NUFFIELD COUNCIL ON BIOETHICS

GENETIC SCREENING ETHICAL ISSUES

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GENETIC SCREENING
ETHICAL ISSUES

Preface

The Nuffield Council on Bioethics was established in 1991 to consider ethical issues presented by advances in biomedical and biological research. It had no difficulty in deciding to make genetic screening the subject of its first report.

Genetic research differs from many areas of medical advance in three distinct ways: first, the astonishing speed of its development; second, its inescapable effect not only on individuals, but also on their families and society generally; and, third, the fear it arouses that it may be interfering with the basis of life itself.

Hence the urgency of examining the complex range of ethical issues and exposing them to wide professional and public debate, and of identifying the action to be taken and the further work to be done. To this end the Council set up a Working Party, under the chairmanship of Professor Dame June Lloyd, and has carefully considered and endorsed its report. It now looks to the Government and to other bodies to initiate the reviews and discussions which the report recommends.

As Chairman of the Council, I wish to highlight four important features of the report:-

- **The difficulty in assessing individual health risks exposed by genetic screening.**

  Even with greater medical knowledge there may be a wide margin of error in assessing the risks affecting individuals and their families. This will accentuate the ethical problems relating, in particular, to employment and insurance.

- **The increased complexity of the ethical aspects of confidentiality.**

  The serious implications which screening results may have for a family pose potentially difficult problems in applying the longstanding ethical principle of confidentiality between the professional and the individual screened.

- **The demands made upon professional and health resources by the required ethical procedures**.

  These demands are likely to be heavy, but they must be met if the recommendations of the report are to be fulfilled.

- **The broad framework provided as a safeguard against potential eugenic abuse**.

  Better public understanding of, and education about, genetics are essential. So too are the recommendations proposed on informed consent, confidentiality and the central coordination and monitoring of genetic screening programmes.

The report could not hope to identify exhaustively, let alone answer, all the ethical questions which may confront individuals, families and professionals. But it does outline ethical policies and procedures which should help people to answer the questions and make the decisions which are important for them.

The report is not a consultation document, but the Council will welcome and consider views and comments. It intends to publish next year a shorter popular version. This will assist the public discussions of the report which the Council plans to arrange in London and elsewhere.

Rt Hon **Sir Patrick Nairne** GCB MC
Chairman
Nuffield Council on Bioethics

Nuffield Council on Bioethics

Working Party on Genetic Screening

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Secretariat

Mr David Shapiro
Mr Harry Parker (February - October 1993)
Mrs Jill Batty

Terms of reference

The terms of reference were as follows:-

(1) to survey and report on recent and prospective advances in genetic screening and its applications;

(2) to review experience to date of current and potential benefits and difficulties of genetic screening and associated counselling;

(3) to identify, define and discuss the ethical issues affecting both individuals and society which arise, or may arise in future from genetic screening, including such matters as:-

(a) the general risk of stigma attaching or being attached to those perceived as genetically disadvantaged;

(b) the handling and holding of information;

(c) consent to being screened;

(d) confidentiality in all its aspects;

(e) the implications for employment and insurance;

(f) the storage and use of genetic information for legal purposes.

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Chapter 1

Introduction

1.1 New knowledge about human genetics, and the links between genetic inheritance and susceptibility to diseases, have important ethical implications. Medical scientists can now identify the presence of some abnormal genes by simple tests that are easy to administer. But what uses might be made of this knowledge? Who should share it? What are the implications for people identified as having an abnormal gene or genes? For their families? For society?

1.2 So far many of the findings of research into the structure of the human genome are provisional and imprecise. But they have already led to controversy, both within the scientific community and in the public at large, about their implications for human well-being. Widespread concern about the ethical aspects of screening for the presence of abnormal genes led the Nuffield Council on Bioethics to set up a Working Party to examine the issues and draw up this report.

1.3 This report starts with an account of the scientific basis of medical genetics and of recent developments in genetic screening. Chapter 2 should be detailed enough to clarify the ethical issues associated with genetic screening programmes. We have tried to make this difficult subject accessible to readers who do not have a background in the biological sciences. The use of technical terms is unavoidable, and we have provided a glossary. We should emphasise that although the basic mechanism by which genes from both parents are reassembled and transmitted to the next generation through sexual reproduction is well understood, much has yet to be discovered about the varied and complex ways in which genes are expressed, for example in hair or eye colour, or as serious physical malformation or disease.

1.4 Chapter 3 surveys experience to date with genetic screening initiatives and associated counselling. It should be stressed that many of the genetic screening programmes in the UK described in the report are for the purpose of research and do not form part of a regular clinical service. Some are perhaps better described as testing programmes among people already known to be at risk for a particular genetic disease. This fact has implications both for

the ways in which groups have been selected and invited to participate, and for the resources available for counselling and follow-up.

1.5 The rest of the report covers the specific issues referred to in paragraph (3) of our terms of reference (page iv) : consent; confidentiality; the implications for employment and insurance; and the storage and use of genetic information. Chapter 8, on public policy, addresses the possibility of stigma, along with other social implications of screening for genetic disease. In the remainder of this Introduction, after a brief discussion of the known links between genetic inheritance and susceptibility to disease, we raise some of the ethical issues that are explored in the report.

1.6 In order to understand the complex ethical questions that can arise in connection with genetic screening, some knowledge of the different ways in which genetic inheritance can cause disease, or make people susceptible to a disease, is essential. A key distinction is between single gene diseases, where the causal link is strong and the outcome often largely predetermined, and polygenic diseases, where there may be interaction with the environment and where the significance of genetic factors is much less clear. A second important distinction, among single gene diseases, is between dominant and recessive inheritance.

1.7 The fact that an abnormality in a single gene can cause serious disease has been known for some time. Familiar examples of single gene diseases are cystic fibrosis (CF), Huntington's disease and sickle cell disease. These conditions arise from fundamental defects that are incurable by conventional therapies, though some of them, for example cystic fibrosis and sickle cell disease, may be alleviated by appropriate treatment. Many of them are rare, at least in the UK, and some are more common in specific sectors of the population. Where there is a family history it is often feasible to test selectively, on the basis of a known likelihood that the faulty gene may be present, and to offer individuals and families counselling and advice about the reproductive options open to them.

1.8 Polygenic diseases are a different matter. It is becoming clear that an element of genetic susceptibility is among the factors predisposing people to develop many of the common diseases, including coronary heart disease and some cancers. Several different genes appear to influence susceptibility, but how they interact with each other, and the relative importance of genetic inheritance and environmental factors as causes of these diseases, are still largely unknown. Medical researchers are interested in finding out more about the incidence of particular genetic patterns in association with cancers and other diseases.

Selective screening on the basis of familial susceptibilities is one way of doing this. However, population screening for polygenic diseases is probably some way off; it will be of questionable value until the causative significance of the genetic factors and the relative importance of the environmental influences are much better understood.

1.9 The phrases 'genetic testing' and 'genetic screening' are sometimes used interchangeably. There is, however, a significant difference, though not a completely hard and fast one, between testing an individual for a condition or defect that other evidence suggests may be present, and screening all members of a population for a defect or condition where there is no prior evidence of its presence in the individual. An example of the first is testing for the Huntington's gene in the limited number of families known to be at high risk of developing the disease because they have an affected member. An example of the second is the screening of all newborn children for phenylketonuria (PKU). Testing of a sub-population, such as Ashkenazi Jews for the Tay-Sachs gene, might properly be regarded as screening. Nevertheless, the distinction between testing and screening is important in several respects, including the ethical problems of obtaining informed consent and the handling of unexpected information. In this report we are **primarily** concerned with the ethical aspects of genetic screening programmes.

1.10 We define genetic screening as a search in a population to identify individuals who may have, or be susceptible to, a serious genetic disease, or who, though not at risk themselves, as gene carriers may be at risk of having children with that genetic disease. While it is individuals who are screened, the results will normally have wider implications. Depending on the nature of the genetic defect that is identified and its pattern of inheritance, siblings and other blood relations, as well as existing and future offspring, may be affected. Thus the status of genetic information raises ethical questions that differ significantly from the normal rules and standards applied to the handling of personal medical records. Does the person with a defective gene have a right to withhold this information from other family members? Does he or she have a duty to disclose it? What are the rights and/or responsibilities of the rest of the family? These questions are explored in Chapter 4, on Consent and Counselling, and Chapter 5, on Confidentiality.

1.11 Screening programmes have a useful part to play in a health care system that aims to help people maintain good health as well as treating disease and accidents. Already well-established and familiar are the screening of all pregnant women for their rhesus blood group and all newborn infants for phenylketonuria (PKU).

Both programmes identify potentially serious risks which can be prevented by timely treatment. Other screening programmes offered to individuals known to be at risk because of their sex and age are for cancers of the cervix and breast. While the latter are not **genetic** screening programmes, they share some, though not all, of the ethical issues that are discussed in this report.

1.12 The ethical questions raised by genetic screening differ from the ethical aspects of the relationship between individual patients and the professionals caring for them in some important respects. One key difference, already mentioned, is that genetics and diseases of genetic origin inescapably involve families. Another is that for diseases such as cystic fibrosis, where there is usually no prior evidence to suggest that the gene may be present, screening is initiated by a doctor or other healthcare worker inviting a perfectly healthy individual to undergo a procedure that may have worrying implications. The person may be in no danger of developing the illness himself or herself, but may have to consider whether or not he or she is prepared to run the risk of passing on the gene to one or more children, who may then suffer from the genetic disease. A man or woman, asked to accept screening for a defective gene that, if it is present, is not causing any illness and may never do so, is not being asked to consent to treatment in the ordinary sense of the term. The kind of information he or she needs about the possible consequences of a positive result is different from that sought by a patient considering whether to undergo surgery or other medical treatment. We discuss the question of informed consent to screening in Chapter 4, and the need for a greater public understanding of human genetics and the nature of genetic diseases in Chapter 8 on Public Policy.

1.13 Throughout our report we have kept in mind two fundamental points on the ethics of health care decisions. First, there may be certain courses of action that should be ruled out whatever their seeming benefits. In the context of genetic screening we emphasise that compulsion should be ruled out (see, for example, paragraphs 4.21(i) and 10.4). Second the question must always be posed : does the potential good outweigh the possible harm? This question is not always an easy one for patients or their medical advisers to answer, even in a conventional doctor/patient encounter where a well-established form of treatment for an identifiable disease is under consideration. It is even more difficult in the context of a screening programme, and especially a genetic screening programme, where the potential benefits to individuals and their families must be weighed against possible adverse consequences.

1.14 Genetic screening offers a number of potential benefits to individuals, their families and society. They include:-

(i) the identification of treatable genetic disorders at an early stage;

(ii) giving couples the possibility of making informed choices about parenthood; and,

(iii) more speculatively, and largely in the future, identifying genetic susceptibility to common serious diseases.

As medical knowledge about genetic susceptibility develops further, it may become possible to encourage people at risk to take appropriate preventive measures such as stopping smoking and altering dietary habits.

1.15 At the same time, there are the adverse possibilities already indicated. These include the risk of increasing personal anxieties about health, the difficulties sometimes experienced by individuals and families in deciding whether to pass on genetic information to other family members, and the agonising decision whether to terminate a pregnancy following an adverse prenatal diagnosis. There are also potentially adverse consequences for both individuals and society as a whole if normal prospects for employment and life insurance were to be seriously affected by access to, and the misuse of, the results of genetic screening programmes. One serious potential misuse discussed in Chapter 7 would be an over-cautious interpretation by insurance companies of the as yet limited knowledge of genetic susceptibility, especially to polygenic and multifactorial disease (for example, some heart diseases and some cancers).

1.16 In all our discussions, both of the written evidence we have received, including work being done by international bodies, and of the problems encountered by those members of our Working Party who are actively involved in genetic testing and screening, we have been struck by the need for care in providing information to people invited for screening. We have also been struck by the variety of responses encountered. The factors affecting the acceptability of a screening programme are so diverse that it is difficult to draw general conclusions about the desirability of genetic screening. These factors include the severity of the condition being screened for, people's previous experience of children or family members who have suffered from the disease, the stage at which screening is offered (before conception or during pregnancy), individual moral and religious beliefs, and the available therapeutic options. Any screening programme runs some risk of raising false anxieties or giving false reassurance :

the size of that risk depends on the sensitivity and the specificity of the particular test. Each and every proposed screening service must be assessed on its individual merits. The kind of information that screening is intended to reveal, its confidentiality, and the therapeutic options available, are among the matters that need to be taken into account and are explored in our report.

1.17 The profound moral dilemmas that screening can create are illustrated by the statements of two women who refused an offer of screening for cystic fibrosis early in pregnancy.[1] One of them, who had understood that even if she carried the cystic fibrosis gene there was no cause for concern unless it turned out that her partner also carried the gene, was nevertheless worried:

> "If he is negative the worry is unnecessary. If he is positive, even more worry would result until the prenatal diagnosis when if the baby is negative, again the worry has been unnecessary."

The other was worried about the moral choice that she might face:

> "I think I would face a very difficult moral dilemma if I discovered, whilst pregnant, that both my husband and I were CF carriers. I would then want to have the baby screened, and if it had CF I would be very worried about making a decision to have an abortion, which in theory I'm opposed to, but realistically, I don't know what I'd do."

1.18 The views cited above are minority views (see paragraph 4.13). For the majority of the women who accepted screening for cystic fibrosis the benefits outweighed any temporary psychological stress. The screening offered an opportunity to avoid both a child born to suffering and the lifelong emotional cost to the rest of the family in caring for a child in such a condition. But the minority views are important precisely because one test of ethical sensitivity is the way in which minority views are taken into account and given an appropriate response. We discuss these matters later in the report.

Chapter 2

Scientific basis

What genes are

2.1 The inheritance of all our characteristics, including susceptibility to genetic diseases, is dependent on **genes** and **chromosomes**. Genes are large molecules made up of a substance, DNA, whose double helical structure allows both copying and division. The particular sequence of individual chemical sub-units in a gene serves as a molecular code to specify the manufacture of a particular protein; an alteration (mutation) at even a single position of the DNA sequence may cause serious malfunction of the resulting protein. Modern advances in genetics are due to the ability to study DNA directly. It is estimated that about 75,000 different human genes exist. At present we have information on only one third of them at most.

2.2 The genes are arranged in a fixed order on the chromosomes. **Chromosomes** are elongated strings of DNA and protein which occur in the nucleus of every cell in the body. Unlike genes, chromosomes can be seen through a microscope, especially when they become compact during cell division. In the normal human there are two sets of 23 chromosomes, 46 in all. One set of 23 is received from each parent. The members of 22 of the 23 pairs appear identical : these are the autosomes. The remaining pair, the sex chromosomes differ between males and females. Female sex chromosomes are designated XX and male XY.

The scientific basis of genetic screening

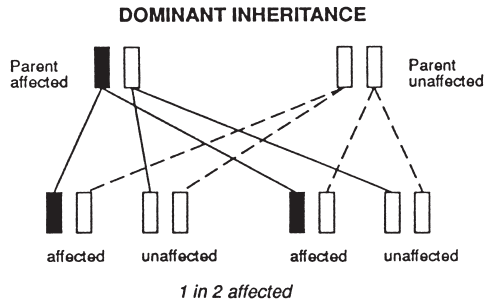
2.3 **Medical genetics** is the part of human genetics concerned with the role of genes in illness. Traditionally, the analysis of the genetic contribution to illness and human characteristics has been divided into :

(i) disorders due to changes in **single genes**;
(ii) disorders influenced by more than one gene (**polygenic**);
(iii) **chromosomal disorders**.

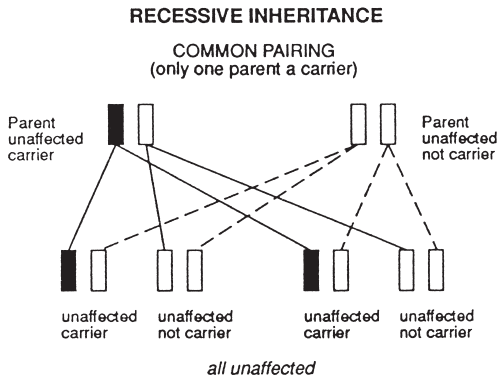
In addition to the genetic contribution, the environment will often play an important part in influencing both the onset and severity of disease particularly in the polygenic disorders.

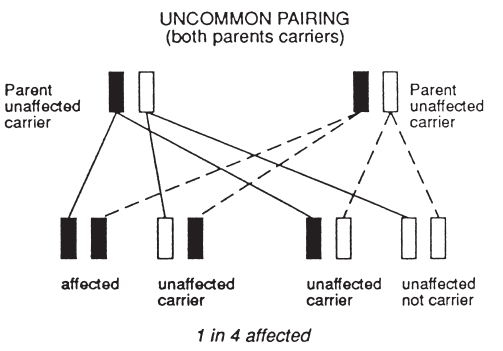
Single gene diseases

2.4 Inherited single gene diseases may show three common types of inheritance pattern:-

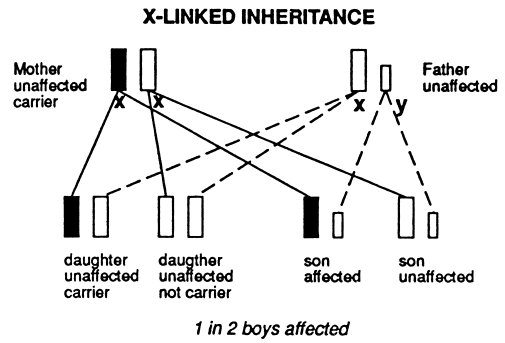


(i) autosomal **dominant** : such diseases (for example, Huntington's disease) result from one of a pair of matched autosomal genes having a disease-associated alteration (shaded in the diagram), the other being normal. The chance of inheriting the altered gene is 1 in 2 in each pregnancy. Autosomal dominant diseases commonly affect several individuals in successive generations.





(ii) autosomal **recessive** : such diseases (for example, cystic fibrosis) require the inheritance from **both** parents of the same disease-associated abnormal autosomal gene. The parents are usually themselves unaffected but are gene **carriers**. When both parents carry the same altered gene, the chance of inheriting two altered genes and so of having the disease is 1 in 4 in each pregnancy. Autosomal recessive diseases usually only affect the brothers and sisters within a single generation; the risk of disease in individuals in previous or subsequent generations is usually very small. Hence diseases with this form of inheritance tend to occur 'out of the blue'.



KEY affected indicates presence or development of disease

□ normal chromosome

■ chromosome bearing disease related gene

(iii) **X-linked** : diseases due to genes on the X chromosome (for example, haemophilia) show a special inheritance pattern; they are also known as sex-linked disorders. Most X-linked conditions occur only in males who inherit the abnormal gene from their mothers; these mothers are carriers of the altered gene but are usually unaffected because their other X chromosome has the normal gene (as in autosomal recessive disease). Females may occasionally show some features of the disease, depending on the condition. An affected male never transmits the disease to his sons. When the mother carries a gene for an X-linked disease, the chance of inheriting the altered gene is 1 in 2 in each pregnancy for both boys and girls, but only male offspring will be affected. X-linked disease may thus give rise to disease in males in several different generations, connected through the female line.

Polygenic disorders

2.5 Many common diseases with a genetic basis result from abnormalities in more than one gene. The inheritance pattern is complicated because of the larger number of different genetic combinations and uncertainties about how the genes interact. Environmental factors frequently play a major part in such disorders, which are more often known as multifactorial diseases. Because of this, screening can yield results that are less clear-cut. At the same time, as our knowledge of all the environmental and genetic factors involved advances, it will become possible to identify individuals at increased risk for a disorder who could benefit from advice on how to minimise this risk. This could lead to screening for genetic predisposition to common diseases, such as coronary heart disease and some cancers.

Chromosomal disorders

2.6 Chromosomal disorders fall into two broad categories:

(i) where an entire chromosome is added or is missing. For example, in Down's syndrome there is an extra (third) copy of chromosome 21 found in the cells of affected individuals (hence the technical term for it, Trisomy 21). In Turner's syndrome, one of the X chromosomes in girls is missing. This type of disorder is **not** inherited but occurs during conception;

(ii) rearrangement of chromosomal material. If this involves either net loss or gain of chromosomal material, harmful clinical effects are likely; on the other hand, if a simple exchange between chromosomes (translocation) or within them (inversion) has occurred, the chromosome make-up is 'balanced' and serious clinical effects are much less frequent.

