4.5 The right not to know

In the context of potentially heritable disorders, good medical practice requires the taking of a family history to determine who else in the family had the disorder in the past, who might have it now and who might be at risk of developing it in the future. Those in the family who are potentially at risk of the disorder can be informed about that possibility and the options available to them. In general, family members who are contacted will appreciate the approach and the underlying concern for their welfare.

It cannot be assumed that everyone will wish to know that they might have inherited a disorder present in their family, that it is possible to test them to determine whether or not the mutant gene has been inherited or that prenatal diagnosis is available for the disorder, which could occur in their children.

Sometimes a family member will have clearly stated that he/she does not wish to discuss the family's illness because of the difficult problems and decisions that are associated with it and the emotional consequences of talking about them. In particular, it may have been made clear that it would be offensive to be approached with information about the availability of prenatal diagnosis. In such circumstances it would fail to respect that person's autonomy to insist on providing him/her with the information he/she has said he/she does not want. To do so would assume that another family member or a health professional is a better judge of what is in the person's best interest.

A more common situation is that the views of a family member are not known, or that he/she appears to dislike discussing health matters in general. If such a person is kept ignorant of his/her situation with regard to the family illness, he/she will have no opportunity to consider the problem and to decide how to proceed. There is a strong argument for informing such people in a sensitive way, almost always through a family member with whom they relate well. If more appropriate, in particular circumstances, a health professional can undertake the task, having been introduced by a family member when possible and having had permission from the person to be contacted for contact to be made.

With regard to the results of genetic research, there will be some research studies which may reveal, as a result of testing, genetic information of potential significance to the health of individual participants. If so, the *National Statement* requires that each research participant is asked, at the time of giving consent, whether or not he/she wishes to receive the results of the tests. If not, his/her wishes should be respected. (Refer to the NHMRC *National Statement on Ethical Conduct in Research Involving Humans* (1999) for guidelines on human genetic research.)

CHAPTER 5

DISCLOSURE OF GENETIC INFORMATION

5.1 Stigmatisation and discrimination within society

Stigmatisation relates to the perception of an individual by others that may result, for example, in an individual being spoken of adversely or considered undesirable as a friend or as a marriage partner by members of a community. The term discrimination can be used to simply mean the recognition of differences between people, but is more often used to refer to the unfair treatment of individuals based on such a perceived or actual difference. The following discussion refers to 'unfair discrimination' rather than 'discrimination' so that the intended meaning is clear. It also focuses on discrimination rather than stigmatisation as the former represents the mechanism that may result in harm to individuals and families.

Genetic tests can reveal that people have, or have a genetic predisposition to, a disorder. Stigmatisation and discrimination could occur within many aspects of everyday life, with regard to family relationships, insurance and employment. They already occur for those who are considered 'different' or 'disabled'. Genetic information, by adding another reason for such treatment, has the potential to increase the number of people so affected.

There are two basic types of discrimination: direct (where a person with a disability is treated less favourably than he/she would have been had they not been disabled); and indirect (requirements or conditions which do not take into account the particular needs a person with a disability may have in a given situation).

There are many situations for potential unfair discrimination. Legislation in Australia, including the *Disability Discrimination Act* 1992 (Cth) and parallel State/ Territory legislation, prohibits many forms of discrimination against people on the grounds of disability. However, for this legislation to protect people against discrimination on the grounds of genetic condition, the definition of 'disability' would need to cover genetic presymptomatic, susceptibility and carrier status.

5.2 Possible uses of genetic information which could harm individuals

In this section, several situations are mentioned to highlight how genetic information could potentially be used in ways that would harm individuals. While some are real issues now, others are more speculative.

The family

Revealing genetic test results to family members can alter the way in which an individual is perceived and treated by the family, for better or worse. For example, early-age onset Alzheimer's disease (dementia) is sometimes caused by a mutation in a dominantly inherited gene. If a man is shown to have inherited such a mutated gene, his siblings could provide emotional support in the short-term and practical

help and care once the dementia begins to limit their brother's functioning. In contrast, they could begin to withdraw by reducing contact with their brother and his family. Another sibling who was also tested and shown not to have inherited the gene, may feel guilty that he/she has escaped while the affected brother has not, and may therefore feel an obligation to care for him as his dementia worsens.

There are many uses of genetic testing, discussed in earlier sections of this document, which can lead to improved health care and provide people with information they wish to have. The genetic register is a tool for maximising the health benefits of genetic information for families and the reader is referred to the NHMRC's *Guidelines for Genetic Registers and Associated Genetic Material* (1999) for additional information.

