Report on genetic testing for late onset disorders : September 1998 / Advisory Committee on Genetic Testing.

ADVISORY COMMITTEE
ON GENETIC TESTING

REPORT ON GENETIC TESTING FOR LATE ONSET DISORDERS

September 1998

Health Departments of the United Kingdom 1998

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SECTION 1 SUMMARY

ACGT's aim in this report is to set out the issues to be considered before genetic testing for late onset disorders is offered and during the provision of such tests. Summarised here are the major issues identified in the report. These relate principally to requests for genetic testing from healthy relatives of patients with a late onset genetic disorder. Population based genetic screening, diagnostic testing of symptomatic individuals and genetic susceptibility testing for common disorders are briefly considered in Annexes A, B and C.

Why do people request genetic testing for late onset disorders?

Most healthy people requesting genetic testing do so because of perceived risk from their family history of developing or passing on the disorder. Depending on the condition, the perceived benefits of testing may be:

a. medical, with the possibility of early treatment or preventive measures before symptoms develop; and for those shown not to be at significant risk, they may be able to discontinue or avoid medical procedures.

b. personal, allowing freedom from uncertainty and planning of major life decisions. For some even an abnormal result may be preferable to continuing uncertainty.

c. primarily for the benefit of family members, present or future. A normal test result may spare relatives the harm that may result from continued risk and uncertainty.

Many people requesting genetic testing will have a combination of these aims and concerns. However others, even though in an apparently comparable situation, may not request testing, or may decline it if it is offered.

Scientific and clinical validity of the test

Before any genetic test is used in clinical practice the scientific and clinical validity should be established. When genetic tests are validated scientifically, the following need to be established before the test is considered as valid in a service setting:

a. The error rate and failure rates should be known; and

b. Where possible the disorder and particular genetic change being tested for should be confirmed in an affected family member.

Laboratories undertaking genetic testing for late onset disorders

All laboratories providing genetic testing services should be closely linked with other genetic services, and be appropriately accredited for this as well as taking part in internal and external quality control schemes. Research laboratories should not normally be the basis for genetic testing services; where they are, because of the rarity of the disorder or other factors, the service delivered should aim to conform to the same standards expected in service laboratories.

Information needed by those being tested

Information on the disorder being tested for should be full, accurate and appropriately presented, in a clear and simple manner that is readily understandable. Complex information should be provided face to face by an appropriately trained and experienced person. Individuals should be given adequate time to absorb the information provided, before a decision is taken to be tested or a result is given.

Support in relation to genetic testing

Appropriate support in preparation for and subsequent to genetic testing should be considered as part of the genetic testing process. The costs of the potential support needs of genetic tests should be considered when such services are evaluated and commissioned.

Consent to genetic testing

Where an individual is able to give consent, specific freely given consent is required before testing. In the case of presymptomatic genetic testing of healthy individuals, written consent should always be obtained, though written consent is not in itself a substitute for careful face to face explanation.

For adults permanently incapable of giving consent (eg. because of a learning disability) the legal position is that the decision will be made by the doctor responsible for the person's clinical care. They will be guided by the best interests of the individual and where appropriate take into account, the views of the family or other close carers. It should be noted that the best interests of the

individual and of the family and close carers may not necessarily be the same. If the incapacity is temporary, genetic testing should be delayed until consent is possible unless it is essential in the individual's therapy.

Testing of young children and adolescents for late onset disorders

Presymptomatic genetic testing of young children for disorders not currently influenced by therapy, and where onset is normally in adult life, is not recommended.

Any request from those with parental responsibility, for pre-symptomatic genetic testing of a young child unable to give consent, should be fully discussed in the context of the particular family situation, the nature of the disorder, the possible medical or other benefits, and the implications of testing for the child and family. In all cases the views of a child or young person should be obtained where possible and taken into account in any decision.

Where genetic tests are being used diagnostically in the context of a child with a family history of a late onset disorder showing clinical features, it is essential that these clinical features are relevant to the nature of the family disorder.

Requests from adolescents for presymptomatic genetic testing for late onset disorders should be considered, taking into account the circumstances of the individual and their family. If the adolescent is competent to give consent but there are no clear benefits of testing, some might suggest that testing should be deferred until the age of majority is reached. However, the competent adolescent is entitled to make a personal decision on this matter after a full discussion and exploration of the issues.

Prenatal genetic testing for late onset disorders

Prenatal genetic testing for late onset disorders should only be undertaken in the context of full genetic counselling.

"Over the counter" genetic testing for late onset disorders

Tests for late onset disorders should not be supplied direct to the public. Any medically qualified person requesting or providing genetic testing for late onset disorders should ensure that they, or another suitably qualified medical practitioner, are actively involved in the process.

Genetic testing and results of research studies

Research studies that generate identifiable genetic test results on individuals should only be done with appropriate consent and following approval of a designated ethics committee.

Those giving consent to participation in research should be made aware that they will not normally receive genetic test information that forms part of research, nor should such data normally be placed on the medical record.

FOREWORD

A. The Advisory Committee on Genetic Testing (ACGT)

1. ACGT was established, under the Chairmanship of the Rev Dr John Polkinghorne KBE FRS in 1996. A full list of ACGT's members is at Annex D. ACGT's remit covers the whole of the United Kingdom.

2. ACGT's Terms of Reference are:

   i. to provide advice to Ministers on developments in testing for genetic disorders;

   ii. to advise on testing individuals for genetic disorders, taking account of ethical, social and scientific aspects; and

   iii. to establish requirements, especially in respect of efficacy and product information, to be met by manufacturers and suppliers of genetic tests.

3. ACGT's Secretariat is provided by the Department of Health. That Department, the Office of Science and Technology and the Human Genetics Advisory Commission (a separate non-statutory advisory body, of which the Chairman of ACGT is a member) send observers to ACGT's meetings.

B. Late Onset Disorders and Genetic Testing

4. Late Onset Disorders are those disorders with a genetic component that normally become symptomatic in adult life. During their inquiry into human genetics the House of Commons Select Committee on Science and Technology highlighted the issue of late onset genetic disorders.

5. Because of these concerns and the increasing emphasis given to testing for late onset diseases by researchers, industry and patient support groups, ACGT recognised, the high priority that should be given to consideration of issues raised by genetic testing for late onset disorders. ACGT therefore established a Sub-Group, chaired by Professor Peter Harper, to prepare this report.

6. Genetic testing may help in diagnosis by establishing the cause of symptoms or of a disorder. It may also indicate that a person will develop a disorder in future; or that they are a carrier of a condition, so that although they will not themselves be affected, they may have affected children. Tests for genetic susceptibility to common diseases such as cancer, heart disease and diabetes are being developed and an increasing range of tests can be anticipated. In the UK genetic testing services are most often provided through the National Health Service, and most people requiring these services obtain them by referral from their general practitioner. Consultant-led NHS genetics services are available throughout the UK, and ACGT recognises the importance and achievements of these services. The UK Regional Genetics Centres can supply information to clinicians and members of the public on the range of services they provide, and their addresses and contact telephone numbers are listed at Annex E.