Types of genetic tests

2.7 All forms of genetic test aim to identify particular genetic characteristics but approach this in different ways.

Chromosomal tests (cytogenetics)

2.8 Microscopic examination of chromosomes from cells in blood, amniotic fluid or fetal tissue may be used to detect the chromosomal changes mentioned above. Until recent years it was only possible to detect large alterations on a chromosome involving many genes, but new techniques are making it possible to detect much smaller defects, allowing disorders involving only a small amount of genetic material to be recognised.

Tests for disorders involving a single gene

2.9 Genes cannot be seen using the microscope, so in the past tests for single gene disorders have been largely indirect, involving what the gene produces (protein), or another substance affected by it, rather than the gene itself (see paragraph 2.15). Since the protein is still unknown for the majority of genes, testing for single gene disorders has been very limited until recently.

Direct tests

2.10 A variety of techniques have now been developed for identifying important human genes directly. There are two main approaches:-

(i) the gene may be isolated if the product (protein) it normally produces is known. This approach was used for the genes involved with the main blood cell protein haemoglobin (important for tests involving sickle cell disease and thalassaemias). The genes for some metabolic diseases, where a specific chemical defect involving an enzyme was already known, have also been isolated in this way;

(ii) the gene may be isolated if its position on a chromosome is known (**positional cloning**). This approach is increasingly successful in allowing genes to be isolated even when we know nothing about their function or what protein they normally produce. One reason for this success is that detailed **genetic maps** of the different chromosomes are being produced. This approach not only pinpoints the chromosome region where the gene lies, but can provide **genetic markers** (identifiable pieces of DNA) which lie close to the gene, and can enable an accurate test for a genetic disorder to be made even before the gene itself is isolated.

2.11 Once the gene responsible for a disorder has been isolated it is possible to study the different changes (**mutations**) in it that can result in disease. These may range from complete absence of the gene to faults in a single chemical sub-unit of the gene. A single gene disorder may be caused by many different changes in the gene responsible. By careful study of particular populations of people it may be possible to determine which mutations for a disease are the commonest and most important, and to design a programme of testing accordingly.

2.12 Direct genetic testing by DNA techniques differs from most other forms of medical testing in several important respects. Any body tissue can be used since genes are present in almost all cells. Although blood is most commonly used, cells obtained by mouthwash are proving especially suitable for some screening programmes. Since genes do not usually change during life, a DNA test can be performed at any time from conception onwards. This is a practical advantage for tests in early pregnancy, as it can allow the detection of a serious genetic abnormality that would not show itself until after the child is born. However, this raises difficult ethical problems, especially in relation to diseases which do not appear until later childhood or adult life.

2.13 Major scientific advances have also occurred in the sensitivity of genetic techniques, allowing minute amounts of DNA or protein products to be analysed. A particularly important advance has been the **polymerase chain reaction** (PCR), which allows a single copy of a small part of a gene to be amplified many thousand times. Testing of single cells may make preconception testing of a single egg feasible, and may also allow testing of fetal cells in the mother's blood during early pregnancy. The dried blood spot taken onto filter paper from all babies in the newborn period can be stored and could be used for a wide range of genetic tests. Such techniques increase the potential impact of genetic testing since they are often suitable for mass population screening.

2.14 An important discovery has been that many stretches of normal DNA vary between different people and together provide a pattern that is unique for every individual (apart from identical twins). This powerful technique, known as **genetic fingerprinting**, has many applications, especially in legal and criminal cases. There are important ethical issues as to when and how it should be used. As the legal issues have been addressed by the Royal Commission on Criminal Justice, we have not attempted to consider them in this report.

Indirect (biochemical) tests

2.15 These tests detect not the gene itself, but some aspect of its function. The most nearly direct are for the specific protein that the gene produces. In a genetic disorder tests may show that the protein is not being made or is present in reduced amount; or it may be altered so that it does not function adequately. Such tests are still important, for example, for abnormalities of haemoglobin (in thalassaemia or sickle cell disease).

2.16 Where the gene or its product cannot easily be tested, it may be possible to measure some other substance whose amount is altered in the disease. Thus the screening test commonly used in all newborn babies for the disorder phenylketonuria (PKU) is based on measuring the amino acid phenylalanine, which builds up in the blood of affected patients.

Ultrasound

2.17 A quite different but very important technique is ultrasound imaging, which gives a virtually risk-free method of identifying structural and some functional abnormalities which can result from genetic disease. This technique is widely used for the detection of fetal malformations during pregnancy, of which some, but not all, are genetic in origin. Some early manifestations of serious genetic disorders that may develop in later life, such as polycystic kidney disease (enlarged kidneys with cysts) or certain types of cardiomyopathy (heart muscle disease) can also be detected.

The importance of genetic variation

2.18 Most of the genetic differences that can be detected between individuals represent normal genetic variation and are not associated with disease. This variation has been essential for human evolution and is seen both within and between populations.

2.19 Whether a genetic characteristic is harmful or not may depend on factors in the environment. Thus in countries where malaria is common, individuals, particularly children, who are carriers for genes causing disorders of haemoglobin, such as sickle cell disease, have some protection against malaria. The sickle cell gene is thus of benefit in such an environment. Conversely, other genes which may have had no significant harmful effects in the past, may cause problems because they provoke an adverse reaction to certain newly available drugs or anaesthetics.

2.20 Genes and chromosomes are continually undergoing change, rearrangement and interaction as a normal process. Although some harmful genetic changes can be prevented, for example by the avoidance of unnecessary irradiation or harmful chemicals, genetic disorders due to new mutations can never be entirely eliminated.

Chapter 3

Genetic screening : current programmes

Introduction

3.1 Genetic screening programmes are not a new development. Since the 1960s pregnant women have been routinely tested for their **rhesus blood group**, so that damage to babies of rhesus negative women before and after birth can be prevented. Damage is prevented by ensuring that rhesus negative women are given an antibody within a few hours of delivery, miscarriage or abortion. Since 1973 it has been policy to screen all newborn babies in the UK for **phenylketonuria (PKU)**. Severe mental retardation is characteristic of this disease, but can be prevented if dietary treatment is started in the first weeks of life. These two tests have now become an accepted part of primary health care, and are essentially genetic screening programmes.

3.2 Genetic screening may be carried out in the following groups of people:-

(i) the entire population, albeit a section defined by age or sex, where all within the group are at risk. This is appropriate for example in screening newborn babies for **PKU**;

(ii) sub-groups within the population, where the risk is known to be concentrated. This is appropriate, for example, within the Ashkenazi Jewish population for **Tay-Sachs disease**, a fatal brain disease of children especially frequent in this group, where healthy carriers can be detected in order to provide information;

(iii) broad groups in which genetic factors may be responsible for some but not all of certain disabilities. For example, individuals with learning difficulties could be screened in order to detect those with **fragile X syndrome**, and thus identify the families at further genetic risk.

3.3 Individuals with a family history of an inherited disorder may undergo genetic testing. Such testing should be distinguished from population screening, but has important similar societal effects which are considered in this report. Family studies provide the most practical strategy for detection of the abnormal gene in most dominantly inherited and X-linked disorders.

3.4 Screening programmes often have more than one component. A **primary screen** may be offered to all members of the population to identify a 'risk group', which would then be offered further **testing**, leading to **definitive diagnosis**. This sequence applies to many genetic screening programmes, depending on the methodology used. For example, the initial screening test for phenylketonuria (PKU) is by an indirect method (see paragraph 2.16). Babies with a positive result do not always have the disease and further tests are required to confirm the diagnosis. Where, however, direct methods are better (for example, testing for carriers for cystic fibrosis) no further testing is required for those with positive results. In the case of cystic fibrosis, a small proportion of individuals whose genetic defect is not detected by the current test will be missed.

3.5 Depending upon the mode of inheritance, the genetic abnormality, and the type of test, screening may detect individuals:-

(i) who have the disorder, for example, phenylketonuria (PKU) as presently screened by blood spot in the newborn;

(ii) who are themselves unaffected, but are carriers of a gene for a recessively inherited disorder (for example, sickle cell disease) and thus at risk of having an affected child;

(iii) who may themselves develop a disease after many years, for example, Huntington's disease.

It follows that a variety of different practical and ethical problems may arise.

3.6 Screening may also be carried out for **congenital disorders** where a genetic basis **may** exist but has not been established; for example, ultrasound scanning of a fetus for malformations.

3.7 In the future, increased understanding of the genetic component in common diseases may lead to proposals for screening for genetic abnormalities that confer an **increased risk** for the individual rather than a **certainty** of developing the disease : for example, screening may point to an increased risk of cancer, or diabetes, or mental disease and there may not be simple or guaranteed ways of avoiding the risk or of treating the condition

if it develops. It is therefore important to assess, so far as possible, the character and degree of risk, to study existing experience as it increases, and to improve understanding of the social and ethical, as well as the technical, implications of genetic screening.

Principles of genetic screening programmes

3.8 The traditionally accepted principles and practice of screening for disease were set out in a WHO report in 1968:[1]

1 An important disease
2 Known history
3 Latent or early symptomatic state
4 Reliable screening test available
5 Definite diagnosis possible and treatment available
6 Natural history improved by treatment
7 Cost effective

3.9 These criteria were designed for the detection of disease. They were formulated before prenatal diagnosis with the associated option of aborting an affected fetus was current. They are not entirely appropriate for genetic screening, for example for carriers for a recessively inherited disorder who are themselves healthy (see paragraph 3.5(ii)). For genetic screening three goals have been identified.[2] It should:-

(i) contribute to improving the health of persons who suffer from genetic disorders; and/or

(ii) allow carriers for a given abnormal gene to make informed choices regarding reproduction; and/or

(iii) move towards alleviating the anxieties of families and communities faced with the prospect of serious genetic disease.

3.10 Further experience of genetic screening can be expected to lead to a more precise definition of its principles and goals; **but at present the prime requirement is that the target disease should be serious.** The Clothier Committee on the Ethics of Gene Therapy[3] recommended that the first candidates for consideration for such treatment should be those suffering from a disorder which is life-threatening, or causes serious handicap, and for which treatment is unavailable or unsatisfactory. Such disorders would clearly be classed as serious. In the context of

genetic screening the definition is likely to be much wider and it is difficult to define precisely what is serious. Furthermore the perception of seriousness may vary between societies and will vary according to treatment possibilities. The fact that the severity of some diseases can range from serious to slight, as in fragile X syndrome, adds to the difficulties. Perhaps it is easier to define what should not be included in genetic screening : these are characteristics with a genetic component, but which cannot be classed as diseases.

Existing screening programmes

3.11 In reviewing existing screening programmes, some of which are well established and others barely beyond the pilot stage, we have tried to identify the ethical problems that may arise.

3.12 Screening programmes are broadly divided into four groups, depending on the timing of the testing:-

(i) neonatal (in the newly born)

(ii) older children

(iii) testing of couples or individuals before pregnancy (adults)

(iv) antenatal (during pregnancy).

3.13 There may be no single stage of life at which genetic screening is most suitable. Screening may best be offered in a variety of ways, and the optimal approach may change as the community becomes more informed. For example, genetic screening for thalassaemia in Cyprus and Sardinia (countries where this is particularly common) has progressed from the antenatal stage to the premarital stage towards screening in schools. This type of progression may prove to be a common pattern as genetic screening becomes a more established component of primary health care.

Neonatal screening

3.14 The blood spot test for **phenylketonuria** (PKU) has not created any major ethical problems, although the information given about the condition and the informed consent obtained in many instances have not met the criteria recommended in paragraph 4.6. Likewise the test for **congenital hypothyroidism**, which is carried out on the same sample, does not appear to have raised

any major ethical problems. This may in part be because both diseases are severe and can be adequately treated if detected.

3.15 Nevertheless, there is evidence that many women do not understand what the test is for. A recent study of new mothers' knowledge of the blood test for PKU and hypothyroidism showed that although two thirds said that the test had been fully explained, most did not in fact know what it was for, and a considerable number incorrectly believed the test detects more disorders than is the case.[4] Such results clearly challenge any notion that women are giving informed consent for their babies to be tested, even though they believe themselves to be informed. This issue is discussed further in Chapter 4.

3.16 Some laboratories carrying out neonatal screening for PKU and hypothyroidism, both in the UK and other countries, have chosen to add tests for other serious conditions. It is not always clear to what extent parents are fully informed about these tests. A neonatal screening programme in Pittsburgh, USA, has chosen to employ 'informed dissent', where parents are required to express a wish to opt out if they so desire.[5]

3.17 The present method of screening for PKU, which is recessively inherited, is indirect and does not identify the genes involved. If direct gene testing were introduced, so that carriers as well as affected individuals were identified, a different order of ethical issues would clearly arise. The finding of a carrier child has no disease implications for the child, but may become important to that child in later life when reproductive decisions are being made. How and when the child should be told would require careful consideration.

3.18 Neonatal screening for **sickle cell disease** is cheap and reliable and is recommended for populations with a significant incidence of this disease. Early diagnosis of affected infants reduces childhood mortality and morbidity, and allows parents to be counselled about subsequent pregnancies. In some inner city areas in the UK, all newborns regardless of ethnic origin are now screened for sickle cell disease. Screening, however, does detect carriers as well as affected individuals, and thus raises ethical issues for the families as discussed above.

3.19 Neonatal screening for **cystic fibrosis** (CF) by indirect testing (for trypsin in the blood) is only carried out in certain areas and is still under evaluation. There is some, but not conclusive, evidence that neonatal identification of infants with cystic fibrosis may improve their prognosis, because preventive management can be started before their lungs are damaged. Parents of affected children can also be offered prenatal diagnosis in subsequent

pregnancies. DNA techniques, which identify carriers as well as affected children, have been used for confirmation of the diagnosis in the newborn period.

3.20 Pilot neonatal screening programmes for early identification of **Duchenne muscular dystrophy** have been set up in the UK (in Wales) and several other countries.[6] All of these programmes have been based on an indirect method; the detection of the level of the enzyme, creatine kinase, in the blood. These programmes vary somewhat in detail, and in the manner of obtaining consent : the Pittsburgh study, for example, employs informed dissent (see paragraph 3.16). The X-linked nature of this disease raises particular ethical issues in terms of implications for the extended family (see paragraph 5.13).

3.21 Because neonatal screening for Duchenne muscular dystrophy is essentially still in the pilot stage, evaluation of all the ethical issues is not possible. Most of those involved consider that extensive, well-monitored pilot phases should precede a decision on more general implementation.[6]

3.22 All newborn babies have a **physical examination** which may detect **congenital disorders**, some of which may have a genetic component. Examinations are often carried out in the presence of the mother and the parents are informed about any abnormalities and their implications.

Later childhood screening

3.23 As part of **routine child health surveillance**, all children have a physical examination for a variety of diseases which may in part have a genetic basis; for example, hearing defects may be detected. Programmes of screening for specific genetic disorders are at present in the pilot stage.

3.24 In Montreal, genetic screening programmes directed at high school students have been conducted for **Tay-Sachs disease**, **beta thalassaemia** and **cystic fibrosis**.[7,8,9] All three projects appear to have been well accepted. The vast majority (over 90%) in all programmes approved of screening in high school and understood the significance of the findings. Clearly the community was well informed as genetic screening in the local high schools is regarded as a ‘normal activity’. Most carriers for Tay-Sachs or beta thalassaemia claimed they would want to know the carrier status of an intended spouse; a small minority of the Tay-Sachs carriers would ‘reconsider’ if the prospective partner proved to be a carrier. A follow-up survey of attitudes towards screening for

Tay-Sachs concluded that "students have a very positive attitude toward genetic screening in general. These findings are associated with an effort to expand the human genetics content in the biology curriculum....The screening clinic in the schools, and literature provided by the screening authority, was an effective source of knowledge about the significance of Tay-Sachs heterozygosity [ie of being a Tay-Sachs carrier]."[7]

Adult screening

3.25 Screening of adults may be carried out to detect existing disease or predisposition to a disease, or may identify carriers with a reproductive genetic risk. Most presymptomatic testing for late onset genetic diseases (for example, Huntington's disease) is currently offered to family members at risk. General screening for such late-onset genetic diseases is increasingly becoming technically feasible, though not necessarily desirable.

3.26 Screening programmes for various forms of cancer which may have a genetic basis are currently the main form of genetic screening in the adult population. Testing of the gene itself is now possible for **familial adenomatous polyposis,** an inherited form of **colorectal cancer**. It may shortly become possible to screen a sub-group of women at high risk of familial **breast cancer**, though at present such screening is aimed at early detection of the cancer itself. These testing programmes in families already known to be at risk may be the forerunners of future screening programmes.

3.27 The general screening of individuals who may be carriers for inherited disease genes is currently used only as a service to those in an ethnic group known to have a high incidence of an inherited disease, for example the **haemoglobin disorders** and **Tay-Sachs** disease.

3.28 Pilot projects have been undertaken in several centres to detect carriers for **cystic fibrosis** in adults aged between 16 and 45 years through screening in general practice.[10,11] Preliminary results suggest a high uptake when individuals are offered testing and counselling through personal contact. These projects are discussed more fully in Chapter 4.

Pre-pregnancy and pre-marital screening

3.29 Testing before pregnancy is not systematically practised to any extent in the UK. Screening for carriers for the **haemoglobin disorders** may be offered through family planning clinics and general practice. Insufficient information is available to evaluate such programmes.

3.30 In Cyprus, antenatal screening for **thalassaemia** has been almost totally superseded by premarital screening. The religious authorities had ethical objections to screening during pregnancy on the grounds that it excluded most options other than termination of affected pregnancies. The church in Cyprus therefore insists on testing as a formal prerequisite to church weddings. The certificate required states merely that the partners have been tested and appropriately advised. In this way the confidentiality of the test result is preserved and the couple can exercise an informed choice about reproduction.

3.31 General population carrier screening programmes for **thalassaemia** have been established throughout the Mediterranean area. A comparative study of these programmes has shown they are most rapidly and equitably implemented when a small community at high risk is served by motivated staff working from a single centre, with the help of a lay support association (for example, Sardinia and Cyprus).[12] Such programmes have developed more slowly in larger countries, as they must be delivered through the general health care system, and staff must be trained to integrate screening and counselling into routine services. It has proved particularly difficult to organise carrier screening for haemoglobin disorders when they are not a problem for the whole community but primarily affect ethnic minorities, as in the UK. This problem is the subject of the forthcoming Standing Medical Advisory Committee report on sickle cell, thalassaemia and other haemoglobinopathies. This report, it is hoped, will give guidelines to health service purchasers and providers on the provision of information, screening and counselling services.

Screening during pregnancy

3.32 Screening during pregnancy may be carried out on the mother, on the baby, or on both. If, through screening, a woman is found to be a carrier for a gene for a recessive disorder, her partner may be offered genetic testing in order to find out whether the couple is at risk of having an affected child. If both parents carry the gene for a recessive disorder, or if the mother carries the gene for

an X-linked disorder or if either parent has the gene for a dominant disorder, then tests may be done on the developing fetus. There are several methods of obtaining samples for genetic tests on the fetus, the most common being **amniocentesis** and **chorionic villus sampling (CVS)**. Genetic diagnosis can be achieved before 12 weeks' gestation with CVS, compared with about 16-20 by amniocentesis. However, the risk of miscarriage is slightly higher for CVS (about 1-2% in excess of expectation at this stage of pregnancy) than for amniocentesis (0.5-1%). The emotional trauma engendered by the need to consider a termination and decide whether or not to have one must not be ignored. This is a major ethical issue which applies to many screening procedures where the disease is serious and where there is no effective treatment. Informing parents of the reproductive choices places a considerable burden on them, and counselling and support will be needed whatever the decision.

3.33 In the UK, antenatal screening tests are carried out on all women for **rhesus haemolytic disease** (see paragraph 3.1) and **rubella** (German measles). Rubella screening was the first screening programme undertaken with the objective of offering detection and abortion of potentially affected fetuses. Severe congenital disorders can result from rubella infection during pregnancy.

3.34 Both rhesus and rubella screening appear to be well accepted. Whereas the finding of a rhesus negative blood group results in preventive treatment, a positive rubella test gives rise to the need for very painful decisions.

3.35 Ultrasound scanning of the fetus is generally practised and routine ultrasound may reveal **congenital abnormalities**, some of which may have a genetic basis. Expert fetal anomaly scanning, a specialised form of ultrasound scanning, is offered to women known to be at increased risk of having a malformed fetus because of genetic or other reasons. In addition, it is increasingly offered to all women on a routine basis, as about 70-80% of all severe malformations can be detected. Although the majority of women are aware of ultrasound, the amount of explanation given regarding the possibility of detecting abnormalities varies greatly, as does expertise in interpreting the results.