Insurance

In the past, life insurance companies obtained genetic information by asking questions about the health and causes of death of close family members, and such information was used to determine eligibility for insurance. Recently, as genetic testing for many disorders has become available, insurance companies have stated that if a person has already had a genetic test, this fact must be disclosed to the insurer when applying for life insurance. The insurer may then request the test result if it believes the information is relevant to its decision whether to provide insurance and if so, whether to do so at standard rates. Insurers will not ask applicants to undergo genetic tests. In the future, genetic testing could become, in certain circumstances, a requirement in order to obtain insurance eg for very large policies. These developments have raised concerns that unfair discrimination could occur if genetic test information is used inappropriately by insurers. In Australia, insurance companies are not in breach of the *Disability Discrimination Act* (Cth) if their actions are based on sound actuarial data, and the use of genetic information is not unfair discrimination when used in this way. In some instances, the need to disclose that a genetic test has been performed may cause some people to forego the personal health benefits of genetic testing in order to access life insurance. On the other hand, those at risk of a genetic disorder who are tested and shown not to have inherited their family's genetic predisposition may be keen to reveal that information in order to obtain insurance at standard rates when they would otherwise have been unable to obtain insurance.

Of particular concern would be the use of genetic information to determine eligibility for basic health insurance. Current health insurance provisions in Australia rest upon the notion of 'community rating' and persons cannot be refused private health insurance on the basis of present or possible future health status, although there are waiting times for pre-existing conditions. Social policy related to health insurance may change over time in Australia such that while genetic information revealed now may not have an adverse impact on access to health insurance at this point in time, it may do so in the future. To have had genetic testing may have negative consequences for Australians who move overseas to countries where genetic test results are used to determine eligibility for health insurance.

Employment

Employers may seek genetic information about employees for a variety of reasons. They may wish to identify existing or potential employees whose genetic make-up places their health at risk in a particular work environment and to protect them from the potential harm. The number of known situations in which the work environment is harmful because of genetic susceptibility is very small but includes the carrier state of sickle cell anaemia and work at high altitudes, and glucose-6-phosphate dehydrogenase deficiency and work where environmental oxidants are present. Employers may also decide not to employ people with certain genetic traits in particular work circumstances.

Genetic information about future health could potentially be used to distinguish between job applicants in terms of their ability to remain productive, to take a minimum of sick leave, to not require a special work environment and to not increase the employer's superannuation costs. Such use of genetic information is considered to represent unfair discrimination. However, it could potentially be lawful discrimination in Australia at the present time, if the presence of a mutant gene which creates susceptibility to a disorder fits within the definition of 'disability' in the *Disability Discrimination Act* 1992 (Cth) [s4 (1)]. Then, an employer would be entitled to discriminate against a person who would be unable to carry out the inherent requirements of the particular employment because of the nature of the disability [s15 (1)]. Thus, for example, existing legal provisions may not prevent an employer from discriminating against a young person who has had a test revealing the presence of a gene for Huntington disease, Alzheimer disease or other late onset disorders. Although the individual may not develop symptoms for many years, if at all, the nature of the disorder could prevent the individual from carrying out the inherent requirements of the employment, thus allowing discrimination by the employer.

Finance

There is no evidence at present that Australian financial institutions would wish to access genetic information when determining eligibility for a loan. The possibility of an indirect use of genetic information to determine access to finance is highlighted by the situation in the United Kingdom, where many home loans require a life insurance policy as collateral. It should be noted that United Kingdom insurers do not require genetic information, at the present time, for mortgages below a certain sum. If Australian financial institutions started to require life insurance as collateral for a home loan, and given that Australian life insurers require disclosure of genetic test results, genetic information could then become the basis of unfair discrimination.

Adoption

A child's genetic status may have significant and long-term implications for both a child and his/her adoptive parents. For the present, adoptive parents receive certain personal and family health information about a child's biological parents and this is considered desirable, primarily to assist them in making provision for the future

health care of the child. It is recognised that providing such information could potentially influence whether or not the adoption proceeds. Some information, such as the result of predictive genetic testing of a biological parent would not be given to the adoptive parents (unless the biological parent expressly requested it) as to do so would breach his/her privacy; the fact that a particular disorder is present in the family would be revealed but not the predictive test result.

Some may argue that when a biological parent has a personal or family history of an heritable genetic disorder, predictive or susceptibility genetic testing should be performed on a child prior to adoption in order to determine the child's suitability for adoption. The more generally held view is that the use of genetic information in such a way would represent disrespect for the worth of the child as a human person, would fail to respect the child's autonomy to choose whether or not to be tested on reaching adulthood, and would breach the child's genetic privacy. It also ignores the fact that the results of genetic testing will, in most cases, reflect possibilities rather than certainties.

Health care

Genetic information could potentially be used to determine eligibility for certain health services. For example, a personal history of a genetic disorder, family history of a genetic disorder or evidence of predisposition to a genetic disorder could influence eligibility for assisted reproductive technology and access to donated gametes or organs.

Forensic and legal settings

The sequence of bases in an individual's DNA is unique and as such, provides a means for unambiguous identification of that individual. DNA 'fingerprinting'/ 'profiling' can be used to establish or exclude paternity, and to identify a person who is deceased or who has committed a crime. Australian governments are moving to establish a national DNA criminal investigation database system for forensic use.