7. In its first report ACGT recognised a limited role for the provision of genetic testing services direct to the public ie. outside a clinical setting such as that provided by NHS genetics services, however it saw this testing being mainly relevant to those tests which determine carrier status for inherited recessive disorders, where such status carries no significant direct health implications for the carrier individual (eg. cystic fibrosis). ACGT considered that provision of such testing poses fewer difficulties than provision of testing for inherited dominant and X-linked disorders, for **adult onset genetic disorders regardless of inheritance** (the late onset disorders of this report) or for the genetic component(s) of multifactorial diseases.

8. ACGT continues to regard the provision of tests for late onset disorders as more problematic than other genetic tests and believes that such tests are best conducted in a clinical setting.

C. Conclusion

9. ACGT recognises that clinicians in the NHS and other practice have essential roles to play in the provision of genetic testing services for late onset disorders. ACGT wishes to ensure that such testing is delivered with the best interests of those tested in mind and that such testing is only performed in appropriate circumstances and with suitable information and genetic consultation available.

10. The Government has a public health and consumer protection role to encourage good practice in the provision of genetic testing.

11. It is the aim of ACGT, by means of this report, to set out the issues that need to be considered before offering genetic testing for late onset disorders and during the provision of such testing. ACGT hopes that it may also be of interest to those being tested, patient support groups, testing laboratories, and general medical practitioners and other health care professionals.

DEFINITIONS USED IN THIS REPORT

Please note some of these definitions are specific to this report and may differ from those used in other ACGT reports)

Genetic Testing - Testing to detect the presence or absence of, or alteration in, a particular gene, chromosome or a gene product, in relation to a genetic disorder.

a. **Diagnostic Genetic Testing** - Use of genetic testing in a symptomatic individual to aid in their diagnosis, treatment and management.

b. **Presymptomatic Genetic Testing** - Testing primarily carried out in healthy or asymptomatic individuals to provide information about that individual's future health, with respect to specific inherited diseases. Such a test result may indicate that the individual has a high likelihood of developing the disorder or of excluding it. Presymptomatic genetic testing is most frequently used in late onset autosomal dominant disorders such as Huntington's Disease.

c. **Susceptibility Testing** - Testing which provides information about the genetic component in a multifactorial disorder (see Multifactorial disorders below).

Late Onset Disorders - Disorders that normally become symptomatic in adult life.

Multifactorial Disorders - Disorders whose genetic components are not the sole cause, but which work with other, often environmental factors, in determining a disease outcome. Multifactorial disorders include many cardiovascular diseases, most Alzheimer's Disease of old age and some forms of diabetes.

Mutation - A change in the DNA sequence. Many changes cause a disorder or the inherited susceptibility to a disorder. Only heritable mutations are considered in this report.

Genetic Counselling - A process of consultation by which information is imparted to individuals or families affected by, or at risk of a genetic disorder. It includes information on the nature of the disorder; the size and extent of genetic risks; the options, including genetic testing, that may help clarify the risks; the available preventive and therapeutic measures, and the provision of psychological, social and practical support. In the context of genetic testing it may include responding to the concerns of individuals referred and their families, discussing the consequences of a test, and enabling them to choose the optimal decision for themselves, but not determining a particular course of action.

Autosomal Dominant Disorders - Disorders where inheritance of a mutation from one parent only (or arising anew during egg or sperm formation) can be sufficient for the person to be affected. Important dominant disorders in the UK include familial hypercholesterolaemia, Huntington's Disease, adult polycystic kidney disease and familial adenomatous polyposis.

Autosomal Recessive Disorders - Disorders, where for a person to be affected, a mutation has to be inherited from both parents. Such parents are usually unaffected carriers because they only have a single copy of the mutant gene. Recessive disorders commonly have onset in childhood and include cystic fibrosis, sickle cell disease and thalassaemia. Haemochromatosis is an example of a late onset recessive disorder.

X-Linked Disorders - Disorders due to a mutation on the X chromosome. X-linked disorders usually only affect males, but the disorders can be transmitted through healthy female carriers. Examples include haemophilia and some forms of muscular dystrophy.

GENETIC TESTING FOR LATE ONSET DISORDERS

A. BACKGROUND

Late onset disorders

1. Many serious disorders have their clinical onset in adult life, without preceding symptoms or other features in childhood. Late onset disorders may be progressive and seriously disabling; in high economy societies they account for a considerable proportion of mortality and serious ill health in middle life, often affecting those with major employment and family responsibilities. This document deals with disorders that **normally** do not manifest until adult life including those (like many variable genetic disorders) that may occasionally become symptomatic in childhood.

The genetic basis of late onset disorders

2. Many late onset disorders have long been recognised to run in families to a certain extent, even when clear environmental factors can be identified, but it is only recently that it has become possible to identify specific genetic factors involved. For the purpose of this report, two broad groups can be recognised:

   a. **Mendelian disorders** following a clear cut pattern of inheritance, where alteration of a single gene is largely responsible for the disorder and where risks to relatives may be high. Established NHS genetics services have principally been concentrated on this group of disorders. "Dominant" inheritance, resulting in a 50% genetic risk to offspring of an affected person, is a frequent inheritance pattern in this group. The occurrence of new genetic mutations means that a significant proportion of such individuals may not have a family history of the condition, though their offspring will still be at high risk. These disorders are usually relatively uncommon, but they are numerous (several thousand), resulting in a large amount of disease overall and a considerably larger number of relatives at high risk. Examples include adult polycystic kidney disease (one of the main causes of chronic kidney failure), Huntington's Disease a serious, progressive brain degeneration, familial polyposis of the colon (an inherited form of bowel cancer) and a number of rare familial forms of cancer. A few late onset disorders follow "recessive" inheritance eg. haemochromatosis. Here, if two carriers of the altered gene have a child there is a 25% risk of an affected offspring.

   b. **Multifactorial disorders** showing a significant genetic contribution but where family patterns are rarely clear cut, risks to relatives are relatively low and less clear cut than in Mendelian disorders, and where the disorders are often the result of important environmental influences interacting with genetic factors. Examples include diabetes, coronary heart disease, schizophrenia and disorders of the elderly eg. Alzheimer's Disease.

3. A number of common late onset disorders where most cases do not show a strong genetic component are now recognised as containing a minority of cases following a clear pattern of single gene inheritance, which were not clearly distinguishable from others until the isolation of the specific genes involved. Around 5% of cases of breast and colon cancer are thought to fall into this category.