3.36 The offspring of women with **insulin dependent diabetes mellitus** have an increased risk of stillbirth, neonatal ill health, and major congenital malformations, especially if their diabetes is poorly controlled. In many women with diabetes the diagnosis will already be known, but all women are screened early in pregnancy by blood and urine tests to detect undiagnosed cases. Expert fetal anomaly scanning by ultrasound is offered to all those having the condition.

3.37 In many areas, screening is carried out to detect **neural tube defects** (**spina bifida** and **anencephaly**). Maternal serum **alphafetoprotein** (AFP) estimation is now offered routinely to all pregnant women between 16 and 18 weeks of gestation, but in about half of all pregnancies with a raised maternal serum AFP, no cause can be found, either pre- or post-natally. A raised maternal serum AFP normally leads to expert ultrasound examination for a fetal malformation, with or without amniocentesis for confirmatory biochemical tests.

3.38 Pilot studies of screening during pregnancy for carriers for the common disorder **cystic fibrosis** are currently being undertaken in a number of centres.[13,14,15] In the UK, 85-90% of carriers can be detected by a simple DNA screening test based on a mouthwash sample.

3.39 The various studies of cystic fibrosis screening have devoted considerable effort to the psychological and ethical issues surrounding genetic screening programmes, especially since not all carriers can be detected.

3.40 A study in Edinburgh showed that, of the 2207 women invited for cystic fibrosis carrier screening during pregnancy, 85% accepted it.[16] Only 325 (15%) declined to be tested. Of those who declined, over half did so because of opposition to termination of pregnancy. Other reasons given included the partner's disapproval or non-participation, perceived risk of a CF child being low, the error rate of the test and the generation of unacceptable levels of anxiety.

3.41 The Edinburgh study has assessed the attitudes and responses of the participants and the psychological effects on carriers and their partners. The majority felt that they had had adequate information and were glad to have participated (see paragraph 4.13). There was a consensus that CF carrier testing should be routinely offered to pregnant women, and also that it should be available in family planning clinics and GP health centres, but not in schools. Carriers showed significant symptoms of anxiety and depression whilst awaiting their partner's test result (at this time partners were only tested if the pregnant woman was a carrier : this problem should not occur if couples are tested simultaneously). On receiving the partner's negative test result the carriers returned to normal equilibrium and maintained this.

3.42 Antenatal screening is offered to women in specific risk groups. All **women over an age that varies by area between 35 and 37** are offered testing by chromosome studies for the presence of **Down's syndrome** in the baby. Down's syndrome occurs in approximately 1 in 600 of all births; but it is much less common in

children born to younger women (1 in 1,500 at age 20). Its birth incidence increases with maternal age, being about 1 in 350 at age 35, and as high as 1 in 100 at age 40. Recently, **maternal serum screening** tests have been developed that can be offered to all pregnant women to detect those who may be at increased risk of having a child with Down's syndrome regardless of age, in order to offer them the choice of amniocentesis and chromosome testing.[17] This type of screening is now entering widespread practice and it is estimated that nearly 70% of British districts and health boards have opted to introduce such screening. There are, however, major problems. There is a high false positive rate (about 65 false positives for every true positive or about 1 pregnancy in 10) and false negative rate (about 40%). The practical difficulties relating to consent and counselling and the psychological consequences do not appear to have been given sufficient attention and these are discussed further in Chapter 5. A small study of the experiences of some women who had abnormal results showed that all women were made anxious by their abnormal screening test no matter how they were told.[18] Even after a normal amniocentesis result (ie an unaffected baby) some remained anxious. The practice implications arising from the study are reproduced in Fig A and are, of course applicable to many other conditions for which screening may be introduced.

Fig A[18]

Practice implications

- ► Serum screening for Down's syndrome is increasingly offered to pregnant women in Britain
- ► All screening tests produce a proportion of false positive results
- ► Women who were told that they had an increased risk of having an affected pregnancy became very anxious
- ► Health professionals must recognise women's fears that their unborn baby might have a serious abnormality and their need for information about the implications of such a diagnosis
- ► Protocols concerning the implementation of screening programmes should include adequate psychosocial support for participants

3.43 **Women with epilepsy** requiring treatment with drugs are usually offered expert fetal anomaly scanning by ultrasound in the second trimester of pregnancy because of the increased risk of congenital malformation caused by some drugs.

3.44 It is standard practice in the UK to undertake carrier screening for **haemoglobin disorders** of individuals in antenatal clinics (and increasingly in primary care) who are "not of Northern European origin". Historically the tests used to be part of routine blood investigations, undertaken to detect clinical conditions such as sickle cell disorders. In the process carriers of haemoglobin disorders were identified, but the women were not always informed either that they had undergone a form of genetic screening or of the result. Women found to be carriers are now told by a variety of staff including obstetricians, midwives, haematologists and, increasingly, haemoglobinopathy counsellors (usually nurses and health visitors who have undertaken specialist training).

3.45 Most couples at risk of having children with a major thalassaemia, and about 50% of those at risk of sickle cell disease, request diagnostic tests on the fetus and decide on abortion if the results show the fetus is affected. Screening and counselling may therefore lead to a great reduction in births of affected children, but the emotional costs of the decision to terminate should not be ignored (see paragraph 3.32).

3.46 It is likely that by the time this report is published, some pilot screening programmes may have been extended into more general use and others will be being evaluated. The table opposite summarises current (September 1993) genetic screening programmes in the UK.

CURRENT GENETIC SCREENING PROGRAMMES IN THE UK (September 1993)

It is likely that by the time this report is published, some pilot screening programmes will have extended into more general use and others will be being evaluated. The following table summarises current genetic screening programmes in the UK.

Age Group	Disease	Population screened	Type of screening test	Confirmation required	Other comments
Neonatal	Phenylketonuria	All newborn infants	Indirect	Yes	
	Hypothyroidism	All newborn infants	Indirect	Yes	
	Sickle cell disease	All newborn in some areas; confined to certain ethnic groups in others	Indirect	Yes	Also detects carriers
	Cystic fibrosis	Some areas only (still at pilot stage)	Indirect	Yes	
	Duchenne muscular dystrophy	Pilot studies	Indirect	Yes	
	Other rare metabolic disorders	Family testing	Usually indirect	–	
Later childhood		NONE IN THE UK			
Pre-marital and pre-pregnancy	Cystic fibrosis	Pilot projects in general practice	Direct	No	Detects 85 – 90% of carriers
During pregnancy	Rhesus haemolytic disease	All mothers	Indirect		
	Diabetes mellitus	All mothers	Indirect		Fetuses have expert fetal anomaly scanning
	Congenital malformations	Most fetuses	Routine ultrasound	Yes fetal anomaly ultrasound	
	Down's syndrome	1) All mothers in some areas	Serum screening tests	Amniocentesis with chromosome tests on fetus required for confirmation	
		2) All mothers over 35–37	Chromosome tests on fetus	No	
	Neural tube defects (spina bifida and anencephaly)	All mothers in many areas	Indirect	Fetal anomaly ultrasound	
	Haemoglobin disorders	All mothers not of North European origin	Indirect		Detects carriers
	Cystic fibrosis	Pilot studies	Direct	No	Detects 85 - 90% of carriers

Chapter 4

Providing information and obtaining consent

Introduction

4.1 This chapter considers first the information that people invited for screening need in order to make up their minds whether or not to accept, and the most appropriate way of providing this information. It then discusses the meaning and implications of 'informed consent' in the context of screening. Consent to screening differs in several respects from the consent of an individual undergoing treatment, in particular in the way that families are involved. Informed consent to screening implies that those being screened have thought through the consequences of an abnormal result. These may include an effective therapy, which may however be costly (to the family and/or to the health services), unpleasant, and difficult to sustain over a long period. Where no effective therapy is possible, decisions may be involved about terminating a pregnancy or having children in the future.

4.2 'Family' needs to be understood as covering an extended set of relatives linked by blood ties or by marriage or by both. Members of families may or may not be in close touch. They may live far apart, may be registered with different medical systems, and may sometimes be unaware of the relationship. Nevertheless they may share important genetic traits. Genetic screening may discover information about persons who have neither been screened nor consented to be screened. These points will be particularly important in considering issues of consent, confidentiality and data protection.

4.3 In this chapter the focus is on the ethical aspects of providing screening for genetic defects in day-to-day medical practice. Health services, whether in the general practitioner's surgery or a hospital clinic, are constrained by time and resource limitations that do not apply to most research projects to the same degree. Many of the genetic screening programmes described in Chapter 3 are pilot projects and therefore in the research stage. Research teams may be able to build into their projects ample time for counselling, and to call on the assistance of nurses trained in genetics and other counsellors. Furthermore, only

relatively small numbers of people are involved in most research projects and a high level of support can be offered to such individuals and close members of their families. This may not always be feasible in a normal clinical setting.

4.4 In recent years a number of projects have examined the problems of population screening in a variety of clinical settings for carriers for cystic fibrosis, a serious genetic disease that every year affects about 300 babies born in the UK to parents of Northern European descent. We have drawn on published and unpublished material generated by this work in the discussion which follows.

4.5 We have already drawn attention to some of the differences between a research programme and general clinical practice and we fully appreciate that what is learnt in a research setting is not always easily transferrable into clinical practice. It is also clear that some established programmes have not always followed the ethical principles that we outline, and we have learnt from their difficulties. Our aim in this chapter is to emphasise how screening should be done in the future rather than to dwell on deficiencies in the past.

Information

4.6 The Department of Health's 1990 circular, **A Guide to Consent for Examination or Treatment** is a useful starting point.[1]

> "Patients are entitled to receive sufficient information in a way that they can understand about the proposed treatments, the possible alternatives and any substantial risks, so that they can make a balanced judgement. Patients must be allowed to decide whether they will agree to the treatment, and they may refuse or withdraw consent at any time."

This statement makes four important points relevant to screening:-

(i) those being screened are entitled to receive sufficient information in a way that they can understand about what is proposed;

(ii) they must be made aware of any substantial risks;

(iii) they must be given time to decide whether or not to agree to what is proposed; and

(iv) they must be free to withdraw at any time.

4.7 Screening programmes differ from traditional medical practice in that the process is usually initiated by the health care providers contacting people who are well : these people are being offered the possibility of avoiding detriment to their future health or that of their children. As we have already emphasised, what particularly marks out **genetic** screening are the potential implications for the **family**; in addition, a test result will give the individual tested no certain prediction but rather a range of possibilities that may be quite wide.

4.8 The kinds of information and procedures that people need to help them decide whether or not to be screened for a genetic disorder may be summarised as follows:-

(i) the condition to which the genetic disorder may give rise: how serious is it? how variable is it in its effects? what are the therapeutic options?

(ii) the way in which the disorder is transmitted, ie dominant, recessive and sex-linked mechanisms, and the significance of carrier status;

(iii) the reliability of the screening test, ie the typical rate of false positives and false negatives, and the probability of the development of a serious genetic disease;

(iv) the procedures for informing individuals of the results, negatives (normal) as well as positives (abnormal), and what will be done with the samples;

(v) information about the implications of screening positive (abnormal) for their future and existing children, and for other family members; and

(vi) a warning for pregnant women that genetic screening may reveal unexpected and awkward information, for example about paternity.

It should be made clear precisely what is being screened for at each stage of the screening process. A clear statement of what will be done with the results and with the sample (blood or other bodily fluid) should be provided, and individuals should be able to stipulate that their samples should not be kept.

4.9 This information can be provided during a personal consultation, by means of a leaflet, or through some combination of the two. The evidence of the cystic fibrosis screening pilot projects suggests that a combination is desirable. It is important that both written and oral information is in a language appropriate to the individual.[2]

4.10 A number of pilot screening projects for cystic fibrosis recently carried out have addressed with great thoroughness many of the problems of obtaining informed consent. We have therefore drawn extensively on their experience. The leaflet used in approaching people about screening in a London general practice (Fig B)[3] provides answers to the following questions: what is the nature of the disease? what is a carrier? what are the chances that I will be a carrier? what are the chances that I will have a child with the disease? is it important for me to tell my partner? The question "What does it mean to be a carrier?" is explained in another leaflet given to those whose test is positive.

Fig B

Leaflet issued in a London general practice

Have you heard of.....

Cystic Fibrosis Screening ?

This pamphlet contains information about a disease called Cystic Fibrosis.

• In Britain, about 300 babies a year are born with this disease. About one in every twenty people carry the gene for cystic fibrosis. These people do not have cystic fibrosis but are known as *carriers*. If their partner also has the cystic fibrosis gene, the couple might pass on this serious disease to their children.

• There is now a test to detect those people most likely to pass on cystic fibrosis to their children. If you choose to be tested we can tell you your chance of having a baby with cystic fibrosis. We are offering the test at this health centre as part of a research project.

The test is being offered to both men and women aged between 18 and 45.

• This pamphlet is to help you to decide whether you want the test or not. The result of the test will not affect your health at all. The result could prevent you having a baby with cystic fibrosis.

• Your test result will be treated as confidential.

Please read on.....

4.11 A question and answer sheet used in Manchester (Fig C)[4] goes into the issue of informing other family members. It also raises a question about insurance : the comforting answer, though it may be correct for cystic fibrosis and perhaps other recessively inherited disorders, does not apply to all areas of genetic screening. (The ethical issues relating to insurance are discussed in Chapter 7.)

Fig C

Leaflet issued in Manchester and
other North-West general practices

WHAT DOES IT MEAN TO BE A CARRIER OF CYSTIC FIBROSIS?

1.

Question. Will it affect my health now or in the future?

Answer. No. Because you carry two genes - one from each of your parents the normal gene protects you completely from the effects of the gene carrying cystic fibrosis. It is only when both genes carry cystic fibrosis that you could have the symptoms of the disease.

2.

Question. Are my children at risk in any way?

Answer. They would only be at risk if they had inherited the cystic fibrosis gene from both their parents. If your partner is not a carrier then they have a 50/50 chance of being a carrier like you and a 50/50 chance of not being a carrier at all. Children are not routinely tested for carrier status. Probably by the time they are adults and having children themselves the test will be generally available.

3.

Question. Should I tell any other members of my family that I am a carrier?

Answer. This is entirely up to you. It is likely that if your brothers and sisters are having families themselves they might like to have this test done too.

4.

Question. Will it affect my chances of obtaining insurance in the future?

Answer. Categorically no. All insurance companies take advice at the highest medical level. They accept that being a carrier of cystic fibrosis will not affect your health or your life expectancy in any way.

5.

Question. Why do 1 in 20 people carry the cystic fibrosis gene?

Answer. We don't really know the answer to this. We think that it protected us in some way from other serious illnesses or malnutrition in the past.

4.12 Two of the cystic fibrosis screening leaflets we have seen (Edinburgh and Manchester) outline the treatment options, including prenatal diagnosis of the fetus. The Edinburgh leaflet[5] advises women who are unsure about who is the father of their baby to refuse the test. The reason for this is presumably because, as the fetus can only have cystic fibrosis if the father is also a carrier, antenatal diagnosis would not be contemplated without knowing this fact and the mother might be made unduly anxious.

4.13 The voluntary nature of genetic screening is of particular importance. In connection with the Edinburgh trial of screening for cystic fibrosis a follow-up study of the reasons given by the women who declined testing, after having been informed of the nature of the disease and significance of the test, is of interest. Out of the 2207 women who were invited to participate in the trial, 260 refused. They gave a variety of reasons, including a lack of interest in the result, a wish to avoid anxiety about the result and, in just over half the instances, opposition in principle to the termination of pregnancy, either specifically for cystic fibrosis or in any event.[6] This study underlines the importance of avoiding any hint of coercion in genetic screening programmes; it also illustrates the difficult and delicate task of providing adequate information in a non-directional way. A further illustration is provided in the invented examples in Fig D below:

Fig. D

Jane B and her partner decide to be screened for the cystic fibrosis gene. They have read the leaflets and talked with their family doctor. If they are both carriers they have decided to have prenatal diagnosis and terminate the pregnancy if the fetus has cystic fibrosis. They are found to be carriers and the baby is affected. Jane B is now very doubtful about termination and both parents are excited by reports in the press that gene therapy for the disease is being tried. They are glad to have been screened so that their baby can be treated as early as possible after birth, and may be able to benefit from advances in treatment.

Mary S and her partner are in a similar situation but have gone ahead with termination which is done the day before the press reports about gene therapy. They feel cheated and wish they had never consented to being screened.

These invented examples illustrate also the high level of information that may need to be given to couples at risk. Gene therapy is still in the experimental stage and counselling needs to be readily available when 'advances' or 'breakthroughs' are announced.

4.14 Equally critical ethical issues arise from the identification of late onset diseases such as Huntington's disease or Alzheimer's disease. For Huntington's disease the genetic mechanism causing the disease was discovered in March 1993 and a specific test is now available. Is termination of pregnancy an acceptable option when screening for late onset diseases? Future screening programmes will have to provide information on such matters as the definition of what constitutes 'late onset'; the accuracy and the predictive power of the test for a disease-related gene or genes; whether the causal relationship between genetic and environmental factors is well established; and what treatment options are likely to become available.

4.15 We have so far concentrated on information given in programmes in which the defective gene is detected directly and have pointed out that such programmes are at present research based. But, as described in Chapter 3, many programmes of screening for genetic disease by indirect methods have been in operation for a considerable number of years. The way in which information is given and consent obtained for programmes that are part of normal medical care (for example, phenylketonuria, congenital hypothyroidism, Down's syndrome) seem to be very variable (paragraphs 3.14 and 3.15). The Health Education Authority's **Pregnancy Handbook**, available free to all women pregnant for the first time, now has a section which describes the various methods of prenatal diagnosis and some of the conditions that can be detected, and comments on how couples can make use of the information.

4.16 A review of routine screening for Down's syndrome in antenatal care indicates that the information provided is often not adequate and that women are not always sure of what tests they have undergone or what the results mean.[7] In a recent small study of the psychological consequences of screening for Down's syndrome some of the difficulties surrounding the giving of information are highlighted:[8]

> "One woman did not read the information sheet ... assuming it to be about screening for spina bifida."
>
> "One woman believed she was informed when she had the test but when the news came that she had a 1 in 20 chance of having a Down's syndrome baby, she realised she knew nothing."

Counselling and consent

4.17 In most of the research programmes and pilot projects we have considered, written information has been supplemented by counselling. This has been done either in conjunction with giving out a leaflet or by emphasising the availability of a trained counsellor to answer questions and talk through the problems. In two trials of screening for cystic fibrosis in primary care, through general practices in inner and outer London, the take-up of an invitation by letter to be screened, without any counselling or discussion with a doctor, was low, around 10% of the sample.[9] Those approached (both sexes aged 16-44 in one trial and aged 18-45 in the other) were neither pregnant nor known to be contemplating having a child. It may therefore have been lack of interest, rather than informed refusal, that led to the low take-up.

4.18 Follow-up studies in the Edinburgh[5] and Manchester[3] programmes indicate that the implications of the test were well understood by a majority of the participants. They included the recessive character of the defective gene, the fact that the test would not identify all carriers, and the probability of a child of two carriers being born with cystic fibrosis. These are complex matters requiring an understanding of the basic patterns of inheritance and disease transmission, and of risk analysis, and it is encouraging to note that they can be explained, and the information retained for some time, by means of written material plus a brief discussion. The general practitioners in the Manchester trial estimated that cystic fibrosis counselling added about 10 minutes to a normal prenatal consultation.

4.19 The results of the two London trials illustrate one of the problems associated with introducing screening for a genetic disease in a population which has no direct experience of the disease; namely how to convey adequate information to people who do not perceive a need for the knowledge that the test would supply. It is not clear what meaning can be attached to providing information and obtaining informed consent in such circumstances. The take-up among patients approached 'opportunistically' by a member of the trial team when visiting the surgery was much higher, around 70% in the participating practices. The take-up among women and couples approached in family planning clinics was even higher than this at 87%.

4.20 The evidence suggests that written information needs to be supplemented with a face-to-face discussion about the facts and the choices and moral issues that may arise from a positive test result. This is not necessarily so very different from the kind of discussion that a patient may have with his or her general practitioner (or hospital consultant) before agreeing to diagnostic

tests for any potentially serious disease. Screening large numbers will put pressure on staff resources, but the successful introduction of screening for high risk of heart disease and strokes in general practice, using trained practice nurses as counsellors, suggests that the task is manageable. Health care staff would require training in the basic principles of genetics, in the particular characteristics of the disease for which screening is being introduced, and in handling the moral issues, especially in respect of conception and pregnancy. Artificial insemination by donor or egg donation may be an option in certain circumstances, and termination is an option that couples may need to consider carefully if screening takes place during pregnancy. Health care staff may also need training in the best ways of exploring the familial implications of a positive test result. Individuals or couples with positive test results will need further counselling and support, perhaps over a considerable period.