Governments and government agencies

Governments could potentially use genetic information to determine eligibility for health services in certain circumstances. For example, a government could make the availability of financial support for those with genetic susceptibility contingent on adherence to prevention strategies, or make those who are unwilling to use prenatal diagnosis bear the full cost of care of affected children. Concern about future use of health services by immigrants could result in a government requiring genetic testing, or using existing genetic test results, to determine eligibility to migrate to Australia. Governments, as policy makers and sources of funding, could also require and misuse genetic information as a means of eugenic practice. Individuals or groups of individuals could be disadvantaged economically, socially and politically because they have, or do not have, a certain genetic profile. The use of genetic information in these ways would be ethically unacceptable.

5.3 Psychological difficulties

Disclosure of an individual's genetic information to others may cause them to treat him or her differently. As a direct consequence this may result in psychological problems for the individual, or there may be an indirect effect if the individual's own perception of him/herself is changed for the worse.

5.4 A possible consequence of concern about discrimination

Concern about the possibility of stigmatisation or discrimination could discourage a person from taking advantage of the medical benefits of obtaining genetic information, with consequent adverse effects on his/her health. This could have effects for current and future family members as well as for the individual. The chance that this outcome will occur can be minimised if there is legislation to prevent unfair discrimination based on the results of genetic testing, and if the community is educated about the potential benefits of genetic testing and has factual information about the circumstances in which it is necessary for test results to be revealed.

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GLOSSARY

Achondroplasia —A heritable (autosomal dominant) disorder which is the most common cause of severe short stature (dwarfism). In addition to short stature, it is associated with limb shortening that is more severe than the shortening of the trunk, a relatively large head and a characteristic facial appearance. Intelligence is normal. In almost all instances it is caused by a specific mutation in the fibroblast growth factor receptor 3 gene (FGFR3) on chromosome 4.

Aetiology —The underlying cause of a disorder.

Alzheimer's disease —A degenerative disorder of the brain resulting in dementia. This is mostly a multifactorial disorder with very little known about the genes which create susceptibility, although one variant of the apolipoprotein E gene, $ApoEe_4$ is one. However, there is a rare form of Alzheimer's disease that is dominantly inherited, has an early onset and can be caused by mutations in specific genes.

Amino acid —One of the building blocks of proteins. There are 20 amino acids.

Amniocentesis —A diagnostic procedure performed during pregnancy to obtain a sample of amniotic fluid for testing.

Anonymous —see De-identified.

Autosomal —Associated with one of the 22 pairs of autosomes, chromosomes that are not sex chromosomes. Hence autosomal gene and autosomal inheritance.

Beta-thalassaemia —A severe inherited (autosomal recessive) form of anaemia caused by the inability to make adequate amounts of the protein beta-globin, and hence haemoglobin. Affected children require regular blood transfusions and treatment to remove the excess iron that accumulates in their bodies as a consequence of the transfusions. It results from mutations in the beta-globin gene on chromosome 16.

Carrier —An individual who has a disease-causing mutation but will not develop the disorder in question. Most commonly used with regard to autosomal and X-linked recessive disorders and refers to the situation in which the individual has one normal and one mutant gene in a particular gene pair. Can also be used to refer to an individual with a balanced chromosome rearrangement.

Carrier test —Test to determine whether or not an individual carries a recessive gene.

Chromosomal mosaicism —The situation in which a tissue or person has a mixture of cells, some with normal and some with abnormal chromosomes. It is found in about 1 per cent of all placental samples obtained by chorionic villus sampling (CVS) and is usually confined to the placenta ie. not present in the foetus.

Chromosome —Structures within the nucleus of cells that contain hundreds or thousands of genes arranged end to end. Each cell normally contains 46 chromosomes as 23 pairs. 22 pairs are called autosomes while the remaining pair is

the sex chromosome pair, two X chromosomes in females and an X and a Y in males.

Chromosome rearrangements —Chromosome abnormalities involving abnormal arrangement of parts of chromosomes. Examples include translocations, in which parts of chromosomes are translocated from one chromosome to another and inversions, where as the name suggests, part of a chromosome is inverted. A chromosome rearrangement is said to be 'balanced' if all the chromosome material is present even though it is arranged abnormally. Chromosome rearrangements can be inherited from a parent, or occur for the first time in an individual as the result of a chromosome error during the formation of the ovum or sperm from which the individual developed.

Chorionic villus sampling (CVS) —A diagnostic procedure performed in early pregnancy to obtain a sample of the developing placenta (chorion) for testing.

Coded—see Potentially identifiable.

Colectomy —Surgical removal of the colon.

Complex socially significant characteristics —This concept refers to characteristics of individuals or groups of individuals that have a complex multifactorial basis, some of which are genetically determined, and which may determine how they are perceived and treated by society. It thus includes characteristics such as intelligence, race, personality, sexuality, physical appearance and susceptibility to drug addiction, among others.