New developments in genetics

4. New techniques in genetics have made it possible to identify and isolate specific genes involved with important human disorders, including an increasing number of those with late onset. This is already having important consequences, including:

   a. Greater understanding of the disease process by identifying the nature of the protein normally produced by the gene, its relation to other body processes and how changes in the gene result in disease. Since many late onset disorders have been poorly understood, this increased understanding is of great importance in the development of future treatments. Identification of specific genes is also improving our knowledge of the variability and natural history of the disorders.

b. Genetic testing is now frequently feasible, based on changes in the specific genes involved, or on tracking the family pattern of normal variations in, or adjacent to, them. This may give possibilities of accurate risk prediction for relatives.

c. If specific changes (mutations) in a gene can be identified as causally related to a disease, they may be used in diagnosis of possibly affected individuals or in population screening, even in the absence of a family history of the disorder.

Differences between genetic tests and other tests in medical practice

5. Most medical tests are able to detect evidence of a disease process that is already present and help to resolve its nature. Some (eg. sensitive imaging techniques) may detect changes in those at risk before symptoms occur, but they still reflect an early stage of the pathological process. There is no absolute distinction between tests based on genetic technology and other tests on individuals at risk for an inherited late onset disorder, and this report's definition of genetic testing ("Testing to detect the presence or absence of, or alteration in, a particular gene, chromosome or a gene product, in relation to a genetic disorder") is a purposefully wide one. However we consider that genetic tests, particularly those based on analysis of the genetic material itself (DNA), differ from other tests in a number of important ways:

a. Since the DNA a person inherits and passes on remains largely unchanged throughout life, genetic testing for inherited disorders, based on analysis of DNA, can potentially be carried out at any point from conception to old age.

b. The presence or absence of an abnormality in a genetic test is unaffected by whether the individual has symptoms of the disease or not.

c. Since DNA is present in most body cells, any tissue sample can be used for a test for inherited disorders not just that affected by the disease. Blood or mouthwash samples are examples.

d. DNA is extremely stable, and can be analysed using stored samples taken for other purposes (eg. newborn screening or surgical samples) or samples from individuals no longer living.

e. Genetic tests for inherited disorders differ from most other clinical tests which only involve a single individual, because they may also reveal important information about relatives and can have a great impact upon families. An adult with no risk of developing an illness may seek advice on their chance of passing on a mutation to their children.

f. Another distinctive feature of some genetic tests is their potential to predict the possible future health of the individual. This possibility to predict with considerable scientific confidence is a totally new feature in medical tests, and has particular significance in relation to employment and insurance.

g. Genetic testing raises serious issues, and some of these may be more complex than those faced in other clinical areas. The test result, which has implications for the family as well as the tested individual, may cause anxiety or alleviate concerns in an otherwise healthy individual. Therefore the consultation before and after a genetic test, to explain the implications and consequences of the result, may be different from that needed in many other types of medical test or treatment. Persons tested, and possibly their families, need to understand before the tests are performed what the results may mean for them. Confidentiality must be appropriately protected but the probable implications for family members need to be understood by the person consenting to genetic testing.

h. An abnormal genetic test result may have a powerful effect on a person's perception of the nature of the disease and whether it can be treated or prevented.

6. There will be a progressive blurring between genetic testing and other tests in clinical practice which can be used as less direct markers for genetic disorders eg. serum lipids in familial hypercholesterolaemia and imaging studies for structural changes in adult polycystic kidney disease. Therefore the issues listed above for genetic testing will need to be considered in the application of other tests, and many of the ethical and other issues listed are relevant to other areas of medical and surgical consultation and practice.

Features of genetic testing especially relevant to late onset disorders

7. All the above points are important, but for late onset disorders, they result in several situations which do not usually arise so prominently in childhood genetic diseases:

   a. Since the genetic change underlying late onset disorders can be identified at any age, there may be an interval of years or even decades between a healthy individual being tested and the onset of the disease. It is also being increasingly recognised that even for some disorders following a clear cut inheritance pattern, a proportion of those showing the genetic change may remain entirely healthy.

   b. The result of a genetic test rarely gives an individual information on timing of onset or likely severity that is sufficiently precise to be helpful.

   c. Because late onset disorders may interfere little with reproduction, in addition to those actually affected there will be many relatives who are healthy but at risk of having the genetic change and many of those at risk may not be aware of it.

Practical experience of genetic testing for late onset disorders

8. This is currently limited, since most of the disorders where genetic testing initially became possible, were those of childhood onset. Significant experience is limited to a small number of genetic disorders, notably Huntington's Disease and some forms of familial cancer. For the common "multifactorial" disorders there is almost no experience in a service setting since the range of specific genes and environmental factors involved has rarely been sufficiently established to allow accurate prediction.

9. The experience from Huntington's Disease, a disorder giving severe, progressive physical disability and often mental deterioration, is of particular value. Genetic testing has been available for 10 years, different centres world-wide have used thorough and comparable protocols, capable of evaluation; genetic testing was introduced in expert centres cautiously, in conjunction with guidelines supported by the lay groups, with full information and support for those tested. Over 2,000 individuals at risk for Huntington's Disease had been tested in Britain by the end of 1996.

10. It is thus not surprising that the experience of Huntington's Disease has been used as a model for genetic testing in other late onset disorders and that it has identified many of the issues detailed later in this report. Data are now becoming available from some forms of familial cancer but there is an urgent need for such data to be collected on other late onset disorders and for testing protocols appropriate to individual late onset disorders, to be developed. Experience with HIV testing has shown that while AIDS is not a genetic disorder, many of the issues arising in testing are comparable to those outlined later in this report.

Current service provision

11. Established medical genetics services, both laboratory based and clinical, have been centred on clearly defined genetic disorders (late onset as well as childhood) that are mostly relatively uncommon, even though in aggregate they amount to a large burden of serious disease. Most genetic testing is carried out within the NHS and is based upon regional genetics centres which serve groups of health authorities. Other genetic testing services may be provided by general practitioners, clinicians in private practice, by such specialities as oncology and haematology and within research settings; many of these tests may be carried out in collaboration with regional genetics centres. UK genetics services are characterised by a number of important features that can be utilised to advantage in the appropriate development of genetic testing services. These include:

a. Based in regional centres, serving relatively large populations (commonly 2-5 million people), but allowing personal links with referring clinicians in the region.

b. Extremely close links between laboratory and clinical genetics services, allowing planned service development, appropriate clinical input to laboratory test results, and the involvement of clinical geneticists and genetic nurse specialists in genetic counselling, pre-test preparation and other aspects of the overall service.

c. Close collaborative links across the UK and beyond, permitting a network of highly specialised services for rare disorders for which testing can only be efficiently provided in a very few centres.

d. Strong links with academic medical genetics units, allowing new basic research findings and technology to be introduced quickly into service provision, and encouraging more applied Research and Development activities. This is an essential feature of such a rapidly changing field as genetics.

e. Awareness of the important issues outlined later in this report means that genetics services are an important safeguard against the inappropriate or excessive use of genetic testing. They are also a major source of education for other clinicians who are increasingly requesting tests.