4.21 There is general agreement that counselling at each stage of the screening process should be 'non-directive', as far as possible. In practice a dialogue that helps an individual to explore the facts and issues in the context of his or her particular social and moral background is unlikely to remain completely neutral : experience of genetic counselling suggests that a completely neutral stance can seem cold and unhelpful to some. The key ethical principles of genetic counselling should be:-

(i) the voluntary nature of genetic screening, and the freedom and responsibility of the individual or couple to decide;

(ii) the importance of ensuring that the individual or couple offered screening understand the purpose of the test and the significance of a positive result;

(iii) an assurance of confidentiality in the handling of the results, coupled with an emphasis on the responsibility of individuals with a positive (abnormal) result to inform partners and family members; and

(iv) an appropriate emphasis, at each stage in the screening process, on the fact that consent to screening, or to a subsequent confirmatory test, does not imply consent to any specific treatment, or to the termination of a pregnancy.

It is important that interpreters are available when seeking informed consent from individuals who do not speak English.[10]

4.22 Although the training and supporting of professional staff is clearly essential, there is little empirically based work to guide practice. There is a need to evaluate the effectiveness of different approaches to the provision of information and the obtaining of consent. Such evaluation should be built in to all screening programmes.

Persons requiring special safeguards

4.23 In some cases, it may not be possible to obtain properly informed consent. The testing of the following categories of persons should be subject to special safeguards:-

(i) minors;

(ii) the mentally ill and those with severe learning difficulties.

Minors

4.24 The Family Law Reform Act 1969 permits a person between the ages of 16 and 18 to give consent to medical treatment which is carried out for his or her benefit. Following the decision of the House of Lords in *Gillick v DHSS*[11] a child below the age of 16 may also give valid consent to medical treatment if he or she has the ability fully to understand what is involved in the medical procedure or treatment in question. Otherwise consent must be given by the parents of the child, and may only be given to promote the interests of the child. Under the Children Act 1989 consent may be given by one and is not required to be given by both parents.

4.25 Genetic screening of children which is not of immediate benefit to them should normally be deferred until they can give valid consent. An exception may be where testing of the child is essential for the diagnosis of a family member, though it may be difficult to argue that such testing is always undertaken to promote the interests of the child. The genetic testing of children for late onset/adult diseases raises particularly difficult issues of informed consent and is likely to become increasingly important as a growing number of genes which predispose to disease in later life are being discovered. The child, when adult, may not wish to know the increased risk of developing a disorder. This again is an area where there is no ready answer or right procedure, even for testing within families for a particular disorder. So particular

caution is needed when any wider screening of children for later onset genetic disorders is to be considered.

Mentally-ill and those with severe learning difficulties

4.26 So far as genetic testing of the mentally ill is concerned, the legal position has been held by some to be governed by the House of Lords decision in *F v West Berkshire Health Authority*[12], a case which concerned the sterilisation of a 36-year old woman. If strictly followed, it is not clear that genetic testing could ever be properly conducted on someone who is mentally disabled when the purpose of the test is to benefit a family member or someone other than the person being tested. It is a matter for consideration whether genetic tests on mentally ill individuals or those with severe learning difficulties should be permitted in situations where the information gained would be of clear benefit to other family members. For example, should men with severe learning difficulties be tested for the gene for fragile X syndrome in order to find out whether sisters or nieces might be carriers, and therefore at risk of having boys with the disorder? The benefit to the family could be great and the risk of harm to the individual being tested negligible.

Other vulnerable individuals

4.27 Special care is always needed when consent is being sought from vulnerable individuals, such as prisoners, student volunteers, and (as noted in paragraph 4.21) from individuals who do not speak English.

Conclusions and recommendations

4.28 We do not agree with some recent commentators who have taken the view that so much information is necessary for individuals or couples invited to accept screening for a genetic disease that it is not practicable to obtain truly informed consent at all. Provided that the aim is to provide adequate information, with opportunities for reflection, questioning and further explanation before consent is given, it should be possible to obtain consent in a normal clinical setting. The communication of information is at present likely to be easiest, and best understood, in the context of having children, including preconception and antenatal stages. It should, however, become established outside this framework. We discuss the importance of education in human genetics in Chapter 8 on Public Policy.

4.29 **We recommend that adequately informed consent should be a requirement for all genetic screening programmes.** The voluntary nature of the screening process must be emphasised. Adequate information must be provided for all those being invited to enter a genetic screening programme and should include information about the implications for other family members. Information for all genetic screening programmes is best delivered in both written and oral form.

4.30 **We recommend that counselling should be readily available for those being genetically screened, as well as for those being tested on account of a family history of a genetic disorder.** Counselling should be available at all stages of the screening process. This will require the diffusion of an understanding of genetics (at present mainly confined to genetic counsellors) in particular among those engaged in primary health care. The resource implications, including the need to train large numbers of practice nurses and health visitors in the subject matter and the basic principles of counselling, need to be assessed within the broader context of the expansion and extension of primary care.

4.31 Screening of individuals who are unable to give properly informed consent (minors, the mentally ill and those with severe learning difficulties) require special safeguards (paragraphs 4.24 - 4.26).

Chapter 5

The results of genetic screening and confidentiality

Introduction

5.1 In this chapter we deal with questions relating to the handling of the results of genetic screening and the safeguarding of the information obtained. These questions are particularly complex in the area of genetic screening, because (as noted in paragraph 4.2) screening may reveal information not only about those who have given their consent to screening, but about members of their families who have not. Genetic screening has to take account not only of the way in which difficult information is to be disclosed to individuals who have been screened, and ways in which the confidentiality of data is to be secured, but also of the interests of family members who have not been screened. Family members may have a strong interest in disclosure of information that is closely relevant to their own genetic make-up, and also in such information being disclosed promptly and in sensitive and effective ways.

Disclosure to the individual

5.2 After undergoing genetic screening, or indeed any other form of testing, an individual should **normally** be fully informed of the results, both positive (ie abnormal) for the disorder being screened for, or negative (ie no defect is found).

5.3 Difficulties can arise when the screening process yields results which are unexpected, unwanted, and have not been covered by consent. For example, a sex chromosome abnormality may be revealed when carrying out prenatal testing for Down's syndrome, or a different inherited disease may show up on a test designed for another purpose. To fail to disclose a serious disease accidentally discovered by testing for which consent had not been explicitly given raises ethical problems. To reveal findings affecting an individual which will not have any clinical implications and may provoke anxiety requires careful individual consideration. Sometimes information may cause distress to the family, although

future decisions about having children could be seriously affected if information is concealed. Unexpected information can present ethical dilemmas for which there are no easy answers, or indeed any correct answers.

5.4 Even when the result has been obtained, the sample may be preserved for a number of reasons : to check the results, for future diagnostic needs, including those of the family, and for research purposes. Both the individual and the family may benefit if samples are kept in case a genetic defect could be identified at a later date. Testing of samples as a research procedure may help to improve our understanding of genetic variation and the prevalence of other genetic diseases in the population. Authorisation for such uses should have been obtained when initial consent for screening was given, even when the samples are to be used anonymously, and special care is needed to ensure the confidentiality and security of stored samples.

Disclosure to family members

5.5 Our main concern, however, is not with disclosure to the individual, but where the interests of others are concerned. This raises some of the most serious issues in this report. The perceived interests of members of the same family sometimes clash. Such clashes can usually be resolved in careful discussion with experienced professionals. But we need to consider the problems that unhappily do not reach such a resolution. These problems are much more acute for X-linked and autosomal dominant diseases, as illustrated by the example in Fig E.

Fig E

A man diagnosed with a mild form of adrenoleukodystrophy (ALD), an X-linked condition that can be carried by healthy females, did not wish his diagnosis or the genetic implications to be discussed with his family. Seven years later, his niece gave birth to two successive boys who have a more severe form of ALD. The illness only came to light in them when the elder boy started to display symptoms. The mother's sister, the man's other niece, has also given birth to a son subsequently diagnosed with ALD. Both families are bitterly resentful that the medical services did not warn them of their genetic risk.

5.6 We have reviewed existing case law, professional guidelines and current academic writing on applying the principle of confidentiality to the special circumstances of information arising from genetic screening that may be vital to the well-being or future of other family members. **In such clearly defined contexts** it may be appropriate to treat those family members as a 'unit' and to place less emphasis on individual patient autonomy. This may not always be feasible, for example where blood relations have lost contact with each other, but even in such cases the individuals being screened should be made aware of the implications for their relations.

5.7 We have based our approach on the following general principles:-

(i) the accepted standards of the confidentiality of medical information should be followed as far as possible;

(ii) where the application of such standards might result in grave damage to the interests of other family members, then the health professionals should seek to persuade the individual, if persuasion should be necessary, to allow the disclosure of the genetic information. That task would be eased if it were accepted, and as we have recommended (paragraph 4.29) that genetic screening programmes should include in the information leaflets and the counselling a clear indication that the consequences to the family of genetic information may in some cases make it unfair to confine the information gained solely to the individual who has been screened;

(iii) in exceptional circumstances, health professionals might be justified in disclosing genetic information to other family members, despite an individual's desire for confidentiality. For example, confidentiality might justifiably be broken if an individual refused to disclose information which might avoid grave damage to other family members.

5.8 We begin by examining the issue of confidentiality, considering in particular why it is important and how it is currently protected by the law and by other means. We then ask whether there are circumstances in which the confidentiality of genetic information ought properly to be overridden to permit disclosure to those interested third parties who, it is sometimes said, have a 'right to know.'

The importance of confidentiality

5.9 Article 8(1) of the European Convention on Human Rights provides that "Everyone has the right to respect for his private and family life, his home and his correspondence." The right to private life, or to privacy, clearly includes the right to be protected from the unwanted publication or disclosure of intimate personal information. Although there is disagreement in this country about the extent to which personal privacy should be protected by law, there appears nevertheless to be widespread acceptance that, to the extent that there is such a thing as a right to privacy, it includes at least "privacy of information, that is the right to determine for oneself how and to what extent information about oneself is communicated to others."[1]

5.10 These general principles are particularly important in medicine. Respect for privacy is vital to the doctor/patient relationship. The relationship is one which must be built on trust and confidence if patients are to reveal information essential to the proper diagnosis and treatment of their condition. Yet trust and confidence would soon be shattered if doctors were to fail to respect the confidentiality of intimate personal information. Indeed it has been suggested that this would have unhelpful implications for both public as well as private health: in a High Court decision it was stated that: "In the long run, preservation of confidentiality is the only way of securing public health; otherwise doctors will be discredited as a source of education, for future patients will not come forward if doctors are going to squeal on them."[2]

5.11 The case for confidentiality in medicine must apply with equal force in the specific area of genetic screening. Individuals agreeing to be screened need to be confident that no personal information about the results will be made available to anyone other than themselves and their medical advisers without their explicit consent. Otherwise people may be reluctant to participate, with damaging implications possibly for themselves, their families, and potentially other third parties. If doctors were to break the confidence relating to genetic information, this would have adverse implications for other areas relating to the care and treatment of the patient. And how could the patient be confident that other medical information might not also be disclosed to a third party?

5.12 But, although the right to privacy generally and the confidentiality of personal medical information in particular are of the greatest importance, it does not necessarily follow that both should be wholly unqualified. Article 8(2) of the European Convention on Human Rights provides, for example, that the individual's right to personal privacy may be overridden by requirements prescribed by law introduced to protect health or morals, or the rights and

freedoms of others. This acknowledgement may be particularly important in the area of genetic screening. Information gained in the course of genetic screening will have implications for other family members which could clearly affect the future conduct of their lives. (The information might also be deemed to be relevant by employers and insurers; these issues are dealt with in Chapters 6 and 7 respectively.)

5.13 Here we are concerned particularly with family members who may claim to have a legitimate interest in being informed about the results of genetic screening. The claims may vary in strength. An individual may have an interest in knowing whether a partner or prospective partner is likely to suffer from, for instance, familial colon or breast cancer, or Huntington's disease in the future. But such an interest, while understandable, falls far short of any right to claim knowledge. The emphasis is somewhat different if children with a particular partner are contemplated. For example, a pregnant woman may legitimately want to know the result of the screening test on the father of her child if she herself has had a positive test for the cystic fibrosis or Tay-Sachs gene. A different type of problem may arise with blood relatives where non-disclosure of information might lead to an unnecessary termination, or where a relative, not informed of a high genetic risk, might unknowingly become the parent of a child with a serious genetic disorder (see Fig E on page 42).

Legal protection of genetic information

5.14 The confidentiality of medical information is protected by law, first by the common law principles, and secondly by the Data Protection Act 1984. (In the limited circumstances of infertility treatment confidentiality is further protected by the Human Fertilisation and Embryology Act 1990 as amended by the Human Fertilisation and Embryology (Disclosure of Information) Act 1992.)

Breach of confidence

5.15 At common law personal information held by health professionals about genetic screening is almost always held in confidence. This means that as a general rule there is no right to disclose the information to a third party without the consent of the person to whom the information relates. There is an exception which allows disclosure of information without the individual's consent where the disclosure is in the public interest. The courts recognise that, while "there is a public interest that confidences should be preserved and protected by the law", in some cases "public

interest may be outweighed by some other countervailing public interest which favours disclosure."[3]

5.16 In determining whether confidential information may lawfully be disclosed, a court thus has to balance competing considerations, some which will argue in favour of confidentiality and others which will argue in favour of disclosure. It is difficult to know in advance how this balance will be struck in any particular case, but it has been argued that the law "is necessarily vague to take account of the many different situations which might arise."[4] In a case where a doctor wished to disclose confidential genetic information to a member of the patient's family against the individual's expressed wish, the court would have to balance the public interest in confidentiality against the public interest in enabling individuals to make informed decisions about their health and reproduction.

Data Protection Act 1984

5.17 In addition to the common law duty not to disclose confidential information, there is also statutory protection in the Data Protection Act 1984 which applies to genetic information stored on a computer. The Act applies to "information recorded in a form in which it can be processed by equipment operating automatically in response to instructions given for that purpose" (s 1(2)). It seeks to control the storage and use of 'personal data', a term defined to mean data relating to a living individual who can be identified from the information (or from that and other information in the possession of the data user) (s 1(3)).

5.18 The Act establishes a number of data protection principles and creates a system for the registration and supervision of data users. It also makes provision for the improper disclosure of information. When a data user registers, the entry must include a description of any person or persons to whom it is intended to disclose data. Once registered, the data user must not disclose to anyone who is not described in the entry. These restrictions are qualified in the sense that the information may also be disclosed to the data subject or to another person authorised by the data subject. Disclosure is also permitted if it is "urgently required for preventing injury or other damage to the health of any person or persons." (s 34(8)).

5.19 It is a criminal offence for a data user knowingly or recklessly to disclose information to a third party. The aggrieved individual could also refer the matter to the Data Protection Registrar who is empowered to issue an enforcement notice to the data user directing him or her to comply with the data protection principles. The Registrar may ultimately issue a de-registration notice to a data user who violates the data protection principles. There is no provision in the Act for compensating a data subject who is a victim of the unauthorised disclosure of information by the data user. There may, however, be a right to damages for any loss suffered, arising under the general law of tort. A data subject is, in contrast, expressly entitled to compensation for damage or distress caused by the disclosure of the data without the authority of the data user.

Professional codes of conduct

5.20 Apart from the common law and statute, the confidentiality of medical records in general and genetic information in particular is protected by professional rules of conduct governing at least some health professionals. The General Medical Council's guidance states that:

> "Patients are entitled to expect that the information about themselves or others which a doctor learns during the course of a medical consultation, investigation or treatment, will remain confidential."

The General Medical Council's guidance also states, however, that a doctor's duty of confidentiality is not absolute and may be overridden in the public interest. This appears to reflect (but may not be identical with) the legal obligations already considered.

5.21 Concern has been expressed that professional obligations of this nature do not govern everyone employed in the health service who may come into contact with confidential genetic information. This concern is misplaced. There are professional codes, similar to those laid down for doctors, for disciplines such as nursing, from whom the majority of genetic counsellors are drawn. Other health service staff are likely to be employed under a contract of service which either expressly or by implication prohibits the disclosure to unauthorised persons of confidential medical (including genetic) information. Breach of any such condition could lead to the dismissal of the employee responsible.

5.22 Do additional measures need to be taken to deal specifically with the unauthorised disclosure of genetic information by health service employees? Does genetic information raise any questions of confidentiality which are radically different from those which apply to other sensitive personal medical information? Why should the confidentiality of genetic information be singled out for special treatment beyond that accorded to other medical information about individual patients? We appreciate that there are concerns about confidentiality generally, recently expressed for example in the Report of a Working Group on the Access to Named Data by Management and Administration under the chairmanship of Professor Roy Weir in 1991.[5] In our view the confidentiality of genetic information is best seen as an aspect of the problem of confidentiality generally. Nevertheless it is a serious issue in the context of genetic screening and, before programmes are set up, the mechanisms for ensuring confidentiality should be defined and secured.

The disclosure of genetic information

5.23 Thus the confidentiality of genetic information is protected in a number of ways, involving the common law, statute, professional codes of practice and contracts of employment. But the duty of confidentiality is not absolute. At common law confidential information may be disclosed where it is in the public interest to do so (paragraph 5.16). Under the Data Protection Act 1984, protected information may be disclosed where it is urgently required for preventing injury or damage to the health of any person or persons (paragraph 5.18). And under the General Medical Council's Guidance to doctors confidentiality may be overridden in the public interest (paragraph 5.20).

The ethical dilemmas

5.24 We discuss first the responsibility of the individual in resolving the dilemmas and next the role and responsibility of the doctor or other professional adviser. The main ethical dilemma arises from a conflict between the right of the individual to personal privacy on the one hand and the interest of family members to be made fully aware of available information which would play a part in making important life decisions on the other. A balance needs to be struck between the two. A further complicating factor is that some family members may not wish to be presented with the

information. We note that this would become a much more serious problem if widespread screening were introduced for X-linked or autosomal dominant diseases.

The individual's responsibility

5.25 The question of responsibility has at least two dimensions in this area. The first is the responsibility of the individual to pass on relevant information to other family members, and the second is the responsibility of the other family members to receive the information. As a starting point, we adopt the view that a person acting responsibly would normally wish to communicate important genetic information to other family members who may have an interest in that information, and that a responsible person would normally wish to receive that information, particularly where it may have a bearing on decisions which he or she may be called upon to take in the future. We are also of the view that the primary responsibility for communicating genetic information to a family member or other third party lies with the individual and not with the doctor who may, however, do this at the request of the person concerned.

5.26 The situation regarding family members who may not wish to know can be more difficult. If family members were unaware that a relative had been screened, they would be unable to know whether or not they would wish to be informed about the result. In these circumstances the individual who had been tested would have to take care about the manner in which other family members were informed.

5.27 Evidence submitted to us suggests that in practice the withholding of genetic information obtained by a screening procedure from those who may need to know is not a common occurrence, although it does happen from time to time. Some submissions to us raised the possibility of creating a legally enforceable duty on the part of the individual to communicate genetically relevant information to interested family members. Although serious problems can arise as a result of non-disclosure, and certain family members may clearly have a legitimate interest in the information, we do not consider that this should always supersede the individual's right to privacy, whatever the circumstances. We have difficulty in contemplating how any such legal obligation would work and how any legal right of family members (assuming that they could always be identified) could be enforced. In any event, in certain circumstances there may be perfectly good reasons why an individual would not wish to inform family members about the result of a genetic test. For example, a woman who has discovered she is a carrier for Duchenne

muscular dystrophy may not wish at that time to tell her sister who is seven months pregnant.

5.28 The best way of ensuring that genetic information is appropriately shared with family members (and occasionally with other third parties) is through the information and counselling procedures that we have discussed in Chapter 4. Although the desirability of sharing information with family members can be emphasised, disclosure ought not to be made a condition of participation in a screening programme. Inevitably some individuals will refuse to allow disclosure and this can present the doctor or health professional with an ethical dilemma.

The doctor's dilemma

5.29 Just as we have rejected the suggestion that there should be a legally enforceable duty placed on people who have been screened to inform family members or other third parties about the results, so too we reject the idea that doctors could be placed under a legal duty to reveal information against the wishes of the individual concerned. No such duty is acknowledged by law in this country, though the position may be different elsewhere. The furthest the law appears to go is to recognise that in exceptional and ill-defined cases the doctor may have discretion to disclose genetic information to third parties. This is as far as we believe the law ought to go, although even here we are reluctant to suggest that the wishes of the individual should readily be overruled.