Cystic fibrosis (CF) —A serious inherited (autosomal recessive) disorder affecting the lungs and digestive system of babies, children and young adults. Affected individuals have sticky mucus in their lungs and are prone to chest infections. They also have difficulty digesting food and may later develop liver problems. It is caused by mutations in the CFTR gene on chromosome 7. About 1 in 20 Australians is a carrier of a CFTR mutation and about 1 in 2,500 have the disorder.

De-identified (not identifiable, anonymous) —Genetic information or material is referred to as 'de-identified' if identifiers have been removed permanently or the genetic information or material has never been identified. The process is irreversible. It should be recognised that the term 'de-identified' is used frequently in other documents to refer to sets of data from which only names have been removed. Such data may remain 'potentially identifiable'.

Diagnostic test —A test performed to make a diagnosis of a specific disorder in a person who already has symptoms.

DNA (deoxyribonucleic acid) —A linear sequence of deoxyribonucleotides (nucleotides for short) which encodes genetic information. Genes are composed of DNA. See nucleotide.

Dominant —The form of inheritance in which a genetic disorder or characteristic manifests when only one of the two copies of a gene is abnormal (mutated).

Down syndrome —A chromosome disorder resulting from the presence of three copies of chromosome 21 instead of the normal two. It is associated with specific physical characteristics and usually with intellectual disability. Trisomy 21, the situation in which there are three separate chromosomes 21 is not an inherited problem. The chance of having a child with the disorder increases as the age of the mother increases. Translocation Down syndrome is the situation in which the third chromosome 21 is attached to another chromosome and in this case, the disorder may have been inherited from a parent who is a 'balanced translocation carrier'. The parent, and possibly other family members, may have an increased chance of having children with translocation Down syndrome.

Duchenne muscular dystrophy —A serious progressive genetic (X-linked) disorder of muscle which affects boys from early in childhood. Affected boys usually require a wheelchair by 12 years of age. It results from mutations in the dystrophin gene on the X-chromosome.

Enzyme —A protein that acts as a catalyst to speed up the conversion of one chemical in the body into another.

Factor V Leiden —A variant of the blood clotting protein Factor V that predisposes to venous thrombosis.

False-negative —The proportion of those with the disorder who are not identified by the test.

False-positive —The proportion of those who are not affected which the test incorrectly identifies as being affected.

Familial adenomatous polyposis (FAP) —An inherited (autosomal dominant) disorder which results from mutations in the APC gene on chromosome 5. Hundreds/thousands of polyps develop within the inner lining of the colon from teenage years onwards and ultimately cancer develops in one or more of them. Children of affected individuals have a 50 per cent chance of inheriting the disorder and need to have regular sigmoidoscopic surveillance of the colon for polyps. Colectomy is usually recommended once polyps have started to appear, in order to prevent cancer of the colon.

Familial hypercholesterolaemia —An inherited (autosomal dominant) disorder associated with very high levels of cholesterol in the blood and predisposition to coronary heart disease and disease of other arteries. It results from mutations in the LDL receptor gene on chromosome 19. About 1 in 500 individuals have the disorder.

Fragile X syndrome —An inherited (X-linked) form of intellectual disability, associated with characteristic physical features, resulting from mutation in the FMR1 gene on the X-chromosome. It affects about 1 in 2,000 boys.

Gamete —Egg (ovum) or sperm cell.

Gene—The fundamental physical and functional unit of heredity consisting of a sequence of DNA, occupying a specific position on a specific chromosome. Each

gene encodes the information required to produce a protein or ribonucleic acid with a specific structure and function.

Gene product —The RNA or protein encoded by a specific gene.

Genome —The total genetic complement ie. complete DNA sequence. The term can be used with reference to a cell, an organism or a species.

Genotype —This term may refer to (a) the particular DNA sequence of one of an individual's genes, or (b) the sum total of such sequences for all the individual's genes.

Germ-line DNA —The DNA that an individual will pass on to his/her children in the sperm/egg. It is distinguished from somatic DNA which exists in cells other than reproductive cells and which cannot be transmitted to offspring.

Germ-line mutation —A mutation in germ-line DNA.

Glucose-6-phosphate dehydrogenase deficiency (G6PD deficiency) —An inherited (X-linked recessive) disorder of red blood cells which affects mainly males, about 400 million people worldwide. It can cause neonatal jaundice and acute haemolytic anaemia (sudden breakdown of red blood cells). Haemolytic anaemia can be triggered by a number of drugs, infections and certain foods. The disorder results from mutations (over 400 different ones) in the glucose-6-phosphate dehydrogenase gene on the X chromosome.

Gonadal mosaicism —The situation in which a gonad (ovary or testis) contains a mixture of cells, some with normal and some with abnormal genetic constitution. There can be gonadal mosaicism for mutations in single genes or for chromosome abnormalities. A person with gonadal mosaicism is not thought of as a carrier of the abnormality but could potentially have multiple children with the disorder that is associated with the genetic abnormality.