12. Because of the increasing use of genetic testing by all clinical disciplines it is important that the skills learnt by many clinical geneticists, not only in relation to collecting and analysing genetic data but also such general aspects as empathy, information giving, acknowledgement of family issues and confidentiality, are taught within the medical school curriculum.

Regulation of Genetic Tests and Reagents

13. The proposed European *In Vitro* Diagnostics Directive (IVD) is presently undergoing negotiations in the Council of Ministers' Economic Questions Working Group. It is a single market initiative with the primary intention to remove technical barriers to trade between Member States. On completion of the Directive and its acceptance, regulations will come into force in each Member State of the European Union which will in the future **require** *in vitro* diagnostic medical devices to be CE-marked in declaration of conformity with the Essential Requirements of the Directive in order to be placed on the market. These essential requirements are likely to address safety aspects, require that products meet the performance claims made by the manufacturer, and require that they do not adversely affect the health and safety of a patient, user or other persons. Genetic tests, and components of them, will in the future be regulated in this way. Such regulations are not intended to be the vehicle for addressing broader aspects surrounding the use of IVDs, such as ethical issues or their use in conjunction with counselling.

ISSUES ARISING FROM GENETIC TESTING FOR LATE ONSET DISORDERS

1. The rapidly increasing number of genes identified for late onset disorders, the special features of genetic testing and the particular nature of the disorders themselves, have combined to create a range of important issues that should be given careful consideration before genetic testing is offered as a service.

2. At present these issues arise mainly in relation to pre-symptomatic genetic testing of healthy relatives with a family history of serious late onset disorders with a clear genetic basis and commonly following dominant inheritance. The following sections deal primarily with this pre-symptomatic form of genetic testing.

3. Three somewhat different areas of genetic testing are dealt with separately later at Annexes A, B and C. These are: population screening for late onset disorders; the diagnostic use of genetic tests in clinically symptomatic individuals; and genetic susceptibility testing for late onset disorders involving multiple genetic and environmental factors. These three categories also raise important issues, but some are additional and specific, while our practical experience in these areas is extremely limited.

Why do people request genetic testing for late onset disorders?

4. Most healthy people requesting genetic testing do so because of perceived risk from their family history of developing or passing on the disorder. Depending on the condition, the perceived benefits may be:

   a. medical, with improved outlook for those detected as carrying the gene in terms of early medical treatment or surgical intervention, or possible preventive measures before symptoms develop. Equally those shown not to be at significant risk may be able to discontinue or avoid such medical procedures.

   b. personal, allowing freedom from uncertainty and planning of major life decisions, even when medical interventions are not feasible or helpful. Even an abnormal result may be preferable for such individuals to continuing uncertainty over many years.

   c. primarily for the benefit of family members, present or future. A normal test result may spare such relatives the harm that may result from continued risk and uncertainty.

5. Many people requesting genetic testing will have a combination of these aims and concerns. However others, even though in an apparently comparable situation, may not request testing, or may decline it, if it is offered.

Scientific and clinical validity of the test

6. Scientific and clinical validity should be clearly established before any genetic test is used in clinical practice, but validity may be especially difficult to establish in late onset disorders, where those carrying the genetic abnormality will be healthy for much of their life, prior to onset.

   a. *It must be clear that the genetic change found is causally related to the disorder, before it is offered as a direct genetic test. Validity should be based on published, peer reviewed evidence.*

   Normal variation in DNA is very great and considerable data may be required before it becomes certain that a genetic change found in association with a disorder is causally related, not coincidental.

   b. *The extent and limitation of the association between the test result and the disorder (false positive and false negative rates) should be accurately known.*

   Even when the scientific validity of the test is clear, there may be important factors that mean the association is not absolute. There may be situations where individuals with the genetic change never develop the disorder (eg. most males and up to 10% of women with mutations in the BRCA1 gene involved in familial breast cancer). There may also be reasons why a proportion of individuals with a normal test result are still at risk of developing the disorder; in particular it may not be possible to test for all

the known mutations in a gene, a proportion of cases may be the result of changes in a different untested gene (genetic heterogeneity), or as in breast cancer a large majority of cases have no known genetic cause.

c. *The use of linked genetic markers (surrogate markers close to but not part of the disorder related gene), poses particular difficulties in interpretation.*

Their use is dependent not only on a correct clinical diagnosis but also on family structure and other factors. Any possible error associated with recombination between marker and disorder gene should be accurately known and be small.

d. *Any correlation between test result and disease severity or age at onset should be recognised, but should only be incorporated into the test result as given to the individual if it is validated and is sufficiently strong to be of use in the context of an individual result.*

When an abnormal genetic test result is obtained it usually does not allow any clear prediction of severity or age at onset, but some specific mutations are being found to be associated with severe or with less severe disease; age at onset has likewise been found to be statistically associated with the extent of the genetic change in some mutations that are variable in size, as seen in Huntington's Disease and myotonic dystrophy. This type of information may be extremely important to those tested, but it should only form part of the test result as given to the individual if the associations have been validated and if the information can be used in interpreting an individual result rather than an overall series. The information should, if requested, be provided as part of post-test counselling.

Is the testing "service ready?"

7. Even when a genetic test is validated scientifically, there are further considerations that need to be established before the test can be considered as valid in a service setting, rather than in research.

a. *The error rate and failure rate should be known to those requesting the test and those being tested.*

This represents the technical or human error rate, as opposed to the inherent false positive or false negative rate. It may be influenced by the complexity or fallibility of technical procedures, by human error or (as in some prenatal tests) by cells failing to grow in tissue culture.

b. *Where possible the disorder and particular genetic change being tested for should be confirmed as present in an affected family member.*

If confirmation is not possible the implications for interpretation of an apparently normal result should be clearly explained. These will vary according to the disorder involved.

Laboratories undertaking genetic testing

8. The following issues are important, but are not specific to late onset disorders.

a. *All laboratories providing a genetic testing service should be appropriately accredited for this as well as taking part in internal and external quality control schemes.*

All laboratories offering genetic testing services should be appropriately staffed and equipped, and should:

i. be an appropriately accredited laboratory;

ii. join an appropriate external quality assessment scheme; and

iii. perform adequate internal quality control.

All such systems should reflect current best practice. Examples of **i.** and **ii.** are registration with a National Accreditation Body and conformity with the requirements of BS EN ISO 9002 (Formerly BS 5750 Part 2). Continued registration is dependent on satisfactory audits that are performed at prescribed intervals by the Accreditation body to ensure compliance with the appropriate standards, and accreditation by the Clinical Pathology Accreditation (UK) Ltd. Accreditation by this company involves external audit to standards reflecting best professional practice for clinical laboratories.

ACGT believes that such standards are applicable to all laboratories performing genetic testing services, including those in the NHS.