5.30 But while we are firmly of the view that privacy and confidentiality should be respected and maintained, we also accept that there may be exceptional circumstances where these might properly be overridden by the doctor. We have in mind here, for example, a case submitted to us in evidence where the information was withheld out of malice. We do not suggest that the wishes of the individual should be overridden only in this type of case. But it does illustrate how exceptional is the type of situation where it may be appropriate and reasonable to subordinate the individual's privacy to the interests of others.

5.31 It is impossible to prescribe in advance all the circumstances in which a doctor might properly disclose confidential information to family members. Although it may be helpful to develop guidelines to help the doctor in taking decisions, and to seek clarification of the legal position to ensure that disclosure within the framework of such guidelines can be made within the requirements of the law, the actual decision to disclose can only be made case by case. This imposes a heavy burden of responsibility on the health

professional. Two factors stand out as especially relevant. The first is the consequences of the refusal to share information. There would be a stronger case for overriding individuals' objections where the information would influence a decision having potentially damaging rather than merely inconvenient consequences for other family members. The second is the reason for the individual's refusal to give permission. If it can be determined that the reasons are malicious, the decision may be straightforward. However, if the reason were a fear that the information might yield compromising evidence about paternity, the ethical issues would be quite different. If information about non-paternity were not disclosed, a man who incorrectly believed himself to be the father of a child with a particular genetic status might make the wrong decisions about having children. On the other hand, for the health professional to reveal such information might lead to harm to the woman concerned, not only because of the breach of confidentiality itself, but also because of its impact on the woman's relationship with the man involved. For this dilemma there is no easy answer.

Genetic registers

5.32 So far, we have considered the consequences of individual results and their disclosure. In the context of genetic screening, where large numbers of tests are being undertaken, this may be recorded in the form of a genetic register or similar database. Special consideration has therefore to be given to the implications for security of these grouped results.

5.33 A register can be defined as a systematic collection of relevant information on a group of individuals. Genetic registers record information on individuals with specific genetic disorders, and may include relatives at risk of developing or transmitting the condition. The information may be recorded by hand, or may be held on computer. Genetic registers may be set up for a variety of reasons, including research on the disorder, the effective provision of services to those on the register, and the systematic offering of genetic counselling to family members. The amount and type of information recorded also varies greatly, as does the presence of identifying details.

5.34 A number of general ethical issues concerning genetic registers exist. Here we outline those issues relating to genetic screening. They need to be seen against the background of the following points:-

(i) a genetic register may be the starting point for genetic screening; for example, the systematic testing of relatives of individuals with fragile X syndrome or Duchenne muscular dystrophy;

(ii) genetic screening may also be based on a register which is not specifically genetic in its basis; for example, registers of specific cancers or of those with severe learning difficulties; and

(iii) a genetic register may be the result of a genetic screening programme; for example, a register of carriers for cystic fibrosis or sickle cell disease in a population screened for the purpose.

5.35 Consent of individuals on a register to be screened is clearly essential as stated earlier, but it is also important that individuals know that they are on the register.

5.36 Consent of individuals for long term storage of information resulting from genetic screening has also been emphasised earlier; but should this form the foundation of a genetic register, separate and specific consent should be sought for any subsequent tests or other measures.

5.37 While confidentiality of all medical information is essential, this is particularly the case for genetic registers, which may contain highly sensitive and potentially identifiable data on large numbers of individuals with, or at risk for, serious genetic disorders.

5.38 Computer-based genetic registers are subject to the Data Protection Act, but there is need for additional safeguards for all genetic registers, including storage of information in a safe place and manner, restriction of access to those specifically responsible for the register, and the removal of identifying information when data are used for research purposes.

5.39 This is an important area of concern. In our view the Department of Health should consider with health authorities and the appropriate professional bodies effective arrangements for the preservation of confidentiality, particularly in relation to genetic registers, and should issue the necessary guidance.

Conclusions and recommendations

5.40 We regard it as axiomatic that:-

(i) individuals should normally be fully informed of the results of genetic screening, and in particular of the implications of those results for the family; and

(ii) the accepted standards of the confidentiality of medical information should be followed as far as possible.

5.41 When genetic screening reveals information that may have serious implications for relatives of those who have been screened, health professionals should explain why the information should be communicated to other family members. **We recommend that in such circumstances health professionals should seek to persuade individuals, if persuasion should be necessary, to allow the disclosure of relevant genetic information to other family members.** They should also seek to ensure that treatment, counselling and other appropriate support are made available to those to whom such unsought information is disclosed.

5.42 We note that both the law and professional guidelines provide for exceptional circumstances, when an individual cannot be persuaded to inform family members with a legitimate right to know. In such exceptional circumstances the individual's desire for confidentiality may be overridden. The decision can only be made case by case. **We recommend that the appropriate professional bodies prepare guidelines to help with these difficult decisions.**

5.43 **We recommend that the Department of Health should consider with health authorities and the appropriate professional bodies effective arrangements for the preservation of confidentiality, particularly in relation to genetic registers, and should issue the necessary guidance.**

Chapter 6

Employment

Introduction

6.1 The possibility that genetic information could be used in the context of the employment relationship has been recognised for some time. In 1938 J B S Haldane wrote:

> "The majority of potters do not die of bronchitis. It is quite possible that if we really understood the causation of this disease we should find out that only a fraction of potters are of a constitution which renders them liable to it. If so, we could eliminate potters' bronchitis by regulating entrants into the potters' industry who are congenitally exposed to it."[1]

6.2 It has been pointed out that Haldane's reasoning could be extended : if individual genetic variation is a significant contributor to the incidence of workplace disease, and if people could be identified and steered away from workplaces in which they were particularly susceptible to exposures, then the overall burden of occupational disease could be diminished.[2] At the present time there are few work related hazards known to have a genetic origin, though there are some; alpha-1-antitrypsin deficiency in a polluted environment is an example. The position may, however, change in the future as scientific developments help more clearly to identify a larger number of diseases which are affected by a particular workplace environment.

6.3 Employers, in addition to identifying employees who may be exposed to any particular risk arising from a particular employment, may also wish to use genetic screening to exclude people who might be at risk of non-occupational diseases, which are likely to develop regardless of the working environment of the individual in question. Although the onset of the disease may not be caused by or exacerbated by the workplace, the development of the disease may have implications for the manner in which the work is done, and possibly also the safety of the workplace for the individual concerned as well as for fellow employees and other third parties.

Possible reasons for genetic testing in employment

Employers' interests

6.4 Many employers already request a medical examination before granting employment, and there are reasons why an employer might wish to use genetic tests for occupational diseases, or might wish to have access to genetic information about other diseases which may have implications for the employment relationship. Competition drives employers to take advantage of opportunities to reduce costs and improve efficiency. They might thus be concerned to exclude employees or job applicants who could be identified as being at an increased risk of developing a work related illness or an illness which will impair work performance. Healthy workers cost less : they are less often absent through illness, there are lower costs for hiring temporary replacements or for training permanent replacements, and there are fewer precautions which would need to be taken to deal with health and safety risks.

6.5 Market forces and the drive for economic efficiency do not, however, provide an adequate justifation for any behaviour which is ethically unsound. Ethical standards are not determined only by economic considerations, which although clearly relevant, must be balanced against the needs of others as well as of the community as a whole. Businesses are constrained by a wide range of restrictions which may be thought to impede efficiency; those seek to protect employees, consumers and in some cases the environment from the misuse of corporate power.

Employees' interests

6.6 There are good reasons why genetic screening could be in employees' interests. It would enable employees to assess their own susceptibility to occupational disease, permitting them to make free and informed choices concerning the type of employment undertaken, while giving due consideration to personal health and safety. Employees would, in principle, be empowered to avoid occupations which would increase the risk of ill health and which in the long run might be life threatening. In this way they could protect the economic security of themselves and their families. It would also help to provide employers with information necessary for the protection of employees by indicating who needed the protection of special health and safety measures to safeguard against the increased danger of ill health.

6.7 There are also foreseeable circumstances in which genetic screening might prejudice the interests of employees. It could operate to restrict job opportunities to those who, with few employment prospects, or for personal reasons, were prepared to assume the risk of ill health. It could provide a convenient excuse for employers to refuse either to take the reasonable steps necessary to accommodate those at higher risk or to employ certain categories of people able to work normally for an indefinite period. Moreover, there would be no obvious benefit to those employees who might be excluded because of a non-occupational genetic risk. The use of genetic information in these cases would serve only to reduce the opportunities of people with genetic risks which are not occupationally related and for whom the use of genetic information by employers is likely to have few, if any, advantages.

The public interest

6.8 Apart from the private interests of employers in genetic screening or testing, there may also be a public interest in this issue. Screening might in principle lead to a reduction in the incidence of occupational disease. This, if it became feasible, might in turn lead to a reduction in the burden both on the health care system in terms of treatment and also on the social welfare system. On the other hand, if some people were, in the future, entirely excluded from the labour market as a result of genetic screening, the Government would need to review their position, taking into account experience of employment policy and the disabled.

6.9 It is already accepted that people with certain diseases may be debarred from certain occupations. For example, sufferers from epilepsy cannot obtain an HGV licence. Genetic screening may make it possible in the future to identify individuals with a high risk of developing late onset serious conditions. There would be a public interest in such results only if the individual concerned both was in an occupation that put third parties at risk and also was at risk for a condition with a sudden and unpredictable onset.

6.10 But the public interest is not solely concerned with potential benefits. There is the danger that genetic screening could lead to discrimination against those with a genetic disease. Such discrimination could be based on fear, prejudice and misunderstanding or other irrational grounds unrelated to the needs of the employer, leading to the possibility of widespread genetic discrimination, with its attendant social and economic costs. There is in this country no legal protection against genetic discrimination. In some cases, as we shall consider, it may be possible to argue that any such discrimination would be unlawful

under either or both the Sex Discrimination Act 1975 or the Race Relations Act 1976. Discrimination on grounds other than those expressly forbidden by these Acts may well also be against the public interest.

The legal framework

6.11 There would be no specific legal regulation of genetic screening by employers in this country, if it were to be introduced. The position would therefore be governed by the general principles of employment law as they currently exist. Any screening might properly be seen in the general context of the employer's duty to provide a safe place of work, although employers would appear not yet to be required to screen for genetic disease in order to comply with their legal obligations in this field. Employers on the other hand would not be prohibited from undertaking such screening programmes and questions would then arise as to the refusal to employ people as a result of the screening. Questions would also arise if people were dismissed or relocated to other work if screening were introduced after the employment relationship had started.

6.12 There are very few direct legal restrictions on employers' hiring policies in British law. Subject to statutory provisions such as the Sex Discrimination Act 1975 and the Race Relations Act 1976, it would be lawful to require job applicants to agree to genetic screening and to refuse to employ people who refuse. As a general rule it would also be lawful to refuse to employ someone because of the employer's concern about the results of the screening. An employer is not under a duty to give reasons for refusing to employ a job applicant, though under the Access to Medical Reports Act 1988 an employee may have a right of access to a medical report sought in connection with the employment.

6.13 Possible sources of legal protection for job applicants are the Sex Discrimination Act 1975 and the Race Relations Act 1976. In both cases discrimination is defined to include direct discrimination and indirect discrimination. It would be unlawful direct discrimination (on the grounds of less favourable treatment) for an employer to require members of one sex only or one ethnic group only to be screened. It might also be unlawful indirect discrimination (conduct which appears non-discriminatory in principle but which is discriminatory in practice) for an employer to screen for conditions which are confined wholly or mainly to the members of one sex or one racial group. A good example of this might be sickle cell disease, the screening for which may be unlawful

because of its discriminatory impact, unless it can be shown to be justified in the interests of the business.

6.14 The position would be different where the employer introduces genetic screening and applies it to existing employees. One question which would arise is whether the dismissal of an employee following the introduction of screening would be unfair under the terms of the Employment Protection (Consolidation) Act 1978, Part V in the case of those employees who are still protected by the legislation (and many are not). Problems could arise in two quite different situations, one where the employee refuses to participate in the screening programme, and the other where questions have arisen about the results in those cases where the employee has agreed to participate in the programme. There is no clear answer to the question of whether dismissal in either case would be fair or unfair. Much would depend upon the employer's reasons for dismissing the employee and the manner and circumstances of the dismissal. Potentially also relevant would be attempts made by the employer to secure alternative work for the employee. The discrimination legislation discussed in the previous paragraph may be relevant in the context of dismissal as well as in the context of hiring.

The practice of genetic screening in employment

The position in the UK

6.15 Despite extensive enquiries, the Working Party has been unable to identify any employer, with the sole exception of HM Forces, that requires employees or job applicants to undergo genetic testing. From this we could conclude that despite the availability, albeit limited, of genetic screening, employers have so far decided that it is not necessary or in their interests. This is in itself significant. It is perhaps also significant that employers have not been compelled to introduce such testing as a result of pressure from insurance companies who provide liability insurance for employers. Some employers now screen for a variety of other conditions, such as drugs, alcohol and HIV.

6.16 In the one genetic screening programme currently in use by a UK employer, those who apply to join occupational categories of HM Forces which involve exposure to atypical atmospheric conditions undergo sickle cell screening. An example is aviation. Candidates who are carriers of the sickle cell gene are considered to be unfit for duty in such occupational categories. They may,

however, be accepted for other duties. This is primarily because of the risk of sickling on exposure to reduced atmospheric pressure or hypoxia. (Sickling is a change in the shape of the red blood cells which can lead to blockage of blood vessels.) Candidates with sickle cell disease are considered to be unfit for any form of service. This screening process is not part of a NATO-wide programme although other NATO Forces undertake sickle cell screening and may have different policies on acceptability.

The position in the USA

6.17 In the United States, where health insurance is usually provided by the employer, genetic screening of employees has more serious implications. Employers who provide health insurance may seek to avoid hiring people who may be sources of higher medical bills. The health of both the employee and the employee's family may be at issue. There is also the danger that employees with health coverage may find it impossible to change employment without losing insurance cover in whole or in part. A family's life may be restricted by the necessity for a parent of a child with a genetic disorder to maintain employment in the same state and at the same job in order to have health insurance.

6.18 In 1982 the US Congressional Office of Technology Assessment (OTA) conducted a survey to determine the extent of genetic screening in the workplace.[3] Confidential questionnaires were sent to the 500 largest US industrial companies, the 50 largest private utility companies, and 11 major unions that represent the largest numbers of employees in those companies. Of the 366 organisations responding, 6 were currently conducting genetic testing, 17 used some of the tests in the past 12 years, 4 expected to use the tests in the next 5 years, and 55 stated that they would possibly use the tests in the next 5 years. These results were widely construed to suggest that genetic screening by employers was likely to increase dramatically.

6.19 The OTA conducted a further survey in 1989[4] which demonstrated that no such increase had in fact occurred. Using a similar base of large industrial companies, private utilities and unions, the survey found 12 companies currently using genetic screening tests and 8 that had used them in the past 19 years. Companies were also asked if they expected to conduct such tests in the next 5 years : biochemical genetic tests and direct DNA tests were asked about separately. Four companies answered yes about biochemical genetic screening, 25 were unsure, and 218 said no. No company expected to use direct DNA testing, 23 were unsure, and 224 said no. The available evidence suggests

that at the present time there is no major demand for the genetic testing of employees, though the possibility of more widespread use in the future should not be ruled out.

Ethical issues

6.20 In our view people should be excluded from employment opportunities only where this is shown to be absolutely necessary. We see no reason why people should be required by employers to undergo genetic screening unless the illness or condition will present a serious danger to third parties. Where the concern is limited to the health of the employee, it should be a matter for the individual employee to decide whether or not to participate in the screening programme. Where an individual does participate in a screening programme, we accept that a responsible employer may not wish to employ someone disclosed to be at risk of a condition, particularly if its onset is unpredictable, that might imperil the employee or third parties. But even here steps would have to be taken to ensure that individuals were not unfairly treated and that there were in place, through agencies such as the Employment Services' Placing Assessment and Counselling Teams (PACTs), procedures to assist the individual and to facilitate his or her employment in other areas.

6.21 So far as existing genetic information is concerned, this should not normally be used to exclude people from employment unless the condition had developed so as to impair efficient performance in the job. It would be particularly inappropriate to rely on this information where the risk of disease was misunderstood by the employer or where the risk did not lead to the onset of the disease. In relation to screening for late onset genetic disorders (for example, Huntington's disease) it is important for all involved to recognise that the genetic defect is detectable from birth, but that the individual is only likely to develop the actual disease from a relatively late age, being healthy for most of his or her life. We do not overlook the likelihood for some people that a disabling disease may develop in the future. But it would be possible at that stage for an employer to transfer the employee to other work. There is a legal requirement for employers to ensure that 3% of the workforce are registered disabled.[5] It should only rarely be necessary to dismiss such an employee. We have no information at present about any employment discrimination against people in this category, but we are concerned that discrimination could occur if genetic information had to be disclosed on job application forms, or could properly be made available to employers who seek medical reports about potential employees.

6.22 There is clearly a need to strike a balance which takes into account the competing interests in this area. We are concerned to ensure that nothing should be done to undermine the employer's ultimate responsibility to provide a safe working environment. Genetic screening should not be an excuse for cutting costs on health and safety standards, nor should it become a justification for excluding people from the labour market. Indeed in view of the sensitive issues raised, it is open to question whether the decision to introduce a screening programme ought properly to be that of the employer alone. It may be appropriate that such a programme should be implemented only in consultation with workplace representatives, with the coordinating body proposed in paragraph 9.7 and possibly also only with the approval of the Health and Safety Commission.[6]

6.23 Subject to this prior consultation and authorisation, genetic screening of a workforce for increased occupational risks ought to be contemplated in our view only where:-

(i) there is strong evidence of a clear connection between the working environment and the development of the condition for which the screening is conducted;

(ii) the condition in question is one which seriously endangers the health of the employee or is one in which an affected employee is likely to present a serious danger to third parties;

(iii) the condition is one for which the dangers cannot be eliminated or significantly reduced by reasonable measures taken by the employer to modify or respond to the environmental risks.

But although it may be appropriate to introduce a screening programme on these limited grounds, it should only be done if accompanied by safeguards for the employee, as indicated in paragraph 6.20.

A need for further legal provision?

6.24 Under the law as it presently stands, employers may introduce genetic screening, and may require potential employees to be screened as a condition of employment. There are no pre-conditions to be satisfied before a screening programme is introduced, and there are no safeguards against misuse or abuse where such a programme is introduced. The absence of specific

legal regulation does not appear to be peculiar to this country, though there are a number of jurisdictions where there is more direct legal intervention.

Legal regulation elsewhere

6.25 In Europe draft legislation has been introduced in Denmark which would prohibit an employer from demanding or making use of a genetic test at the time of appointment or at a subsequent stage.[7] This would be subject to a proviso to permit the Minister of Labour to authorise genetic tests for "any disorders which might jeopardise other people in the relevant function or job." Rather different forms of regulation in a number of jurisdictions in the United States prohibit discrimination in employment on the basis of one or more genetic traits. Florida, Louisiana, and North Carolina prohibit discrimination based on sickle cell trait, the prohibition in the last case extending also to haemoglobin C. New Jersey goes further in prohibiting discrimination on the additional grounds of carrier states for thalassaemia, Tay-Sachs disease and cystic fibrosis.[8]

Legal Intervention in Britain?

6.26 In the light of our comments about the circumstances in which genetic screening ought properly to be conducted in this country, and in the light also of the lack of any regulation of the practice, the question arises as to whether it would be appropriate to introduce legislation such as that now in draft in Denmark or provided in some of the states of the USA. We are reluctant to recommend any initiative at this stage because of the lack of evidence which we have been able to uncover about the systematic use of genetic screening programmes by employers in this country. Still less is there evidence of any systematic abuse by employers.

Conclusions and recommendations

6.27 At present, the use of genetic screening by employers in the UK does not appear to be a cause for concern. We have found evidence of only one existing screening programme : that programme can be justified quite readily on the grounds of safety, not only of those being screened but also of third parties. Nevertheless we recognise that the matter needs to be kept under review. **We recommend that the Department of Employment keeps under review the potential use of genetic screening by employers.**

6.28 Subject to prior consultation with workplace representatives, and with, as necessary, the Health and Safety Commission, **we recommend that genetic screening of employees for increased occupational risks ought only to be contemplated where:-**

(i) there is strong evidence of a clear connection between the working environment and the development of the condition for which genetic screening can be conducted;

(ii) the condition in question is one which seriously endangers the health of the employee or is one in which an affected employee is likely to present a serious danger to third parties;

(iii) the condition is one for which the dangers cannot be eliminated or significantly reduced by reasonable measures taken by the employer to modify or respond to the environmental risks.