Guthrie test —The original test to screen newborn babies for phenylketonuria using blood obtained by heel prick spotted onto blotting paper and mailed to the laboratory. Subsequently, the blood spots came to be used for screening for disorders such as hypothyroidism, galactosaemia and cystic fibrosis.

Haemochromatosis —An inherited (autosomal recessive) disorder resulting from mutations in the HFE gene on chromosome 6. It is associated with progressive accumulation of iron in the tissues, the toxicity of which ultimately leads to organ damage. Treatment involves regular removal of blood from the body. As many as 1 in 10 people are carriers of mutation in the HFE gene.

Haemoglobin electrophoresis —The process of separating different types of haemoglobin using the fact that haemoglobin molecules with different electrical charges move at different rates in an electrical field.

Haemophilia A and B —Inherited (X-linked) disorders of blood clotting resulting from mutations in the factor 8 and factor 9 genes, respectively, on the X-chromosome. This results in bleeding into joints and bruising after minor injury.

Prevention and treatment of bleeding uses pure factor 8 and 9. About 1 in 10,000 boys are affected.

Hereditary non-polyposis colorectal cancer (HNPCC) —An inherited (autosomal dominant) disorder resulting from mutations in genes (MLH1, MSH2, MSH6, PMS1, PMS2) which repair errors in DNA. Affected individuals have a high risk of developing colorectal cancer as they get older and for women, there is also a high risk of endometrial and ovarian cancer.

Heterozygote —See Carrier.

Histological block —Tissue embedded in a solid material such as paraffin to enable the cutting of thin slices of the tissue for examination with a microscope.

Homozygote —Individual with a mutation in both genes of a particular pair. When used strictly, the situation in which both mutant genes have the same mutation. The term compound heterozygote is used when the two genes of a given pair both have mutations, but the mutations are different.

Huntington disease —A progressive inherited (autosomal dominant) degenerative disorder of the brain which begins in mid-adult life and results in a particular type of involuntary movement called chorea, often associated with change in personality and later on with dementia. It results from mutations in the IT15 gene on chromosome 4 and affects about 1 in 10,000 people.

Hypercholesterolaemia —See familial hypercholesterolaemia.

Hypothyroidism —Inadequate production of the thyroid hormone thyroxine by the thyroid gland. Newborn babies are routinely screened for hypothyroidism. If detected and treated early, the children will be normal and will avoid the intellectual disability and growth failure that would otherwise occur.

Identified —Genetic information or material that allows the identification of a specific individual is referred to as 'identified' information or material. Examples of identifiers may include the individual's name, date of birth or address. In particularly small sets of data even information such as a postcode may be an identifier.

Monogenic disorder— See single gene disorder.

Multifactorial —A term which denotes that a disorder or characteristic is determined by multiple factors which may include one or more genes, one or more environmental factors, and chance.

Multiple endocrine neoplasia type 2A —A heritable (autosomal dominant) disorder which creates a predisposition to cancer (medullary carcinoma of the thyroid and phaeochromocytoma) and parathyroid gland hyperplasia. It results from mutations in the RET gene on chromosome 10.

Mutation —A variation or change in the sequence of nucleotides in a gene's DNA that is permanent, may be transmissible to children, and may cause, predispose to or modify a disease process.

Myotonic dystrophy —An inherited (autosomal dominant) disorder which causes progressive muscle weakness, myotonia (inability of muscles to relax normally after use), cataracts, frontal baldness and several endocrine abnormalities including predisposition to diabetes and testicular atrophy. It results from mutation in the myotonin kinase gene on chromosome 19.

Nucleotide —The basic chemical unit of DNA consisting of one of four bases (adenine, guanine, cytosine and thymine) together with deoxyribose and phosphate.

Pathogenesis —The process of sequential steps or mechanism by which cells and/or tissues go from normality to a disease state.

Penetrance —The frequency with which individuals having a particular disease genotype develop the disorder. Thus, the penetrance of mutations in the BRCA1 gene in women is 60-85 per cent ie. only 60–85 per cent of those with a mutation in this gene will develop breast cancer.

Phenylketonuria (PKU) —An inherited (autosomal recessive) disorder resulting from mutations in the phenylalanine hydroxylase gene on chromosome 12. Affected children are unable to rid the body of the amino acid phenylalanine that is toxic to the developing brain. Newborn babies are routinely screened for phenylketonuria. If detected and treated early with a special diet, the children will be normal and will avoid the intellectual disability that would otherwise occur.

Phenotype —The biochemical, physiological and physical characteristics of an individual that result from the interaction of his/her set of genes with the environment and chance events. Often used when referring to the particular features of a genetic disorder which can be observed in an affected individual.

Polyp —A benign tumour that grows from cells in the lining of the gut, most often in the colon. Some polyps will change with time and become cancers.