The accrediting body may vary according to the nature of the genetic testing, which may be based on DNA, chromosome or biochemical analysis, but it is essential that the main requisites of a genetic testing service are addressed, regardless of the technology used.

b. *Genetic testing should be undertaken only by laboratories closely linked with other genetic services.*

Many general pathology laboratories use genetic techniques to investigate disease, while the detection of somatic (non-inherited) genetic changes forms an important part of laboratory analyses of tumours. Although the technology may be the same, genetic testing for inherited disorders, in particular pre-symptomatic testing, requires different approaches, and should not be undertaken by general laboratories unless they form part of or are closely affiliated to a genetic testing service, and meet the provisions for accreditation and level of expertise appropriately.

c. *Research laboratories should not normally be the basis for a genetic testing service; where they are, because of the rarity of the disorder or other factors, the service delivered should aim to conform to the same standards expected in an approved service laboratory.*

If the early stage of development of the genetic test means that the field is still at the borderline of research and service, this should also be made clear, and the test should not be offered or promoted as an established service. Some genetic disorders are so rare that only a research laboratory may be able to undertake testing. Such laboratories should only offer a service if they follow expected service standards, but equally it should be made clear to those requesting testing or being tested that the research nature of the laboratory may involve limitations.

d. *There should be full, equitable and satisfactory access to genetic testing services throughout the UK.*

Current demand on laboratory and clinical genetics services makes this difficult to achieve and emphasises the need for cooperation between centres, particularly in relation to rare disorders.

Information needed by those being tested

9. The communication of various types of information outlined in this section comprises a considerable part of the process known as genetic counselling whether it is given by clinical geneticists, genetic nurse specialists or by other professionals.

a. *Information on the disorder being tested for should be full, accurate and appropriately presented, in a clear and simple manner that is readily understandable.*

While some individuals requesting predictive genetic testing for a late onset disorder will have extensive experience of the condition from their own family, others will not, or the information may be incomplete. This information is essential if individuals are to make appropriate decisions regarding testing. Written information should be provided in an understandable form, and particular consideration should be given in providing information to those with hearing or visual disabilities, or whose first language is not English.

b. *Full information should be provided on the test, its consequences and limitations, and its scientific and clinical validity.*

Some individuals being tested may have inaccurate expectations as to what a genetic test can deliver in terms of removing or confirming risk, or in predicting severity or age of onset. This may also apply to some clinicians requesting tests.

c. *Individuals should be fully informed of potential adverse consequences, such as for insurance, employment, and effects on other family members.*

Experience with genetic testing for Huntington's Disease and other serious late onset disorders has shown that while many individuals are well informed in advance, there are almost always significant issues that have not been already considered and which are important to enable them to make an appropriate decision.

Genetic testing may directly or indirectly have effects on family members who have not themselves requested testing. Thus an abnormal result in a person at 25% risk for a serious genetic disorder (with an affected grandparent), would imply that the intervening healthy parent would also be likely to develop the disorder, even though they did not wish for testing. Such implications need full discussion before testing.

d. *While written information is important, complex information should be provided face to face by an appropriately trained and experienced person.*

In genetic testing for serious late onset disorders, there are frequently complex and sensitive issues that require discussion, rather than simply provision of information. While not all such issues require involvement of specialist genetics services, these have an important role when they are complex and time-consuming, or when they involve members of the extended family. Genetic Nurse Specialists and other professionals may play an important role in pre-test preparation and in post-test home visiting to ensure that necessary support is explored and that information has been received and understood.

e. *Voluntary organisations involved with genetic disorders can also be a valuable source of information for those considering genetic testing.*

Many voluntary bodies have helped to provide valuable guidance for testing in their particular field, both in terms of written information and of support from their staff.

f. *Individuals should be given adequate time to absorb the information provided, before a decision is taken to be tested or a result is given.*

For serious late onset disorders such as familial cancers and Huntington's Disease, a two step approach has been found to be important in allowing time for reflection. Since a premium is often placed on avoiding delay in other laboratory testing situations, it is important that this time interval is protected.

Consent to genetic testing

10. Where an individual is able to give consent this is required before testing is undertaken.

a. *In the case of presymptomatic genetic testing of healthy individuals, written consent should always be obtained. The main purpose of written consent is to provide evidence that consent was sought and obtained and that an explanation of the proposed procedure was given. Written consent is not in itself a substitute for careful face to face explanation.*

Written consent is already established practice in presymptomatic genetic testing for Huntington's Disease and most other serious late onset disorders. As such testing becomes more widespread this should be a general policy. In diagnostic testing of symptomatic individuals current policy is more variable; we consider written consent desirable here also.

b. *Consent should be specific.*

New technology may make it possible to test for many genetic diseases at one time and could generate results relating to disorders that the individual was not even aware of, a situation which should be carefully avoided. If testing is for a group of allied disorders, this should be made clear when consent is being obtained.

c. *Where an adult is permanently incapable of giving consent (eg. because of a learning disability) the legal position is that the decision will be made by the doctor responsible for the person's clinical care. They will be guided by the best interests of the individual and where appropriate take into account the views of the family or other close carers. It should be noted that the best interests of the individual and of the family and close carers may not necessarily be the same. When assessing an individual's best interests consideration should not be limited to "best medical interests". Other factors that may be considered include: psychological health, well being, quality of life, ethical, moral, spiritual and religious welfare, relationships with other family members and financial interests. If the incapacity is temporary, genetic testing should be delayed until consent is possible unless it is essential in the individual's therapy (the special case of testing children is considered below).*

The issues of testing of the incapacitated are complex and in relation to genetic disorders it is necessary to distinguish between the situation in which testing is necessary in furtherance of the individual's treatment, when it will be clearly in their best interests; where testing might be proposed essentially in the interests of furthering the diagnosis, but without implications for treatment; and where testing is pre-symtomatic, with no symptoms likely to be related to the disorder being tested for.

In psychiatric practice, mental illness may result in temporary incapacity to consent and the clinician must then be guided by consideration of the individual's best interests. Where possible testing should be delayed until the patient has recovered. However, many mentally ill people retain the capacity to consent but assessment of that capacity can at times be difficult. It is important to guard against the risk of an individual giving consent during a period of mental illness which they would have withheld had they been in normal health by ensuring that the individual fully understands the nature of the proposed test and its likely consequences and is able to balance these issues appropriately in making their decision.

d. *Consent should be freely given, without pressure from third parties.*

There has been public concern that pressure for genetic testing for serious late disorders might come from insurers or employers, though currently there is no clear evidence of this happening directly. The insurance issues raised by genetic testing have been addressed by the Human Genetics Advisory Commission amongst others.

A more frequent, and more difficult to resolve, issue is that of pressure to be tested from family members. This may only be recognised when the issues are discussed before testing. Clinicians should likewise not exert pressure and should present information in a way that permits a free choice. It should be noted that consent given under pressure is not valid.