Although it may be appropriate to introduce a genetic screening programme on these limited grounds, it should only be done if accompanied by safeguards for the employee, and after consultation with the coordinating body recommended in paragraph 9.7.

Chapter 7

Insurance

Introduction

7.1 The subject of genetic screening in relation to insurance is not new. In 1935 R A Fisher addressed the International Congress of Life Assurance Medicine on the topic, noting that "linkage groups should be sorted out, in order to trace the inheritance and predict the occurrence of other factors of greater individual importance, such as those producing insanity, various forms of mental deficiency, and other transmissible diseases."[1] However, it is only during the past few years that molecular techniques have provided the opportunity to realise this goal. We are now seeing rapidly increasing numbers of serious disease-causing genes mapped and isolated, with a corresponding ability to predict or exclude their presence in family members at risk and in the general population.

7.2 At present, much of our experience of the insurance-related ethical issues comes from Huntington's disease. This dominantly inherited disease is rare (affecting less than 1 person in 10,000), of late onset and can be predicted with a high level of certainty. Nevertheless, many of the issues it raises also apply to other diseases which may have a genetic basis.

7.3 Insurance is unlikely to create any new ethical issues in connection with genetic disorders whose symptoms are already manifest at the time of application. Standard insurance proposal forms have for many years asked about recent medical treatment as well as relevant elements of family history. Insurance companies already require applicants to give consent to the companies' access to medical records. These records may now, and will increasingly in the future, include the results of genetic screening. New ethical issues are most likely to arise as testing for late onset disorders becomes more widespread, and as genetic screening increasingly identifies individuals with a predisposition to develop certain diseases, though they will not necessarily know of any relevant family history.

7.4 As this report has emphasised, a genetic predisposition to disease is not always an indication of future ill health. The probability that a disease will develop can vary greatly. It may also be very difficult to predict for any given individual the age at which a disease is likely to become manifest. Any prediction is further complicated by the fact that environmental factors often play a major role in many late-onset diseases. Thus, in some cases it will be particularly difficult, if not impossible, for insurance companies to calculate the chance of an individual developing a disease, especially when little is known about its cause, and where statistical information is limited. Huntington's disease, for example, lies at the extreme end of a spectrum. It is a dominantly inherited disease where there is a high level of probability that those having the defective gene will develop the disease. On the other hand, in familial hypercholesterolaemia, another dominantly inherited disease, by no means all of those with the gene will develop coronary heart disease at an early age, and environmental factors such as diet, smoking and exercise may play a major part.

7.5 Although the treatment of some genetic disorders (for example, cystic fibrosis) may increase their frequency in later life, treatment of others (for example, phenylketonuria) has removed the associated disability, while the birth incidence of many other genetic disorders amenable to genetic testing (for example, thalassaemia and Tay-Sachs disease) is falling. This is occurring because significant numbers of families have used the information made available by these tests to avoid the birth of affected children. Thus the introduction of genetic screening may actually decrease the burden to insurance companies; a factor that needs to be taken into account by the insurance industry. It is likely that in the future, as genetic screening becomes more widespread, such a reduction will continue. But this depends on encouraging the acceptance of genetic screening. This will not occur if families are penalised in insurance matters.

Life insurance and health insurance

7.6 Insurance of all types is based on the complementary principles of solidarity and equity in the face of uncertain risks. In insurance, solidarity has been taken to imply the sharing by the population, as a whole or in broad groups, of benefits and costs; while equity has been taken to imply that the contribution of individuals should be approximately in line with their known level of risk.

7.7 Life insurance and health insurance are the two forms of insurance to which genetic screening is most relevant. Their relative importance varies between different societies. In the UK, where only a minority of individuals currently depend on private health insurance, health insurance is less important than in countries such as the USA, where it is the principal means of paying for health care and, increasingly, has become employer based. In the future, the largely American concern with health insurance in relation to genetic testing may need to be taken into account in the UK, but the need for this consideration would become serious **only if** there should ever be a major shift in the balance of health care costs from the public to the private sector.

7.8 For most people in the UK, life insurance is normally linked to home purchase and the covering of basic family responsibilities. It is therefore of great importance to individuals that they are not excluded from life insurance, and it is to this form of insurance that genetic screening has most relevance. The issue goes wider than the concerns of individuals. If large groups of people categorised by genetic conditions were to become effectively excluded from life insurance, then there would be serious consequences for public policy (including, possibly, for social security).

Different viewpoints

7.9 Those applying for insurance, the insurance companies, and professionals in medical genetics, see the issues raised by genetic screening from different perspectives. Each group has valid concerns.

The applicant's viewpoint

7.10 Applicants are likely to have the following concerns:-

(i) pressure to be screened for genetic risk when seeking to obtain basic life and health insurance;

(ii) demands for disclosure of existing test results;

(iii) refusal of cover or premium increases out of proportion with the risk detected; and

(iv) fear of possible divulgence of test results to third parties.

7.11 **Pressure to undergo genetic testing** when seeking to obtain insurance is an important issue. It is difficult to assess in the UK the degree to which it is currently affecting individuals' decisions to undergo screening or how it might do so in the future.

7.12 The **need to disclose results** of genetic tests that are being or have been done for reasons entirely unrelated to insurance is an issue of great concern. This would particularly be the case in population screening programmes where there is no specific family history. There is the fear that such disclosure, whether by the individuals concerned or their doctors, would make insurance difficult or even impossible to obtain.

7.13 A further concern is that insurance might be prejudiced by **misinterpretation** of the finding of a harmless carrier state, for example of the cystic fibrosis gene, or by **uncertainty** regarding the significance of the results.

7.14 The **storage of genetic information on databases** that may be shared by a number of insurers is another important issue. There is also the fear that such information might reach employers and others.

The insurers' viewpoint

7.15 The insurance companies' main concerns are summarised as follows:-

(i) adverse selection, especially when large sums are insured;

(ii) competition between companies; and

(iii) the avoidance of unnecessary discrimination and of consequent adverse public opinion.

7.16 **Adverse selection** is the foundation of all the fears that insurance companies have in relation to genetic testing. The term relates to the essentially unfair position faced by the insurance company if the applicant is in possession of relevant information that the company does not have, such as the result of a genetic test. Adverse selection is particularly feared by insurance companies when the policy is for an unusually large sum, a situation already experienced in relation to HIV infection.

7.17 **Commercial competitiveness** in the insurance industry is intense. Access to the results of genetic screening would be in the insurers' interests as it would enable them to refuse cover, or raise the premiums, of individuals found to be at increased risk. This would in turn enable insurers to offer cover at a lower premium to individuals thought to be at low risk. There is the understandable fear that if one company does not use genetic testing, but its competitors do, the company would lose custom from those shown to be at low risk, while carrying the increased burden of those with an undisclosed high risk. Equally however, companies wish to avoid unnecessary testing, partly on the grounds of medical and administrative work, but also to avoid losing customers.

7.18 As far as the **avoidance of unnecessary discrimination** is concerned, the Association of British Insurers emphasises that over 95% of life insurance policies are obtained at standard premium rate, while less than 1% of proposals are declined due to the mortality risk being too high.[2] The concern is that the widespread use of genetic testing might sharply alter this balance.

The health professionals' viewpoint

7.19 Most health professionals share the applicants' concerns, since undue pressure to be screened, inappropriate demands for disclosure of test results, the misinterpretation of results and the breaking of confidentiality all run counter to established ethical practice.

7.20 The new element that is introduced by genetic screening is that programmes of benefit to individuals, families and society may be hampered by fears relating to insurance. For example, genetic screening may identify individuals who are predisposed to late-onset diseases which are treatable or avoidable, such as familial colon or breast cancer. It is important that such individuals do not deny themselves the benefits of genetic screening because of concerns about insurance.

7.21 Professionals are particularly concerned that the results of genetic testing might be misinterpreted by insurers, with healthy carriers in some cases denied coverage, as happened previously with sickle cell testing in the USA.[3] The opportunity for such misinterpretation is likely to increase with testing for greater numbers of disorders, often rare and unfamiliar. The consequences of denial of health insurance may be immense in countries, such as the United States, without a comprehensive

national system of health care; these may also extend to loss of employment, since the majority of health insurance systems are employment based.

Current Practice

7.22 The insurers' current practice in dealing with applications is to ask for medical details, including family history, then to ask for the individual's permission for a medical report and examination and for the results of any tests that have been done previously.

7.23 Our understanding of the way in which insurers treat information on family history suggests that there is unlikely to be a major difference between declaring a family history and declaring that the gene is actually present. Tables used by the insurance industry show that insurers treat a 5% risk of developing Huntington's disease in the same way as a 50% risk : such individuals may be declined insurance or offered insurance at an increased premium, depending on their age at the time of application. Insurance prospects for individuals with a family history of Huntington's disease only improve when the risk is below 5%.

7.24 The Association of British Insurers (ABI) in their submission to us stated their position clearly (a comparable position has been taken by insurance companies in the USA):-

> "From the point of view of insurers, genetic diseases can be divided into two main groups. The first is the known genetic diseases such as Huntington's disease, cystic fibrosis or Duchenne muscular dystrophy, for which specific tests are already in use. In these cases the insurance industry already has experience of individuals who have had a genetic test because of a medical history and insurers treat the results of such tests in exactly the same way as the results of any other medical test."
>
> "The UK insurance industry does not intend to ask proposers for life insurance to undergo screening for genetic information within the foreseeable future, but where individuals have had a specific genetic test as part of their medical assessment these tests will fall into the same category as other medical tests and will need to be declared on proposal forms."

7.25 According to the ABI's position it would seem that there is a clear duty for individuals and their doctors to disclose the results of any genetic test. It could be questioned, however, whether tests carried out in the context of genetic counselling should be regarded as part of 'medical assessment'; such assessment would be expected to involve only those tests relating to past or family history of disease or current illness.

Resolving the ethical issues

7.26 It is important that the concerns of applicants, insurers and health professionals be reconciled in such a way that the principles of consent and confidentiality are maintained while at the same time balancing the principles of solidarity and equity. An appropriate balance has also to be found between the public health benefits of genetic screening, the ethical concerns of individuals and the principles of solidarity and equity.

7.27 At present, genetic screening or testing is most likely to occur in families with a known risk. Where an individual is aware of a family history of a genetic disorder, good faith on the part of both applicants and insurers requires that this information be declared on insurance proposal forms. Insurers already take into account the risk as determined by the family history when deciding whether to insure and at what premium. As insurers interpret this information cautiously, there is unlikely to be a major difference in insurability between an individual with a family history of a genetic disorder and an individual who has had a positive genetic test result.

7.28 If the individual who has a family history of a genetic disorder chooses to have a genetic test and it is positive, we suggest that this result, with the specific consent of the proposer, may be made available to the insurer, but that the insurance decision based on the family history should not be changed. Thus premiums would be the same for individuals who have tested positive for a genetic disorder as for those who have declared a family history but have not had a genetic test.

7.29 For those with a negative (ie normal) test result, however, we would expect them to benefit from this information and be granted premiums similar to those without a family history. In this way we hope that applicants will not be deterred by fears relating to insurance from having genetic tests and that insurers, by continuing their present practice based on family history, will not be adversely affected. Both parties should indeed benefit. For example, if there is a family history of Huntington's disease, an

individual may find it impossible to get insurance; if genetic testing is positive, and the result declared, the situation for both parties does not alter. But, if the test is negative, the applicant can be insured and the insurer gets a new customer. If this principle can be accepted, there will be no need for insurers to ask for genetic testing, and the freedom of individuals to decide whether or not to be tested will not be hampered by insurance considerations.

7.30 Population screening raises quite different ethical issues, as the majority of individuals participating in such programmes would be unaware of any family history of the disease being screened for. In addition, according to the principles laid out at the beginning of this report (paragraph 3.9), such screening is likely to be offered only if something can be done to reduce the risk following a positive result. The presence of an abnormal gene for a recessive disorder, for example cystic fibrosis, has no effect on the health of the individual concerned. It is not therefore relevant to life insurance companies to be informed about the results of carrier screening for recessive disorders.

7.31 If insurers were to demand access to the results of population screening for polygenic or multifactorial disease (for example, for genetic predisposition to breast cancer), and premiums were increased for those who tested positive, many people would clearly be discouraged from participating in such programmes. This could have adverse consequences both for the health of individuals and for the public health.

7.32 At present, we have no experience of such discrimination by insurers and indeed their statement indicates they currently have no intention of requesting any genetic testing before insurance. We suggest therefore that, at least for the present and until we have more experience of screening programmes, individuals should not be required to disclose the results of population screening tests when applying for life policies for reasonable sums. This would parallel the moratorium agreed in 1990 by the insurance companies in the Netherlands to run for a trial period of five years.

7.33 For unusually large sums, however, insurers should have the right to ask for results of all tests. The exact sums would need to be discussed with the insurance industry and take into account matters such as housing costs. A feature of the moratorium in the Netherlands is that only for sums over the equivalent of £65,000 (200,000 guilders) should genetic screening results be declared.

7.34 If insurance companies are to have access to the results of genetic tests, they must have the ability:-

(i) to interpret the risk accurately if undue discrimination is to be avoided;

(ii) to ensure the absolute confidentiality of all genetic test results, because of the concern that interested third parties, such as employers, might gain access to genetic information disclosed to insurance companies.

7.35 We consider that the principle of free and informed consent should not be compromised by insurance considerations. Therefore, genetic testing should **not** be made a prerequisite of obtaining insurance.

Conclusions and recommendations

7.36 Our recommendations about the use of genetic screening and genetic tests by insurance companies follow from the following considerations:-

(i) the difficulty of assessing what may be slender evidence on the genetic susceptibility of individuals to develop polygenic and multifactorial diseases (for example, some cancers and some heart disease);

(ii) an awareness that ordinary commercial practice will lead companies to be over-cautious in their assessment of the risks derived from medical data; and

(iii) the possibility of abuses.

7.37 **We recommend that British insurance companies should adhere to their current policy of not requiring any genetic tests as a prerequisite of obtaining insurance.**

7.38 In the light of the arguments summarised in paragraph 7.36, **we recommend that there should be early discussions between the Government and the British insurance industry about the future use of genetic data, and that pending the outcome, the companies should accept a temporary moratorium on requiring the disclosure of genetic data.** There should, however, be two exceptions:-

(i) first, in the case of those individuals where there is a known family history of genetic disease that can be established by the conventional questions about proposers' families, then individuals may be asked to disclose the results of any relevant genetic tests (see paragraph 7.28); and

(ii) the moratorium should apply only to policies of moderate size. The limit would be a matter to be settled between the Government and the industry in the context of arranging the moratorium.

The importance of the discussions that are recommended is highlighted by the considerations set out in paragraphs 7.7 and 7.8.

Chapter 8

Genetic screening and public policy

8.1 By their nature, most genetic screening programmes involve large numbers of people. This is so even for programmes limited to defined groups of the population which may be at risk of developing a serious disease or transmitting it to the next generation. We have therefore attempted to assess the present level of understanding of the science of genetics and its significance for the health of individuals, as well as the potential for improving public health.

8.2 Such evidence as there is suggests that there is widespread misunderstanding of the mechanism of inheritance, in particular of the importance of recessive genes and carrier status. Much ignorance about how genetic diseases are transmitted is mixed up with notions about the inheritance of physical characteristics, such as height, eye colour etc. Genetics can be confused with eugenics (see paragraph 8.16), and there are concerns about possible stigmatisation which may or may not have a basis in fact.

8.3 A broad public understanding of the scientific basis of medical genetics is essential if informed public policy decisions are to be taken about the introduction of genetic screening programmes. Such programmes, as we have emphasised throughout our report, have both an individual and a public dimension.

Public understanding of genetics

8.4 If an individual is to be well enough informed to be able to give consent to genetic screening, he or she needs to have some general understanding of genetics. This means that the public as a whole needs to have a greater knowledge and awareness of the genetic processes that can affect us all.

8.5 Some relevant teaching about human genetics is included in the National Curriculum for 14 to 16 year olds under **Life and Living Processes**:-

> "[Pupils] should consider the interaction of genetic and environmental factors (including radiation) in variation. They should be introduced to the gene as a section of a DNA molecule and study how DNA is able to replicate itself and control protein synthesis by means of a base code. Using the concept of the gene, they should explore the basic principles of inheritance of how sex is determined in human beings and how some diseases can be inherited."

8.6 Teaching of the principal modes of inheritance is particularly important. This knowledge is needed to understand most genetic disorders; and, since it conveys the message that all healthy people can carry genes which are abnormal but which only rarely result in disease, it may help to prevent misinformation and prejudice. It may be helpful for people to know that most healthy carriers of genes for recessively inherited disorders will have no family history of that disease. If there are to be screening programmes for recessively inherited conditions, the public must have some knowledge of the recessive mode of inheritance and, most particularly, the meaning of being a 'healthy carrier'.

8.7 Accurate information on genetics and genetic disease should be available both for the public and for health workers. This should include general information about reproductive risks and specific material for individual disorders appropriate for particular screening programmes. A wide range of educational aids about genetic screening is required. We hope that the Department of Health will take the lead in addressing the different sections of the community, enlisting the media to help with the task. Appropriate voluntary bodies can also help; we have noted that in the Department of Health's recently (June 1993) issued outline guide **Population Needs and Genetic Services**[1] it is stated that:-

> "voluntary bodies, by virtue of the special experiences and knowledge of their members, and the sources of expert advice available to them, have important roles in providing information and giving support to individuals and their families."

What are the dangers of stigmatisation?

8.8 Stigmatisation has been defined as 'branding, marking, or discrediting because of a particular characteristic.' It has been suggested that genetic screening could lead to stigmatisation of carriers.

8.9 Concern has been expressed that routine screening for carriers of a genetic disorder might be viewed as a tacit requirement that the birth of children with handicapping genetic conditions should be avoided. Stigmatisation of carriers is likely to focus on beliefs that it is irresponsible and immoral for people to have children who could transmit disability to them.

8.10 There have always been some negative social reactions to disability in all its forms. These social reactions can be related to conflicting feelings, for example not knowing how to talk to parents or people with a specific problem, fear of creating offence by being healthy, a consciousness of good fortune because one does not have a similar problem and has no idea how one would cope if one had. There is a fear that a known genetic cause of handicap could add to social isolation, because, due to prevailing ignorance of genetics, people are inclined to feel that inherited disorders affect only a few families, and fortunately 'this could **not** affect me'.

8.11 It has been argued that the availability of prenatal screening and diagnosis, together with the termination of seriously affected pregnancies, both reflect and reinforce the negative attitudes of our society towards those with disabilities. Indeed medical genetics may add a new dimension if genetic disorder came to be seen as a matter of choice rather than of fate. On the one hand, there is an effort to create an environment in which people with a disability are accepted into society and seen as having a worthwhile life; for example, integration into mainstream schooling and changes in the language used to describe people with disabilities. At the same time as encouraging a more positive environment for people with severe disabilities, resources are spent on preventing their births. Given the option of prenatal diagnosis and abortion of affected fetuses, some parents may feel that to produce a child with a potentially diagnosable disability is to be blameworthy for that child's birth.

8.12 It has been further suggested that an emphasis on genetic differences between ethnic groups could increase social differences and discrimination. Ethnic groups with a high prevalence of genetic disorders might be additionally stigmatised. Members of an ethnic group may feel stigmatised, although other communities do not in fact attach stigma to that group.

Evidence on stigmatisation as a result of genetic screening

8.13 We have noted the unhappy consequences of the introduction of sickle cell screening programmes in the USA during the 1970s. A study by the Office of Technology Assessment of the US Congress reported :

> "Some who participated in screening programs and were found to be carriers of sickle cell trait experienced discrimination at work and from insurance companies that raised their premiums. Apparently, discrimination in the workplace sometimes occurred because it was believed that those with sickle cell trait could experience the painful episodes characteristic of sickle cell disease (which occur when sickle-shaped red blood cells occlude the normal flow of blood). The result for some job applicants was denial of employment based on their carrier status and removal for some who were already employed. In some cases, life insurance companies either raised premiums for carriers or denied coverage for applicants with sickle cell trait. At that time, laws were enacted in Florida, Louisiana, and North Carolina that prohibited such discrimination. Since the mid-1970s, many of the State laws requiring mandatory sickle cell testing have been repealed."