Polycystic kidney disease —A progressive inherited (autosomal dominant) disorder resulting from mutations in either the PKD1 gene on chromosome 16 or the PKD2 gene on chromosome 4. Cysts may develop in the kidneys from childhood onwards and can cause kidney failure. About 1 in 1,000 individuals has the disorder.

Polygenic —Sometimes used synonymously with 'multifactorial' but strictly, caused/controlled/modified by, or associated with, the action of more than one gene.

Population screening —The application of a screening test to an entire population or large group within a population. Examples are newborn screening for hypothyroidism, phenylketonuria and cystic fibrosis and maternal serum screening for Down syndrome and neural tube defects.

Potentially identifiable (coded, re-identifiable)—Genetic information or material may have identifiers (name, date of birth, address) removed and replaced by a code. In such cases it is possible to use the code to re-identify the person to whom

the genetic information or material relates, that is the process of de-identification is reversible. In these cases the data are referred to as 'potentially identifiable'.

Predictive test —A test performed on a person who has no symptoms of a specific disorder at the time of testing, to determine whether or not he/she has a gene which has a high probability of causing symptoms of the disorder to appear at some time in the future. See Presymptomatic test.

Prenatal test —A test performed during pregnancy, sometimes presymptomatic and sometimes diagnostic, usually to detect or exclude the presence of a particular disorder in the baby. These tests are accurate when performed on cells from the foetus obtained by chorionic villus sampling or amniocentesis, and can determine with certainty whether or not a foetus has a particular condition eg molecular testing for thalassaemia or chromosome testing for Down syndrome. Some prenatal tests are imperfect because they assess the foetus indirectly (eg maternal serum screening for Down syndrome) and can only determine whether or not the foetus has an increased chance of having the condition sought. For those at increased risk, a further test is needed to determine with certainty whether or not the disorder is present.

Presymptomatic test —A test performed on a person who has no symptoms of a specific disorder at the time of testing, to determine whether or not he/she has a gene which is almost certain to cause symptoms of the disorder to appear at some time in the future. See Predictive test.

Protein —A molecule composed of many amino acids linked together, folded into a particular shape in order to carry out its function. There are many types of protein including enzymes (eg the digestive enzyme trypsin), hormones (eg growth hormone and insulin) and structural proteins (eg collagen).

Recessive —The form of inheritance in which a genetic disorder or characteristic manifests only when both copies of a gene pair are abnormal (mutated). One abnormal gene will have been inherited from each parent who in most cases will be carriers. A recessive gene can be an 'autosomal recessive' if the gene is located on one of the 'autosomes' (the chromosomes which are not sex chromosomes) or an 'X-linked, or sex-linked, recessive' if the gene is located on the X chromosome.

RNA (ribonucleic acid) —A linear sequence of ribonucleotides (nucleotides for short). One type of RNA is messenger RNA, or mRNA. In order to make a protein, the genetic information in DNA is copied into mRNA, which carries it from the nucleus to the protein producing part of the cell. There the information is translated using the mRNA as a template and is reflected in the amino acid sequence of the corresponding protein. See nucleotide.

Screening test —A test performed to detect or exclude the presence of a mutant gene(s) in an individual or group of individuals who are not known to be at increased risk of having the mutant gene(s).

Sensitivity —The sensitivity of a test is the proportion of those affected by the disorder who are correctly identified by the test as being affected.

Sex chromosomes —The X and Y chromosomes. Females have two X chromosomes and males an X and a Y.

Sex-linked —See X-linked.

Sickle cell anaemia —An inherited (autosomal recessive) disorder characterised by lifelong breakdown of red blood cells (haemolytic anaemia) and a variety of complications resulting from increased susceptibility to infection and a tendency to blockage of blood vessels. It is caused by a specific mutation in the beta-globin gene on chromosome 11 in all those affected, which results in the substitution of the amino acid valine for glutamine at position 6 of beta-globin. Beta-globin is one of the components of haemoglobin.

Sigmoidoscopy —The medical procedure during which an endoscope (viewing instrument) is passed into the anus and up into the sigmoid colon so that the rectum and lower part of the colon can be viewed.

Single gene (Mendelian) disorder —A disorder inherited in a dominant, recessive or X-linked fashion that results (predominantly) from mutation in a single gene. The inheritance of such disorders behaves as described by Gregor Mendel.

Somatic DNA —DNA in cells other than the germ-line.

Somatic mutation —A mutation in somatic DNA. Such mutations cannot be passed on to children.

Specificity —The specificity of a test is the proportion of those not affected by the disorder who are correctly identified by the test as not being affected.

Spina bifida —A malformation resulting from abnormal closure of the neural tube. Affected babies are born with a defect on the back that involves the spinal cord and its overlying covering membrane, vertebrae, muscle and skin. The disorder is associated with varying degrees of weakness and loss of feeling in the lower limbs, loss of bladder and bowel control and hydrocephalus. The disorder has a multifactorial cause.