11. Support in relation to genetic testing

a. *Appropriate support in preparation for and subsequent to genetic testing should be considered as part of the genetic testing process.*

Genetic testing for late onset disorders may have consequences extending many years ahead and affecting multiple family members. The testing process itself may also be extremely stressful, but experience from Huntington's Disease and familial cancers suggests that even serious adverse results can usually be well coped with if the person tested is fully prepared and has adequate support. The likely needs for support should be considered and planned for as part of the testing process, otherwise unexpected serious problems could be generated for the individual, for family doctors and for other staff.

As much of the long-term support, follow-up and co-ordination will devolve to primary health care teams it is important that they have the mechanisms to cope with this duty. Such mechanisms include suitable record keeping of genetic tests taken and family history data.

b. *Consideration should be given to the cost of the potential support needs for genetic tests when evaluating and commissioning genetic services.*

The cost of associated genetic counselling and related measures should be costed in addition to and separately from the laboratory aspects of a genetic test. Some genetic tests for late onset disorders, such as that for polyposis coli, may avoid other costly, and for the patient potentially risky, investigations if individuals thought to be at risk can be shown to be free from the relevant genetic mutation. The potential effects of abnormal test results in terms of long term support and medical investigations also need to be considered when the likely overall benefit of the test is being assessed.

12. "Over the counter" genetic testing for late onset disorders

a. *A previous ACGT report has already recommended against such testing and we support this conclusion.*

ACGT considers that the main role for genetic testing supplied direct to the public should be limited to determination of carrier status for inherited recessive disorders in which an abnormal result carries no significant direct health implications for the customer. ACGT considers that the provision of such testing poses fewer difficulties than provision of tests for inherited dominant and X-linked

disorders, chromosomal disorders, for adult onset genetic disorders regardless of inheritance, or for the genetic component(s) of multifactorial diseases including tests for somatic mutations.

The complexity of issues, both scientific and general, involved with genetic testing for late onset disorders makes "over the counter" testing inappropriate for this category of disorders.

b. *Any medically qualified person requesting or providing genetic testing for late onset disorders should ensure that they, or another suitably qualified medical practitioner, are actively involved in the process.*

There is a possibility that medical involvement may be "token" in nature, leading effectively to a situation equivalent to "over the counter" testing. This should not be permitted.

13. Pre-symptomatic Genetic Testing of young children for late onset disorders

a. *"Over the counter" genetic testing of children is not appropriate.*

This was the conclusion of the committee's previous report and we continue to endorse this approach. The issues involved may be complex and they require professional involvement.

b. *Presymptomatic genetic testing of young children for disorders not currently influenced by therapy, and where onset is normally in adult life, is not recommended.*

Since very young children are unable to give consent, it is usually preferable for important decisions relating to their adult life to be left to a time when they can give consent themselves. This has also been the conclusion of other bodies, such as the Clinical Genetics Society working group report, the Genetics Interest Group and the US Task Force on Genetic Testing. The situation for a particular disorder will require reassessment in the light of advances in therapy.

c. *Any request to professionals from a person or persons with parental responsibility, for pre-symptomatic genetic testing of a young child unable to give consent, should be fully discussed in the context of the particular family situation, the nature of the disorder, the possible medical or other benefits, and the implications of testing for the child and family.*

Requests for such testing are frequently part of a more general need for information and require full and sensitive discussion with a professional who can provide this; they should not be simply accepted or declined on ground of general policy. If a child is to be tested, then the consent to be given for the test by the person or persons with parental responsibility should be on the basis that it is in the child's best interest. When assessing a child's best interests consideration should not be limited to "best medical interests"; the child's right not to know should also be taken into account. Other factors that may be considered include: psychological health, well being, quality of life, ethical, moral, spiritual and religious welfare, relationships with other family members and financial interests.

In assessing the best interests of the child the separate, and potentially conflicting interests of children, parents and other family members should each be given careful consideration. Where there is particular concern over what is in the interests of a child in certain circumstances, including where there is any dispute between those with parental responsibility for the child, it may first be necessary to seek an order from the court that the child be tested.

Section 8 of the Children Act 1989 provides courts with the power to make a "specific issue order" for the purpose of resolving a specific question in connection with any aspect of parental responsibility for a child, such as consent for a genetic test.

d. *Where genetic tests are being used diagnostically in the context of a child with a family history of a late onset disorder showing clinical features, it is essential that these clinical features are relevant to the nature of the family disorder.*

Genetic testing is increasingly part of diagnosis in paediatric practice. Where a late onset disorder may occasionally occur in childhood, there is the risk that in a child with symptoms, these might be unrelated to the disorder in the family; this would give a real risk of inadvertent detection of the gene being present, with serious implications for later life. Many clinicians do not at present recognise this potentially dangerous situation.

14. Genetic testing for late onset disorders in adolescents

Requests from adolescents themselves regarding presymptomatic genetic testing for late onset disorders deserve full and sensitive discussion, taking into account the individual and their family. If the adolescent is competent to give consent but there are no clear benefits, whilst some may suggest that ideally testing be deferred until the age of majority is reached, we recommend that they are entitled to make a personal decision on this matter after a full discussion and exploration of the issues.

Adolescents will vary greatly as to their emotional and mental maturity in relation to complex issues for later life. Current experience is that such requests are few but that they need full discussion with an experienced person. Pregnancy could be a special situation where testing needs to be considered.

In some late onset disorders, eg. familial adenomatous polyposis, for which treatment might be possible or for which screening might detect the condition at an early enough stage for treatment to be effective there is good reason to consider early testing of adolescents. In conditions such as familial cardiomyopathy where there may be a family history of sudden death in young family members there may be benefit in carrying out predictive testing in children and adolescents. The situation for each disorder requires careful consideration.

15. In all cases the views of a child or young person should be obtained where possible and taken into account in any decision.

Prenatal genetic testing for late onset disorders

16. *Prenatal genetic testing for late onset disorders should only be undertaken in the context of full genetic counselling.*

Requests for prenatal genetic testing are relatively uncommon for late onset disorders by comparison with serious childhood genetic disease. In general, requests are normally related to severe and untreatable disorders, where the individual concerned has experienced particular adverse effects of the disorder. Prenatal testing also can provide an option for those healthy individuals with an abnormal presymptomatic test result to have children free from the genetic disorder in question. There may be complex situations when a person simultaneously requests presymptomatic genetic testing for themselves and for their pregnancy.

Prenatal "exclusion testing" may need to be considered. For example, a woman at 50% risk of developing Huntington's Disease may wish to exclude the disorder in a pregnancy, whilst not wishing to know her own genetic status. Here the pregnancy is tested to determine whether the parent at risk has

passed on the genotype of the affected or unaffected grandparent, without testing for the specific genetic change associated with the disorder. This would either raise the risk of pregnancy to 50% or exclude the risk.