8.14 The lessons of that episode have been learnt by those responsible for current screening programmes. Such evidence as exists suggests that current genetic screening programmes need not result in any significant stigmatisation. A study of over 3,000 individuals in Hertfordshire looking at the psychological and social consequences of community carrier screening programme for cystic fibrosis reported that fears of possible social costs of screening may be ill-founded.[2] Carriers and non-carriers uniformly approved of screening and were glad to have been tested. Carriers told partners, siblings, relatives, and friends of their result and did not seem to feel stigmatised. A large majority (89%) told their partners. "It is very encouraging that being screened has increased awareness of CF and recessive inheritance even for those testing negative, and it is very unlikely that carrier testing will stigmatise or cause lasting psychological damage to those testing positive." Other studies have concluded that, with a few exceptions, individuals taking part in genetic screening programmes did not feel stigmatised. It should be noted that a high standard of information and counselling was provided in all of these studies. The Fragile X Society stated in its submission to us that "no family has said that it has experienced this (stigmatisation) as a problem; on the contrary, many have found that they and others have found their children

easier to accept and deal with once they have an explanation for their problem."

How can stigmatisation be avoided?

8.15 The dangers of stigmatisation have sometimes been outlined, for the most part, in general and **hypothetical** terms. Proper educational programmes should reduce those dangers. At the same time the quality and extent of education and counselling provided should have a major effect on the extent of stigmatisation perceived by individuals. A well-informed individual is less likely to feel stigmatised than a poorly-informed individual who has received little or no counselling. Indeed, it could be argued that, if we all found out our genetic variations, then there would be less concern about stigma. It is estimated that we all carry mutations for at least one serious recessive disorder and when "everyone realises that he or she is a carrier there can be no stigma."[3]

Limiting the improper use of genetic screening : the legacy of the eugenics movement

8.16 Eugenics is the doctrine which claims that it is possible and desirable, through selective breeding and the elimination of undesirable individuals, to alter the hereditary qualities of a race or population. It thus aims to improve the qualities of the species rather than of an individual. Some societies and governments have attempted to apply this doctrine in practice. The most notable example was provided by the Nazi party in Germany, which supported human geneticists in their eugenic research in return for practical support for the party's race policies.

Eugenics and other societies

8.17 Many societies have been influenced by eugenic doctrines. Thus, for example, early in the century certain legislatures in the United States sought to control social characteristics such as degeneracy, drunkenness, unemployment, criminality, prostitution and alcoholism through a targeted sterilisation policy, combined with restrictive immigration laws. In the 1930s, the Canadian provinces of Alberta and British Columbia passed legislation which permitted the sterilisation of mentally ill persons without their consent. The legislation remained in force in both provinces until 1972.

8.18 The UK has differed in this respect in that no legislation has ever existed to carry forward the eugenics doctrine, although there has been in the past scientific, political and even ecclesiastical support for the ideas reflected in the doctrine.

8.19 Eugenics is often regarded as a subject that belongs to the past, at least in democratic societies, but recent developments in genetic technology have understandably raised fears among the public and professionals that these might be misused for eugenic purposes. It will continue to be important to reassure the public that genetic testing in medicine in the UK is used to help individuals and their families avoid the occurrence of serious inherited disorders or their associated complications. This is also the primary goal of those wider population-based genetic screening programmes that have so far been established.

The dangers and safeguards for our society

8.20 Large-scale genetic screening does raise issues relating to population and public health that might conflict with the interests of individuals. Any genetic screening programme set up with the specific aim of reducing the incidence of a particular disorder may come into conflict with those members of that population who do not wish to be screened. The public health definition of 'success' or 'failure' of a programme may be in danger of turning on too narrow a calculation of costs and benefits. Benefits must not be calculated in purely financial terms of preventing the birth of individuals who may have higher than average health care needs and costs. The benefits should be seen as enabling individuals to take account of the information for their own lives and empowering prospective parents to make informed choices about having children.

8.21 Genetic screening programmes for recessively-inherited diseases (for example, cystic fibrosis and thalassaemia) will have no significant effect on the frequency of the abnormal gene in the population, even though the frequency of the disease at birth may be greatly reduced; in testing for dominantly-inherited diseases, such as Huntington's disease, the gene frequency would be reduced in line with any reduction in births of those likely to develop the disease. Genetic screening in such situations could only be considered 'eugenic' in nature if the decisions of individuals were subjugated to those aims considered to be of benefit to the population or the state.

8.22 As it becomes feasible to test for the genetic basis of many common, usually polygenic or multifactorial disorders, as well as for normal characteristics, the potential for eugenic misuse of genetic testing will clearly increase. The existence of genetic registers (see paragraphs 5.32 - 5.39) requires safeguards against the potential for eugenic misuse. This makes it all the more important for society to keep genetic screening under review and, if necessary, limit misapplications at an early stage. We must ensure that neither specific individuals, nor society as a whole, are harmed by a hasty or ill-considered application of genetic testing.

Conclusions and recommendations

8.23 The threat of eugenic abuse of genetic screening requires safeguards. In a democracy, public understanding of human genetics should serve to create awareness of the dangers of eugenics, and of the possible stigmatisation of those carrying or suffering from genetic disorders. **We recommend the need for improving public understanding of human genetics should be borne in mind in any review of the National Curriculum and in the work of all public bodies concerned with the public understanding of science**.

8.24 We recognise that there are limits to the effects of educational work, however good. We, therefore, regard as essential to the safeguards against eugenic abuse our recommendations on **adequately informed consent, confidentiality** and the **central coordination and monitoring** of genetic screening programmes.

Chapter 9

Introduction and implementation of genetic screening programmes

9.1 Most existing genetic screening programmes are at the pilot stage. The population-wide screening programmes for phenylketonuria (PKU) and for rhesus blood group were introduced many years ago on a judgement of clinical utility and with encouragement from the Department of Health.

9.2 For reasons emphasised in Chapter 8, a careful review will be required of the more difficult ethical considerations arising from future genetic screening programmes that cover the whole population. By whole population we do not necessarily mean the population of the entire UK. Some programmes which have progressed beyond the pilot stage may be introduced to cover the whole of the population being screened in a particular health region or geographical location. In effect, they are being introduced into routine practice. We believe the introduction of such programmes should, however, be subject to the same stringent review. Such a review should examine for each condition for which it is proposed to screen whether:-

(i) adequate pilot studies have been undertaken. We would expect that all pilot studies would have been carried out as research procedures and as such have been examined and authorised by the appropriate local research ethical committees;

(ii) the ethical principles relating to adequate information for consent, adequate counselling and the necessary protection of confidentiality can be applied in a routine situation;

(iii) the programme will be subject to continuing evaluation; and

(iv) due attention has been paid to whether the cost of the programme will be justified by the likely gains in knowledge and experience.

9.3 We emphasise that there should be a review of screening for **each** condition. Although screening may become increasingly automated so that many conditions are screened for simultaneously, each condition needs to be separately reviewed. This is because each may give rise to particular ethical problems depending on the nature of the condition, its severity, its variability and its likely onset. One of the important variables will be the availability and success rate of treatment for those suffering from the condition; this may well change radically as medical understanding of genetic conditions advances.

9.4 We suggest that a central coordinating body should be established to undertake such reviews and should be notified of all pilot studies in progress. The reviews should result in the publication of the considerations that led to the coordinating body's decisions. In this way public understanding and public accountability can be brought to bear. The importance of such understanding and accountability has been argued in Chapter 8.

9.5 The Department of Health would appear to be the appropriate public body to decide, in consultation with the appropriate professional bodies, what form such a central coordinating body should take. In the same context the Department should take the lead in formulating the detailed criteria for introducing genetic screening programmes into routine practice. As a contribution to the discussion of such criteria, we suggest they should include the following:-

(i) the aims and purposes of the entire programme;

(ii) the predictive power and level of accuracy of the particular screening test;

(iii) the value to those being screened of the knowledge gained. For each programme this should have been researched as an integral part of the follow-up to the pilot programme;

(iv) the availability of therapy for the particular condition, accepting that lack of treatment does not necessarily mean that screening is not worthwhile;

(v) the potential social implications; and

(vi) the resource costs.

9.6 The central coordinating body should review genetic screening programmes and monitor their implementation and outcome.

Conclusion and recommendation

9.7 **We recommend that the Department of Health in consultation with the appropriate professional bodies formulate detailed criteria for introducing genetic screening programmes, and establish a central coordinating body to review genetic screening programmes and monitor their implementation and outcome.**

Chapter 10

Conclusions

10.1 We set out our conclusions against the background of the following points established earlier in the report:-

(i) screening for **some** defective genes has become a practical possibility;

(ii) medical knowledge about genetic **susceptibility** to common multifactorial conditions (for example, some heart disease and some cancers) is still developing. Even with increased medical knowledge, the individual's risk may be difficult to evaluate;

(iii) many of the ethical issues associated with genetic screening arise from the inescapable involvement of families (both blood relations and spouses);

(iv) the benefits and disadvantages of screening programmes - for individuals, families and society in general - will need to be carefully assessed for each proposed screening programme. Factors to be taken into account include:-

(a) the predictive power and accuracy of the genetic test;

(b) the benefits of informed personal choice in reproductive decisions and their consequences;

(c) the psychological impact of the outcome of screening for both individuals and families;

(d) therapeutic possibilities;

(e) possible social and economic disadvantage relating for example, to insurance and stigma; and

(f) the resource costs and the relative priority, in view of limited resources, of establishing a screening programme.

10.2 Against this background our recommendations fall under six main headings. In making these recommendations we are conscious that no-one can lay down fixed and immutable guidelines for the future of genetic screening. Medical and scientific knowledge is developing rapidly : some of that development may alter the shape and the nature of some of the ethical issues discussed in this report. Nevertheless, certain ethical principles will remain unchanged and certain ethical responses will be required from the health professions, from health administrators, from the insurance industry, from employers and from Government.

What is not covered in this report

10.3 We emphasise once more that this report has covered genetic screening for **serious disease**. (We have explained our views on what constitutes serious disease in paragraph 3.10. Distinguishing between serious disease and other medical conditions would be a task that would fall naturally to the central coordinating body envisaged in paragraph 10.20.) We recognise that there is a whole area of serious concern about genetic screening for human traits that are in no sense diseases. These issues have been brought to the fore by recent controversies about gender choice, and about the so-called 'homosexuality gene'. We do not dismiss these issues. They call for discussion by professionals with skills other than those represented in our Working Party.

I : Providing information and obtaining consent

10.4 **We recommend that adequately informed consent should be a requirement for all genetic screening programmes.** The voluntary nature of the screening process must be emphasised. Adequate information must be provided for all those being invited to enter a genetic screening programme and should include information about the implications for other family members. Information for all genetic screening programmes is best delivered in both written and oral form. (Paragraph 4.29 summarising paragraphs 4.6 - 4.16)

10.5 **We recommend that counselling should be readily available for those being genetically screened, as well as for those being tested on account of a family history of a genetic disorder.** Counselling should be available at all stages of the screening process. This will require the diffusion of an understanding of genetics (at present mainly confined to genetic

counsellors) in particular among those engaged in primary health care. The resource implications, including the need to train large numbers of practice nurses and health visitors in the subject matter and the basic principles of counselling, need to be assessed within the broader context of the expansion and extension of primary care. (Paragraph 4.30 summarising paragraphs 4.17 - 4.22)

10.6 Screening of individuals who are unable to give properly informed consent (minors, the mentally ill and those with severe learning difficulties) require special safeguards (paragraphs 4.24 - 4.26).

II : The results of genetic screening and confidentiality

10.7 The family implications of genetic screening and genetic testing will sometimes require health professionals to review the application of the current principles governing the confidentiality of medical information. We have in Chapter 5 made a start at examining the implications. This work will need to be carried further by the health professional bodies responsible for producing guidelines that govern the conduct of their members as experience is gained from the screening programmes now being introduced.

10.8 We regard it as axiomatic that:-

(i) individuals should normally be fully informed of the results of genetic screening, and in particular of the implications of those results for the family; and

(ii) the accepted standards of the confidentiality of medical information should be followed as far as possible.

10.9 When genetic screening reveals information that may have serious implications for relatives of those who have been screened, health professionals should explain why the information should be communicated to other family members. **We recommend that in such circumstances health professionals should seek to persuade individuals, if persuasion should be necessary, to allow the disclosure of relevant genetic information to other family members.** They should also seek to ensure that treatment, counselling and other appropriate support are made available to those to whom such unsought information is disclosed. (Paragraph 5.41 summarising paragraphs 5.23 - 5.31)

10.10 We note that both the law and professional guidelines provide for exceptional circumstances, when an individual cannot be persuaded to inform family members with a legitimate right to know. In such exceptional circumstances the individual's desire for confidentiality may be overridden. The decision can only be made case by case. **We recommend that the appropriate professional bodies prepare guidelines to help with these difficult decisions.** (Paragraph 5.42 summarising paragraphs 5.23 and 5.29 - 5.31)

10.11 **We recommend that the Department of Health should consider with health authorities and the appropriate professional bodies effective arrangements for the preservation of confidentiality, particularly in relation to genetic registers, and should issue the necessary guidance.** (Paragraph 5.43 summarising paragraphs 5.32 - 5.39)

III : Employment

10.12 At present, the use of genetic screening by employers in the UK does not appear to be a cause for concern. We have found evidence of only one existing screening programme : that programme can be justified quite readily on the grounds of safety, not only of those being screened but also of third parties. Nevertheless we recognise that the matter needs to be kept under review. **We recommend that the Department of Employment keeps under review the potential use of genetic screening by employers.** (Paragraph 6.27 summarising paragraphs 6.24 - 6.26)

10.13 Subject to prior consultation with workplace representatives, and with, as necessary, the Health and Safety Commission, **we recommend that genetic screening of employees for increased occupational risks ought only to be contemplated where:-**

(i) there is strong evidence of a clear connection between the working environment and the development of the condition for which genetic screening can be conducted;

(ii) the condition in question is one which seriously endangers the health of the employee or is one in which an affected employee is likely to present a serious danger to third parties;

(iii) the condition is one for which the dangers cannot be eliminated or significantly reduced by reasonable measures taken by the employer to modify or respond to the environmental risks.

Although it may be appropriate to introduce a genetic screening programme on these limited grounds, it should only be done if accompanied by safeguards for the employee, and after consultation with the coordinating body recommended in paragraph 10.20. (Paragraph 6.28 summarising paragraphs 6.20 - 6.23)

IV : Insurance

10.14 Our recommendations about the use of genetic screening and genetic tests by insurance companies follow from the following considerations:-

(i) the difficulty of assessing what may be slender evidence on the genetic susceptibility of individuals to develop polygenic and multifactorial diseases (for example, some cancers and some heart disease);

(ii) an awareness that ordinary commercial practice will lead companies to be over-cautious in their assessment of the risks derived from medical data; and

(iii) the possibility of abuse.

10.15 **We recommend that British insurance companies should adhere to their current policy of not requiring any genetic tests as a prerequisite of obtaining insurance.** (Paragraph 7.37 summarising paragraphs 7.22 - 7.25)

10.16 **We recommend that there should be early discussions between the Government and the British insurance industry about the future use of genetic data, and that pending the outcome, the companies should accept a temporary moratorium on requiring the disclosure of genetic data.** There should, however, be two exceptions:-

(i) first, in the case of those individuals where there is a known family history of genetic disease that can be established by the conventional questions about proposers' families, then individuals may be asked to disclose the results of any relevant genetic tests (paragraph 7.28); and

(ii) the moratorium should apply only to policies of moderate size. The limit would be a matter to be settled between the Government and the industry in the context of arranging the moratorium.

The importance of the discussions that are recommended is highlighted by the considerations set out in paragraphs 7.7 and 7.8. (Paragraph 7.38 summarising paragraphs 7.26 - 7.35)

V : Public policy

10.17 The threat of eugenic abuse of genetic screening requires safeguards. In a democracy, public understanding of human genetics should serve to create awareness of the dangers of eugenics, and of the possible stigmatisation of those carrying or suffering from genetic disorders. **We recommend the need for improving public understanding of human genetics should be borne in mind in any review of the National Curriculum and in the work of all public bodies concerned with the public understanding of science.** (Paragraph 8.23 summarising paragraphs 8.4 - 8.7)

10.18 We recognise that there are limits to the effects of educational work, however good. We, therefore, regard as essential to the safeguards against eugenic abuse our recommendations on **adequately informed consent, confidentiality** and the **central coordination and monitoring** of genetic screening programmes. (Paragraph 8.24 summarising paragraphs 8.20 - 8.22)

VI : Implementation of screening programmes

10.19 Further consideration needs to be given to the process whereby genetic screening programmes might be introduced into routine practice. As we have emphasised, existing screening programmes are largely pilot programmes. Pilot programmes should be governed by the ethical codes applying to research procedures.

10.20 **We recommend that the Department of Health in consultation with the appropriate professional bodies formulate detailed criteria for introducing genetic screening programmes, and establish a central coordinating body to review genetic screening programmes and monitor their implementation and outcome.** (Paragraph 9.7 summarising paragraphs 9.1 - 9.4)

10.21 As a contribution to the discussion of criteria for screening programmes, we suggest they should include the following:-

(i) the aims and purposes of the entire programme;

(ii) the predictive power and level of accuracy of the particular screening test;

(iii) the value to those being screened of the knowledge gained. For each programme this should have been researched as an integral part of the follow-up to the pilot programme;

(iv) the availability of therapy for the particular condition, accepting that lack of treatment does not necessarily mean that screening is not worthwhile;

(v) the potential social implications; and

(vi) the resource costs.

Acknowledgements

The Working Party wishes to record its thanks to many professionals and other individuals who have assisted its work. It is particularly grateful to those organisations that prepared submissions : they are listed on p 99.

The Working Party has drawn on a large body of medical and scientific literature. References have been given only in specific support of particular points in the text. Those professionally engaged in the subject will have access to detailed bibliographical tools.

Official and professional reports may be less well referenced. They are listed on pp 100-2. Readers will note that this report forms part of a major international effort to address the issues raised by research on human genetics.

The Working Party has also followed the interest taken in the subject by the media in the UK during the last two years.

Finally, the Working Party wishes to record its gratitude for the assistance given by Professor Martin Bobrow, Mrs Ann Hunt and Dr Andrew Wilkie and to all those associated with the cystic fibrosis screening programmes (see paragraphs 4.10 *ff*) who have given permission for the reproduction of some of their material.

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CHAPTER 4

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2. Ideally interpretation should be through a holder of a recognised qualification in interpretation. See, for example, Nuffield Interpreter Project **Access to Justice : non-English speakers in the legal system** (Nuffield Foundation 1993).

3. The leaflet formed part of a study funded by The Cystic Fibrosis Trust. The study is reported in Bekker H *et al* **Uptake of cystic fibrosis testing in primary care : supply push or demand pull?** BMJ 1993;**306:** 1584-1586. Permission has been given for the reproduction of part of this leaflet.

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CHAPTER 8

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Fragile X Society

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Glossary

Scientific terms

Only those terms mentioned in the text are included here

Amino acid
A simple compound, one of 20 from a selection of which all **proteins** are made. Proteins have different characteristics because in each of their constituent chains particular amino acids are arranged in a particular order. **Genes** specify this arrangement.

Antibody
A **protein** made by the immune system, which forms an important part of the body's defences against infection.

Autosome
Any one of the 22 matched pairs of chromosomes, one of each of which is inherited from both mother and father; in contrast to the sex chromosomes.

Carrier
A healthy individual who has both an abnormal and a normal copy of a pair of genes for a **genetic disorder** or character or characteristic. A carrier of a gene for a recessive disorder will usually remain unaffected through life.

Cell
The basic unit of structure of all living organisms. The central body of the cell is the nucleus which contains the inherited genetic material, **DNA**, arranged in threadlike structures known as **chromosomes**.

Chromosome
A threadlike structure containing **DNA** that carries genetic information arranged in a linear sequence. Humans have 46 chromosomes (23 pairs) in most cells of their body. The sex cells (eggs and sperm) contain only 23 (unpaired) chromosomes.

DNA (deoxyribonucleic acid)
The chemical substance of which a **gene** is made and which encodes genetic information.

Dominant
The form of inheritance in which a **genetic disorder** or character shows itself when only one of the two copies of the **gene** is abnormal (see paragraph 2.4).

Enzyme
A **protein** that acts as a catalyst, speeding the rate at which a body process proceeds, so that it can act repeatedly without being permanently used up.

Gene
The fundamental physical and functional unit of heredity consisting of a sequence of **DNA**, occupying a specific position within the **genome**.

Genetic disease or **disorder**
Conditions which are the result of alterations in the genetic make-up of an individual. They may be the direct consequences of defects in single **genes** (**mutations**); or in whole **chromosomes**, parts of which may be lost, duplicated or misplaced; or from the interaction of multiple genes and external factors.

Genetic fingerprinting
A technique which enables genetic relationships between close relatives, or the identity of individuals to be established - usually beyond reasonable doubt.

Genetic map
The body of information on the relative positions of **genes** on **chromosomes**. Much of the effort of the **Human Genome Project** is directed towards mapping chromosomes.