Susceptibility test —A test performed on a person who has no symptoms of a specific disorder at the time of testing, to determine whether or not he/she has a gene or genes which increase the likelihood (the risk increases are often small) that the person will develop symptoms of the disorder in question at some time in the future. In general, the term is used when testing for disorders where genes and environment interact to result in the disorder (polygenic/multifactorial disorders).

Tay-Sachs disease —A progressive inherited (autosomal recessive) degenerative disorder of the nervous system resulting from mutations in the hexosaminidase A gene on chromosome 15. The disorder usually becomes apparent at around six months of age and causes relentless deterioration in brain and muscle function, leading to death around three–four years.

Thalassaemia —see Beta-thalassaemia.

Thyroidectomy —Surgical removal of the thyroid gland.

X-linked —The form of inheritance in which the mutated gene is on the X chromosome. X-linked disorders may be either dominant or recessive.

APPENDIX 1

AUSTRALIAN SOURCES OF INFORMATION ABOUT GENETIC TESTING

It is not possible in a document of this kind to list all those who perform genetic testing or who can provide information or counselling services, whether in the public or private sector. In general, health professionals are aware of the services available in their area or are able to obtain the information they need but this is not so for members of the community. As a starting point, the regional clinical genetic services listed below can provide information about genetic testing. Their staff members know which tests are available and which testing service provides them, and can provide information about testing, arrange it as appropriate or refer enquirers on to another or more appropriate service.

Australian Capital Territory

The Genetic Counsellor
The Canberra Hospital
Woden ACT 2606

Phone: 02 6244 4042
Fax: 02 6244 3834

New South Wales

Department of Clinical Genetics
The New Children's Hospital
PO Box 3515
Parramatta NSW 2124

Phone: 02 9845 3273
Fax: 02 9845 3204

Department of Clinical Genetics
Liverpool Health Service
PO Box 103
Liverpool NSW 2170

Phone: 02 9828 4665
Fax: 02 9828 4650

South Eastern Area Genetics Service
Department of Medical Genetics
Sydney Children's Hospital
High Street
Randwick NSW 2031

Phone: 02 9382 1705
Fax: 02 9399 6243

Department of Molecular Genetics and Clinical Genetics
Royal Prince Alfred Hospital
Missenden Road
Camperdown NSW 2050

Phone: 02 9515 5050
Fax: 02 9515 7595

Hunter Genetics
PO Box 84
Waratah NSW 2298

Phone: 02 4985 3100
Fax: 02 4985 3105

Northern Territory

See Queensland and South Australia

Queensland

Queensland Clinical Genetics Service
Royal Children's Hospital
Herston Road
Herston QLD 4029

Phone: 07 3253 1686
Fax: 07 3253 1987

South Australia

South Australian Clinical Genetics Service
Women's and Children's Hospital
72 King William Road
North Adelaide SA 5006

Phone: 08 8204 7375
Fax: 08 8204 6088

Tasmania

See Victoria

Victoria

Victorian Clinical Genetics Service
Murdoch Institute
Royal Children's Hospital
Flemington Road
Parkville VIC 3052

Phone: 03 9345 5045
Fax: 03 9348 1391

Western Australia

Genetic Services of Western Australia
King Edward Memorial Hospital
Bagot Road
Subiaco WA 6008

Phone: 08 9340 1525
Fax: 08 9340 1678

APPENDIX 2

MEMBERSHIP OF THE GENETICS WORKING PARTY

Members

Associate Professor Eric Haan (Chair)	Clinical geneticist
Dr Christopher Cordner	Philosophy lecturer
Dr Jane Halliday	Epidemiologist
Dr Christopher Newell	Lecturer in medical ethics and disability studies

Secretariat

Ms Sharon Hill	Office of the NHMRC

INDEX

access to results, 36

adoption, 55–56

autosomal recessive disorder, 17

carrier, 17
  carrier test, 17
  carrier testing of children, 42–44

children
  adopted children, 50
  carrier testing, 42–44
  predictive testing, 42–44
  presymptomatic testing, 42–43
  susceptibility testing, 42–43

chromosomes, 7

commercialisation, 26–27

confidentiality—see privacy/confidentiality

consent, 29–44, 48
  forms, 39, 40
  implicit, 40
  reduced capacity, 44
  special needs, 39
  verbal, 40
  waived, 40

counselling, 26–27, 29–32
  by the professional providing health care, 31
  multiple sessions, 31
  protocols, 32
  qualifications of counsellor, 30
  information to be provided, 32–39
    ability of the person to understand, 32
    complexity, 32
  reason for referral, 32
  role of counsellor, 29–30
  support person, 31

Disability Discrimination Act (Cth), 54

direct marketing, 27

discrimination, 13, 53–57
  Disability Discrimination Act (Cth), 54
  insurance, 54
  employment, 55
  finance, 55
  health services, 56