A particular issue arises when a couple decide to continue a pregnancy after an abnormal prenatal test result. This effectively gives presymptomatic diagnosis for the child after it is born, in contradiction to the recommendations given above. Although this may be an inevitable occurrence on occasions, full discussion in advance of prenatal testing should minimise it.

17. Issues of Prenatal Genetic Testing will be the subject of a later report from ACGT, and Preimplantation Genetic Diagnosis will be the subject of a joint report from the Human Fertilisation and Embryology Authority and ACGT.

Genetic testing and results of research studies

18. Most genetic studies leading to isolation of a disease related gene have involved analysis of affected and unaffected family members. Research on the genes for familial cancers and Huntington's Disease are examples of the importance of such family studies in late onset disorders. Stored DNA samples may be available for testing long after the original study has been completed. This gives the possibility of important results being generated when the individuals concerned may be unaware of this and may not have given specific consent. In the case of late onset disorder an abnormal result may be found in healthy relatives.

a. *Research studies that generate identifiable genetic test results on individuals should only be done with appropriate consent and following approval of a designated research ethics committee.*

Safeguards of this nature are particularly important since the stability of DNA creates the possibility of samples collected originally for a study with no individual implications being used subsequently to generate sensitive genetic information. Where there is a possibility of this, new consent and new research ethics committee permission should be obtained, or the samples should be made completely anonymous. There may be exceptional situations where research information needs to be used, as when an individual is deceased and no further material is available, or when no service is available outside a research setting.

b. *Individual genetic test information resulting from research studies should not be given to participants unless a clear and specific arrangement has been made at the onset; nor should it be placed in the individual's medical record without consent. Those giving consent to participation in research should be made aware that they will not normally receive genetic test information that forms part of research.*

Research information is, by its nature, provisional and the way material is collected and analysed will often make it unsuitable for service use. Where a research participant wishes to have genetic testing as a service this preferably should be done using a separate sample and following appropriate laboratory and clinical service standards. There may be exceptional situations when no service is available outside a research setting.

ANNEX A POPULATION SCREEING

1. Genetic testing for late onset disorders currently takes place mainly in the context of a family history of a disorder, with healthy relatives already aware of their genetic risk and requesting testing to resolve it. The increasing identification of specific genetic changes means that it is now technically feasible to detect those at risk outside the family context, and simplication of technology allows genetic tests to be used for screening large groups, even whole populations, for the detection of mutations underlying late onset disorders.

2. The use of genetic tests for such screening raises important issues over and above those already identified for family based genetic testing, including the following:

   a. The procedures for sample collection and laboratory analysis may mean a greater error rate than when testing results from an individual request. This must be clearly recognised by all involved and confirmation of the initial screening result must be built into the programme.

   b. Those being screened will be likely to know less about the disorder, the test and its implications than those requesting testing because of family history. There is a particular need to ensure full understanding and support, yet the large numbers involved make it likely that this may not be adequately provided, or that it is restricted to those proving to have an abnormal result.

   c. Where a genetic test is used to screen populations of affected individuals to detect a genetic subset (eg. screening all individuals with breast cancer for the BRCA1 mutation), those tested may not have been aware that the disorder was genetic in nature, with consequences for their relatives.

   d. Genetic screening raises general screening, epidemiological and public health issues that need consideration along with the specifically genetic issues. Issues include that screening should only be introduced where:

   - an appropriate and effective treatment (or follow-up action) is available, and
   - where treatment of the disorder at an early stage is of more benefit than treatment at a later stage.

   e. Appropriate support should exist to assist those who prove to have an abnormal test result. It is important to avoid prematurely "medicalising" healthy individuals.

   f. There is a potential conflict in genetic screening programmes between the aim of maximising choice for individuals and what may be promoted as "public health" goals of reducing the frequency of a genetic disorder. The aims of any screening programme should be made explicit from the start.

   g. The National Screening Committee considers all recommendations on the introduction of screening programmes including those involving genetic testing. For those screening programmes involving genetic disorders and testing there will be close liaison between the National Screening Committee and ACGT

ANNEX B DIAGNOSTIC GENETIC TESTING

1. Until recently, most genetic testing neither aimed at nor permitted a specific diagnostic use. Most of the issues discussed above are relevant to the testing of healthy relatives at risk for a late onset disorder that has already been diagnosed and recognised as genetic in nature, in an affected family member.

2. The specificity of genetic mutations for an increasing number of late onset disorders now gives the possibility of a primary diagnostic use of genetic testing in patients showing clinical features thought possibly to be due to a particular genetic disorder, even though there may be no family history of this. This increasingly important use of genetic testing is becoming an important part of overall medical practice and has implications different from those for presymptomatic (predictive) genetic testing.

   a. Diagnostic genetic testing will principally be requested not by the individuals themselves, nor by specialists in genetics, but by a wide variety of medical staff in different clinical specialties and in primary care. Most will have little detailed knowledge of medical genetics and many will be unaware of the important issues outlined in this document and elsewhere.

   b. Individuals being diagnostically tested will be symptomatic; the test result will help identify the nature of a disorder, rather than its presence or absence. However, the possible genetic nature of the illness may not be recognised by the person tested or by their relatives, and this should be made clear, and further information and support offered.

   c. Where a symptomatic patient is being investigated in the context of a family history of a late onset disorder, it is important to ensure that the clinical features support this diagnosis, or that other causes have been excluded as far as possible. If this is not done, an abnormal result may be obtained that is unrelated to the patient's symptoms. In effect a presymptomatic genetic test will have been done, without the appropriate preparation and other measures.

ANNEX C GENETIC SUSCEPTIBILITY

1. Genetic testing in clinical practice currently mainly concerns disorders following clear cut inheritance, determined by a single major gene. Most common disorders of later life however, do not show simple inheritance patterns, even though many are increasingly recognised as having an important genetic contribution to their pathogenesis. Common and serious late onset disorders in this group include diabetes, hypertension, coronary heart disease, Alzheimer's Disease and susceptibility to various infectious agents. Current research is resulting in some of the specific genetic factors being identified, giving the possibility of genetic testing by DNA analysis.

2. At present, there is considerable uncertainty as to the extent of involvement of the specific genes in these common disorders. There may be variation between different studies or different populations, while the finding of association between a particular genotype and disease is rarely based on longitudinal study. The particular genetic changes involved often form part of normal variation in a population, unlike the rare and specific changes associated with single gene disorders.

3. Testable genetic factors in common diseases rarely show an absolute association, but may relate to susceptibility by indicating an increased or decreased likelihood of developing the disorder. There will be many individuals showing the genetic change who will not develop the condition and many others with the disorder who do not show the particular change. The strength of the association will vary, and will represent only one of a number of factors that collectively determine whether the disorder will develop.