Genetic marker
A harmless variable inherited change in DNA or protein that can be used to locate a disease gene on a particular chromosome.

Genome
The total genetic complement of an individual, or of a species.

Haemoglobin
The oxygen-carrying **protein** found in mammalian red blood cells. Various gene **mutations** can result in diseases called the **haemoglobin disorders**.

Multifactorial
A term which denotes that many factors, often environmental (such as diet and smoking) contribute to the development of a disease. Often used interchangeably with **polygenic**.

Mutation
A change in the structure of **DNA**, usually permanent and transmissible. Mutations within genes are the cause of genetic disease.

Polygenic
Controlled by or associated with more than one gene.

Polymerase chain reaction (PCR)
A laboratory process in which a specific **DNA** sequence is amplified many millions of times in only a few hours.

Positional cloning
Isolation of a gene through knowledge of its specific location on a particular chromosome.

Protein
A molecule composed of many **amino acids**, folded into a particular shape so that it may form a specific function. There are many types of proteins, for example, **enzymes** are proteins.

Recessive
The form of inheritance where a genetic defect causes little or no outward effect unless it is present in both of a pair of **chromosomes**, and therefore has been inherited from both parents (see paragraph 2.4).

Sex chromosomes
The X and Y chromosomes in human beings that determine the sex of an individual. Females have two X chromosomes in most body cells; males have an X and Y chromosome.

Translocation
A rearrangement of chromosomal material between different chromosomes, not of the same pair.

Trisomy
The existence of three chromosomes instead of the normal two of a particular chromosome.

X-linked
The form of inheritance in which the **gene** is carried on the X **chromosome**. (see paragraph section 2.4)

Diseases

Only those diseases mentioned in the text are included here. The intention is simply to give a very brief description of the main features and mode of inheritance. For many conditions variations occur and it must be emphasised that no attempt has been made to give a comprehensive account of these.

Adrenoleukodystrophy (ALD)
Mode of inheritance : X-linked

Adrenoleukodystrophy is a very rare inherited disorder affecting boys who normally develop failure of their adrenal glands (producing the hormone cortisol), fits, and deterioration of brain function. For reasons that are not understood, some males (a minority) escape the problems with the central nervous system but may develop Addison's disease in adulthood (see, for example, Chapter 5, Fig E). There is no known cure or satisfactory treatment and death usually occurs in childhood. The disease is inherited through the mother who carries the defective gene on one of her X chromosomes. The risk for boys inheriting the disease is 1 in 2; 1 in 2 girls will be carriers, like their mother.

Alpha-1-antitrypsin deficiency
Mode of inheritance : recessive

The commonest form of alpha-1-antitrypsin deficiency occurs in about 1 in 3,000 people who inherit an abnormal gene from each parent. Almost all those who smoke will develop progressive lung disease (emphysema) in adult life. In non-smokers, emphysema occurs later or may never develop. About 20% of infants with the disease develop jaundice and some of these may develop liver damage. Carriers with only one abnormal gene usually have no problems but may possibly have an increased risk of emphysema if they smoke heavily.

Breast cancer
It is believed that several genes play a role in the 25,000 new cases of breast cancer diagnosed in Britain every year, particularly where onset is early or where multiple family members are affected. A gene that predisposes women in some families to breast cancer has been traced to a region of chromosome 17 and it is likely that the gene itself will soon be isolated.

Congenital disorders
Disorders which are present at birth, not necessarily hereditary. For example the limb deformities caused by the drug thalidomide, or the malformations caused by maternal rubella (German measles), are congenital but not inherited, whereas other forms of malformation may be hereditary.

Congenital hypothyroidism
Mode of inheritance : usually not inherited - about 5-10% of cases due to a known genetic defect

Abnormal development or function of the thyroid gland resulting in lack of production of thyroid hormone (thyroxine) occurs in about 1 in 4,000 babies in the UK. The baby is usually normal at birth because the mother's thyroxine has been able to pass to the baby. Unless treatment with thyroxine is started within the first few weeks of life, growth and mental development will be delayed. Screening is carried out by measuring specific hormones in the blood taken from the baby at around the end of the first week (the same blood sample as used for PKU - see later).

Cystic fibrosis
Mode of inheritance : recessive

Cystic fibrosis (CF) is a serious inherited disease affecting the lungs and digestive system of babies, children and young adults. People with CF have sticky mucus in their lungs and are particularly prone to chest infections. They also have difficulty in digesting foods, especially fatty foods, and may later develop liver problems. Treatment (antibiotics, physiotherapy, digestive enzymes) can greatly help but does not cure the condition. The average life expectancy for a person with CF is about 20-30 years. The disorder is inherited and the change in the gene responsible for about 85% of the cases can now be detected. For the disease to develop, a defective gene must be inherited from each parent. Parents who have only one of a pair of defective genes are known as carriers and are themselves completely healthy. About 1 in 20 of the white population in the UK are carriers of the gene; the disease occurs in about 1 in 2,000 babies born. If both parents are carriers, the risk of any baby having the disease is 1 in 4.

Down's syndrome
Mode of inheritance : usually not inherited

The disorder, which is genetic but usually not inherited, affects about 1 in 600 babies born overall, although the risk of having a child with Down's syndrome rises sharply when the mother is over 35 years of age.

The vast majority of individuals with Down's syndrome have an extra copy of chromosome 21, are born with specific physical characteristics and have severe learning disabilities. A very small percentage are inherited due to a translocation.

Duchenne muscular dystrophy (DMD)
Mode of inheritance : X-linked

Duchenne muscular dystrophy is a serious progressive disease of muscles affecting about one in 3,500 newborn boys. There are no signs of disease at birth, and affected boys develop and grow normally until around 18 months of age. From the ages of 7 to 12, affected boys become wheelchair bound. Death from chest infection or heart failure usually occurs by the early 20s or before.

About a third of cases arise from new mutations and are not inherited from carrier mothers. Women carrying the abnormal gene have a 1 in 2 risk of having a son with the disorder; 1 in 2 of their daughters will be carriers.

Familial colorectal cancer
Mode of inheritance : dominant

Colorectal cancer causes about 20,000 deaths each year in Britain and yet if diagnosed at an early stage it is curable. Two relatively common types of inherited predisposition to cancer of the colon have been identified.

Familial adenomatous polyposis is a dominantly inherited disease accounting for about 1% of colon cancer patients and has a birth frequency of about 1 in 8,000. Individuals with the disorder develop hundreds of polyps in the colon during adolescence, and typically develop colorectal cancer by the fourth decade. The gene responsible has been identified, making it possible to offer genetic testing to individuals at risk, and to provide prophylactic treatment (surgery to remove the colon) to individuals found to be affected.

Hereditary non-polyposis colon cancer may cause between 5% and 15% of cases of colorectal cancer. Individuals with the abnormal gene do not develop numerous polyps, but those that do occur rapidly become cancerous. This form of colon cancer is thought to be associated with a gene on chromosome 2, but other genes may also be involved.

Familial hypercholesterolaemia
Mode of inheritance : dominant

High levels of blood cholesterol are associated with an increased risk of heart disease, especially in men in middle age. In most individuals, raised blood cholesterol results from the interaction of several genes (not all of which have been identified) and environmental factors, such as a high fat diet.

Familial hypercholesterolaemia is the name given to a specific inherited disorder in which the gene causes high levels of blood cholesterol from birth. It is dominantly inherited and individuals with a single abnormal gene have a greatly increased risk of developing heart disease by the age of 50 years; those who inherit the abnormal gene from both parents have extremely high blood cholesterol and many develop heart disease in their teens. It is estimated that about 1 in 500 individuals are born with the disorder but the very serious (both genes affected) condition only occurs in about 1 in 1,000,000.

Fragile X syndrome
Mode of inheritance : X-linked (some female carriers are mildly affected)

Severe learning difficulty due to fragile X syndrome distinguished by a visible change near the tip of the X chromosome, is thought to occur in approximately one in every 2,000 male births. The mode of transmission is complicated, because the change in the gene tends to increase with successive generations, and some males can be unaffected, yet transmit the carrier state to their daughters. Girls may also be affected,

but to a lesser degree : about one-third of girls carrying this genetic abnormality will have some degree of learning difficulty.

Severe learning difficulty is the main characteristic of the disorder, although this varies markedly in severity between individuals. There is no limitation of life expectancy for children with the fragile X syndrome.

Glucose-6-phosphate dehydrogenase deficiency (G6PD)
Mode of inheritance : X-linked

This red blood cell disorder occurs mainly in males and is particularly common in the Middle East, China and West Africa. It causes anaemia and jaundice in the newborn period but usually there are no symptoms after this period unless acute destruction of the red blood cells (causing anaemia and jaundice) is triggered by some drugs, by infections, and certain foods such as fava beans - it is sometimes called ‘favism’.

Haemoglobin disorders (haemoglobinopathies)
The haemoglobin disorders are the commonest of all genetic disorders worldwide. These conditions are caused by a failure of haemoglobin, the substance in red blood cells which carries oxygen, to be produced normally or to carry oxygen efficiently. The two most important groups of haemoglobin disorders are sickle cell disease and the thalassaemias:

Sickle Cell Disease
Mode of inheritance : recessive

An inherited abnormality of the haemoglobin (called haemoglobin S) in the red blood cells may cause deformity of the cells known as sickling. Those at most risk of inheriting sickle cell disorders are people of African, African/Asian Caribbean, Eastern Mediterranean, Asian and Middle Eastern origin. The inheritance of one sickle cell gene (sickle cell trait) generally causes no problems; individuals who inherit the gene from each parent have sickle cell disease.

A child born with sickle cell disease does not generally have problems until after the age of four to six months. After this age most children become anaemic because the sickle cells are destroyed in the blood. The children may also from time to time get additional problems such as hand-foot syndrome (swelling of the hands and feet), mild to excruciating pains throughout the body, chest infections, strokes and damage to various parts of the body including the hips, shoulders, eyes and lungs. These are due to the sickle cells causing blockage of smaller blood vessels and other problems. The majority of affected individuals survive into adulthood but there are occasional deaths of young children and adults due to complications such as overwhelming infections and sickling in the spleen and lungs. Haemoglobin C is another haemoglobin variant that causes similar problems when paired with haemoglobin S. (mentioned in paragraph 6.25)

Thalassaemia
Mode of inheritance : recessive

Thalassaemia is the name given to a group of inherited disorders of haemoglobin production and can be broadly divided into two types : alpha thalassaemia and beta thalassaemia, both of which are recessively inherited.

Most people with **alpha thalassaemia** originate from the Far East, notably Hong Kong, China, Singapore and Vietnam; as well as from Cyprus, Greece and the Middle East. There are two types of alpha thalassaemia, but generally only the severe (alpha zero) type is clinically important. **Alpha zero thalassaemia major** causes a total absence of haemoglobin production in the fetus, leading to stillbirth, usually before the expected date of delivery.

The main groups at risk of inheriting **beta thalassaemia** are people of Mediterranean and Southern European, Asian, Middle Eastern and Far Eastern origin. There are estimated to be about 570 cases of beta thalassaemia major in the UK, with an average of 16 births a year. A child born with **beta thalassaemia major** is unable to make a sufficient amount of haemoglobin and will develop anaemia in early childhood if not treated with frequent blood transfusions. However, this treatment causes too much iron to be stored in the body, so the child has to be taught to use an infusion pump containing a drug (Desferal) to get rid of this excess iron and this is a burdensome procedure. Since the advent of treatment early in life, children are now surviving into their twenties or thirties, and more recently bone marrow transplant- ation has further improved the prognosis.

Haemophilia
Mode of inheritance : X-linked

Haemophilia is a descriptive name for a group of blood disorders, all of which have clotting problems as the basic defect. The most common type, haemophilia A, affects about 1 in 10,000 live male births.

Individuals affected with haemophilia A are unable to produce normal factor VIII, one of a number of factors associated with the clotting mechanism of the blood. Manifestations of the disease include haemorrhages into joints following only minimal injury, bruising in soft tissues from minor bumps, and severe bleeding from minor injuries. Arthritis is a frequent complication. Bleeding episodes can be limited by the prompt infusion of factor VIII, but use of contaminated preparations in the early 1980s caused infection of many haemophiliacs with human immunodeficiency virus.

Huntington's disease
Mode of inheritance : dominant

A disorder affecting about one person in every 10,000 in the UK. The abnormal gene was isolated as recently as March 1993. It is a progressive disease of the central nervous system, characterised by involuntary movements, loss of motor control and dementia. The symptoms most commonly first appear in individuals of between 40 and 50 years of age, with death occurring 15-20 years later.

Hypertrophic cardiomyopathy
Mode of inheritance : dominant

A rare dominantly inherited disorder of the muscle of the heart. It may cause heart failure in infancy, but problems may not arise until later childhood or adult life. It is the most common cause of sudden death from heart disease in young people, particularly athletes.

Neural Tube Defects (NTD)
Mode of inheritance : both genetic and environmental factors involved

These conditions occur if the brain and/or the spinal cord with its protecting skull and spinal column fail to develop properly. They include anencephaly, where most of the brain and skull are absent and stillbirth or death soon after delivery is inevitable, and spina bifida, where the spinal canal is not closed and the spinal cord and nerves may be damaged. Infants born with spina bifida show a wide range of physical disabilities and in the most severe forms the legs and bladder may be paralysed. Hydrocephalus (excess fluid within the brain) is a frequent complication. The causes of NTD are complex, but there is an undoubted genetic component, the risk for subsequent offspring after the birth of an affected child being increased about 10 fold. Maternal diet also plays a part : folic acid has a protective effect.

High levels of a protein called alphafetoprotein (AFP) are found in the amniotic fluid and maternal blood when the fetus has either anencephaly or spina bifida. In many areas of the UK, serum AFP estimation is offered routinely to all pregnant women around the 16th week of pregnancy to identify a risk group for neural tube defects; ultrasound scanning is also used. The incidence of NTD at birth in the UK has fallen from about 4 per 1,000 20 years ago, to about 0.3 per 1,000, partly due to antenatal diagnosis and selective termination of pregnancy, but also because of a primary decrease in frequency.

Phenylketonuria (PKU)
Mode of inheritance : recessive

PKU is a rare inherited disorder, affecting about 1 in 10,000 births in the UK. Affected individuals inherit the abnormal gene from each parent and are unaffected at birth; but, with the introduction of feeding, a substance in the blood (phenylalanine and 10 breakdown products) builds up and causes brain damage, so that untreated children become severely mentally handicapped. Every baby in the UK has a blood test for phenylalanine at about 6 days of age and if the diagnosis is confirmed, a special diet is started. With rigorous dietary control mental development can be normal, although the intellectual status of early treated subjects is not as good as was originally thought. The dietary control has to be continued at least into late childhood and possibly throughout life. Women with PKU require particularly strict dietary control during pregnancy. The current screening test only detects babies who may be affected.

Polycystic kidney disease
Mode of inheritance : recessive (infantile form)
dominant (adult form)

There are several disorders in which cysts occur in the kidneys. Two main inherited types can be distinguished. Infantile polycystic kidney disease is present at birth. It is inherited in a recessive manner and can be detected before birth by ultrasound.
Adult polycystic kidney disease is a common dominantly inherited disorder, with a worldwide prevalence of between 1 in 500 and 1 in 1,000 individuals. Symptoms do not usually appear until around 40 years of age. Small cysts may be detected before birth by ultrasound examination; they enlarge slowly throughout life but only about 50% of affected individuals will develop severe kidney failure by age 70.

Rhesus haemolytic disease

Rhesus haemolytic disease can occur if the mother's blood group is rhesus negative and the father's is rhesus positive (about 85% of people are rhesus positive and 15% are rhesus negative). In this situation, the fetus may also be rhesus positive. If sufficient leakage of fetal blood into the maternal circulation occurs, which is particularly likely at the time of delivery, a rhesus negative woman can develop antibodies against the rhesus positive blood group and subsequent babies may be affected, with destruction of their red blood cells causing anaemia and jaundice. Very severely affected infants have problems before birth; after birth treatment (exchange transfusion) may be needed to correct anaemia and prevent brain damage due to jaundice.

The condition used to cause 1-2/1,000 stillbirths or deaths in the newborn period. It is now largely prevented by screening all pregnant women for their rhesus blood group early in pregnancy and ensuring that all are given an injection of antibody within a few hours of delivery (or miscarriage). This removes any fetal rhesus positive cells from the mother's bloodstream and so prevents her becoming immunised in almost every case.

Rubella (German measles)
Mode of inheritance : not inherited - a virus causing congenital malformations

If rubella is contracted in the early stages of pregnancy (before about 12 weeks) it can cause stillbirth or serious congenital malformations such as blindness, deafness, heart defects and mental retardation. As a result of programmes both for immunising schoolgirls and non-pregnant women against the virus, and by screening during pregnancy, the incidence of children born with severe congenital rubella syndromes has declined from about 3.5 to 0.41/100,000 births between 1980 and 1985 in most of Western Europe.

Sickle cell disease - see **Haemoglobin disorders**

Tay-Sachs disease
Mode of inheritance : recessive

This serious inherited disease is principally found in Ashkenazi Jewish families, where the incidence is about one in every 4,000 live births. Affected individuals inherit the abnormal gene from each parent.

The disorder is characterised by deterioration of brain and muscle function and becomes apparent at around 6 months of age. Such affected infants rarely survive beyond three or four years old. In some cases symptoms do not appear before two to three years of age, with death usually occurring between the ages of five and ten years.

Thalassaemia - see **Haemoglobin disorders**

Turner's syndrome
Mode of inheritance : chromosomal disorder - usually not inherited

Turner's syndrome affects girls who have only one normal X chromosome instead of the usual complement of two. It occurs in about 1 in 5,000 girls and is usually not inherited.

Over 99% of girls with Turner's syndrome are infertile, due to lack of fully developed ovaries. The most obvious feature in childhood is short stature; there may also be heart defects. Intelligence is generally normal, but there may be some learning difficulties.

Procedures for antenatal testing

Amniocentesis

The most widely used technique of prenatal diagnosis, most commonly carried out at 15-18 weeks gestation, although it can be carried out as early as 12 weeks. Ultrasound is used to locate the placenta, and a small quantity of amniotic fluid, which contains cells shed by the developing fetus, is withdrawn through a needle from the amniotic cavity. Cells have to be cultured before chromosome examination (for example, to detect Down's syndrome) or DNA analysis can take place. Genetic diagnosis is not usually possible until 16-20 weeks of pregnancy. There is still some uncertainty about the exact risk to the pregnancy from amniocentesis largely because the risk is so low that it is extremely difficult to measure. The best studies suggest a 0.5-1% excess risk of spontaneous abortion following amniocentesis at 15-16 weeks and a slightly increased incidence of mild respiratory problems in the newborn. Good data are not yet available on the risks of early amniocentesis.

Chorionic villus sampling (CVS)

A procedure whereby a small sample of chorionic (placental) tissue, which shares the genetic make up of the fetus, is removed for prenatal diagnosis. It is usually performed at about 10 weeks of pregnancy with only minimal discomfort and often allows a genetic diagnosis to be achieved before 12 weeks' gestation. CVS requires first-class ultrasound and an expert and well-trained team. The risks are higher than for amniocentesis : an MRC trial gave 2-4% excess miscarriage risk.

Fetal blood and tissue sampling

Fetal blood sampling is used for a variety of purposes : for example, for the diagnosis of the haemoglobin disorders and haemophilia when DNA diagnosis is not possible, and for the assessment of rhesus haemolytic disease. It can be performed safely only after the seventeenth week of pregnancy and only by experts. The initial, highly specialised technique of fetoscopy has now been replaced by the safer and less specialised technique of ultrasound-guided transabdominal needle puncture of the fetal cord insertion. The risk figure for cordocentesis is 2%.

Ultrasound

Ultrasound scanning is now a basic part of obstetric practice. There is a continual increase in the range and capabilities of the best equipment and a decrease in the size and cost of basic machines. Many major structural malformations can be detected by ultrasound in the second trimester of pregnancy (at about 16-20 weeks' gestation). There is no evidence for a harmful physical effect of diagnostic obstetric ultrasound. Its main limitations are the dependence on the skill and experience of the operator and the quality of the equipment, and its main risk is misinterpretation of the image leading to failure to detect abnormalities (false negatives) or to abortion of a healthy fetus (false positives). Another problem is that the natural history of many detectable fetal anomalies, for example, choroid plexus cysts, renal pelvicalcyceal dilation and ventricular dilation, is inadequately documented or unpredictable. This makes it difficult to give advice and can generate unnecessary anxiety.

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Publications

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