DNA, 7

employment, 55

equity of access, 26

family members/shared nature of genetic information, 10, 13, 35–36, 49
  adopted children, 55–56
  affected family members, 22
  deceased relatives, 50
  privacy/confidentiality breaches, 50
  reluctance to share information, 48, 50–51
  right not to know, 51–52
  testing family members, 22
  non-blood relatives, 49

forensic issues, 56

genetic determinism, 14

genetic disorders, 8–9
  monogenic, 8, 11
  multifactorial, 9, 11–12
  predicting, 11–12
  polygenic, 8

genetic enhancement, 5–6

genetic information (see also genetic material), 9–10
  misuse of (see also discrimination), 13
  storage, 24, 36–37, 47–48

genetic linkage, 23

genetic material (see also test material and genetic information), 9
  research, 39
  storage, 24, 25–26, 38–39
  future testing, 38–39

genetic research (see also *National Statement*), 19–20, 25–26
  storage of results, 25

genetic test, 9
  adolescents, 43
  appropriateness of testing, 41
  carrier, 17–19
  children, 42–44
  complexities, 21–22
  cost, 23–24
  diagnostic, 15, 18
  error in, 23
  for monogenic disorders, 11
  interpreting test results, 23
  preimplantation, 18
  prenatal, 11, 17–18
  predicting multifactorial disorders, 11
  predictive, 11–12, 15–16
  presymptomatic, 15–16, 18
  protocols, 32

screening, 18, 22
'starting point', 21
setting, 29
susceptibility, 15–16, 18
test quality, 23
geneticisation, 14
health services, eligibility and access, 56
health promotion programs, 11–12
interpreters, 30
laboratories, 38–39
good practice, 24
interpreting test results, 23
storage of information/material, 24–26, 38–39
test quality, 23
legal issues, 56
insurance (life and health), 54
mutation, 7
multiple mutations, 21–22
identifying the mutation, 21–22
National Statement on Ethical Conduct in Research Involving Humans (see also research), 5, 6, 19, 26, 38, 39, 52
non-paternity/non-maternity (see also counselling), 36
polymorphism, 7
predicting
future disease (the probabilistic nature of genetic information), 12–13
monogenic disorders, 11
multifactorial disorders, 11
privacy/confidentiality, 45–52
Guidelines Under Section 95 of the Privacy Act 1988, 45
exceptions, 45
family members, 48–51
Information Privacy Principles, 45
keeping genetic information in the person's main medical record, 47
legal protection, 45
Privacy Act 1988 (Cth), 45
right not to know, 51–52
Privacy Act 1988 (Cth), 45
proteins, 7
relatives
disclosure, 37, 48–52, 53–54
research (see also *National Statement*), 19–20, 39, 52
resource allocation, 27
RNA, 7
stigmatisation—see discrimination
storage of genetic information, 24 36–37, 47–48
de-identified, 46–47
identified, 46
potentially identifiable, 46
privacy/confidentiality, 47–48
test material (see also genetic material and genetic information), 20–21
test results (see also genetic test)
errors in, 23
variants, 7
disease-causing, 7
susceptibility-creating, 7
harmless, 7
germ-line, 7–8
somatic, 8
X-linked recessive disorder, 17

The National Health and Medical Research Council

The National Health and Medical Research Council (NHMRC) is a statutory authority within the portfolio of the Commonwealth Minister for Health and Aged care, established by the *National Health and Medical Research Council Act 1992*. The NHMRC advises the Australian community and Commonwealth; State and Territory Governments on standards of individual and public health, and supports research to improve those standards.

The NHMRC advises the Commonwealth Government on the funding of medical and public health research and training in Australia and supports many of the medical advances made by Australians.

The NHMRC also develops guidelines and standards for the ethical conduct of health and medical research.

The Council comprises nominees of Commonwealth, State and Territory health authorities, professional and scientific colleges and associations, unions, universities, business, consumer groups, welfare organisations, conservation groups and the Aboriginal and Torres Strait Islander Commission.

The Council meets four times a year to consider and make decisions on reports prepared by committees and working parties following wide consultation on the issue under consideration.

A regular publishing program ensures that Council's recommendations are widely available to governments, the community, scientific, industrial and educational groups.

The Council publishes extensively in the following areas:

- Aged care
- Child health
- Clinical practice guidelines
- Communicable diseases
- Dentistry
- Diabetes
- Drugs and poisons
- Drug and substance abuse
- Environmental health
- Ethics – Animal
- Ethics – Human
- Health procedures
- Health promotion
- Infection control
- Men's health
- Mental health
- NHMRC – National Health and Medical Research Council
- Nutrition
- Public health
- Research
- Sport/Injury
- Women's health
- Workforce

A list of current publications is available from:

The Publications Officer
ONHMRC
MDP 50
GPO Box 9848
Canberra ACT 2601

Phone: (02) 6289 1430 (24-hour answering machine)
Toll free: 1800 020 103
Fax: (02) 6289 1351
E-mail: nhmrc.publications@health.gov.au
Internet: http://www.nhmrc.health.gov.au

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