4. Genetic susceptibility testing is thus very different in nature from conventional genetic testing for single gene disorders and will rarely be relevant to the usual indications for genetic testing in that group. However, there may be important reasons for testing being undertaken, particularly as our knowledge of the genetic basis of common diseases becomes better established. These include:

   a. Greater understanding of disease mechanisms. It may be possible to separate broad disease categories into more specific groups and this may be relevant to therapeutic approaches.

   b. Identification of genetic susceptibility to particular drugs could become important in drug choice and dosage.

   c. Identifying genetic susceptibility to infectious diseases could be relevant in targeting immunisation and related programmes.

   d. Those identified as being at high risk for common chronic disorders could adjust their diet, lifestyle and other factors to reduce the risk of developing the disorder.

5. At present, the evidence that individual genetic testing will give clear benefits in any of the above respects remains preliminary. It is thus important that clinicians, and the general public, are aware of this, and that they do not expect the same accurate predictive and diagnostic results as can now be obtained for many single gene disorders. Data on the scientific and clinical validity will be particularly important to establish, as well as evidence as to real benefit to those tested.

6. One of the commonest and most important disorders of old age, Alzheimer's Disease, provides a valuable example of the issues that may arise in susceptibility testing. With the exception of a very small number of early onset families that follow a pattern of dominant inheritance, most cases are not clearly genetic in nature and are likely to result from a number of interacting factors. However one of these factors has been found to be the genetic marker ApoE which shows different forms in the general population, that are associated with different degrees of association with Alzheimer's Disease. A recent USA conference report has endorsed the general view that at present this marker cannot be used as an accurate test in either diagnosis or prediction. The report is valuable also in raising the broader issues involved, including the perspective of family members and carers, potential pressure for testing from insurers and nursing homes, and problems of

consent. It is also relevant that ApoE was originally studied as a genetic marker in relation to cardiovascular disease, with numerous research studies done, some recorded in patient notes, before any possible link with Alzheimer's Disease was recognised.

7. When genetic susceptibility testing for common late onset disorders does become established in clinical practice, it is likely that it will be applied in a very different way from the genetic tests established for clearly inherited disorders. It is unlikely that specialist genetics services will be significantly involved in the clinical and genetic counselling aspects; these, where necessary, are more likely to be dealt with by those involved in primary care and the relevant clinical specialties. Likewise the laboratory service patterns may well be different from existing genetic testing services; they may form part of more general laboratory services. There may be more use of testing for diagnostic purposes in symptomatic patients where pharmaco-genetics of appropriate treatment are an issue.

8. One subgroup of common late onset disorders requiring special attention is where a small proportion of cases prove to follow a clear single gene inheritance pattern. Important examples of this are seen in breast and colorectal cancer, where around 5-10% of cases are now known to be determined by specific genes of major effect, giving very high risks of disease in those with a particular genetic constitution. A very small number of families with early onset Alzheimer's Disease also follow such a pattern. Separation of such subgroups from the much larger proportion of cases where the genetic risks are relatively small, has proved of considerable importance to those families detected with a specific change and allows genetic testing in them to be considered along the same lines as for rarer genetic disorders. It is likely that comparable clearly genetic subgroups will emerge in other common late onset disorders as their underlying basis becomes clearer.

ANNEX D MEMBERS OF THE ADVISORY COMMITTEE ON GENETIC TESTING

Rev Dr John Polkinghorne KBE FRS	Chairman
Professor Kay Davies *	Dr Lee's Professor of Anatomy and Head of Department, Department of Human Anatomy, University of Oxford.
Professor John Durant	Assistant Director, The Science Museum, South Kensington.
Professor Peter Harper *	Professor and Consultant, Institute of Medical Genetics, Cardiff.
Dr Hilary Harris	General Practitioner, Manchester.
Professor John Harris *	Sir David Alliance Professor of Bioethics, University of Manchester.
Miss Wendy Johnston *	Specialist Health Visitor in Genetics, Belfast City Hospital
Mrs Christine Lavery *	Director of the Society for Mucopolysaccharide Diseases and founding trustee of the Genetic Interest Group.
Professor Sally Macintyre	Director, MRC Medical Sociology Unit, University of Glasgow.
Mr Matthew Parris	Journalist, The Times.
Professor Marcus Pembrey	Mothercare Professor of Paediatric Genetics, Institute of Child Health, London.
Dr Sultana Saeed	Formerly Lecturer in Law, University College London.
Mr Philip Webb	General Manager, Zeneca Diagnostics, Abingdon, Oxfordshire.

* Members of the LOD Subgroup.

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Telephone: 0114 268 7280

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Coxford Road
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OTHER USEFUL ADRESSES

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133-155 Waterloo Road
London SE1 8UG
Telephone: 0171 972 4017

British Society for Human Genetics
Clinical Genetics Unit
Birmingham Women's Hospital
Edgbaston, Birmingham B15 2TG
Telephone: 0121 627 2630

The main academic and professional society for human geneticists. Includes all members of ACC, AGNC, CGS and CMGS (see below), plus others.

Association of Clinical Cytogeneticists (ACC)
c/o Oxford Medical Genetic Laboratories
The Churchill, Headington
Oxon OX3 7LJ
Telephone: 01865 226022

The ACC promotes the science and service of clinical cytogenetics, to ensure the development and maintenance of professional standards and to act as an advisory body on behalf of the profession.

Association of Genetic Nurses & Counsellors (AGNC)
Department of Clinical Genetics
Western General Hospital
Crewe Road
Edinburgh EH4 2XU
Telephone: 0131 651 1012

The AGNC is one of the founding groups of the British Society for Human Genetics. Its role is to represent the interests of nurses and counsellors working in the field of genetics.

Clinical Genetics Society (CGS)
Clinical Genetics Unit
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Edgbaston, Birmingham B15 2TG
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Clinical Molecular Genetics Society (CMGS)
Regional Molecular Genetics Laboratory
St Mary's Hospital, Hathersage Road
Manchester M13 0JH
Telephone: 0161 276 6129

Clinical Molecular Genetics Society - part of the federated BSHG representing diagnostic molecular geneticists mostly working in NHS Regional Genetics Centres.

Clinical Pathology Accreditation (UK) Limited
45 Rutland Park
Botanical Gardens
SHEFFIELD S10 2PB
Telephone: 0114 268 6151

CPA (UK) Ltd accreditation programme provides peer review inspection of pathology departments to assess the quality of service provided.

Contact a Family
170 Tottenham Court Road
London W1P 0HA
Telephone: 0171 383 3555

Provides advice and information to families caring for children with disabilities, including inherited disorders.

Genetic Interest Group (GIG)
29-35 Farringdon Road
London EC1M 3JB
Telephone: 0171 430 0090

GIG is the UK alliance of charities and support groups for people who are affected by genetic disorders.

Royal College of General Practitioners
14 Princes Gate
Hyde Park
London SW7 1PU
Telephone: 0171 581 3232

Royal College of Pathologists
2 Carlton House Terrace
London SW1Y 5AF
Telephone: 0171 930 5861

Promotes the science and practice of pathology - the study of the cause and effect of disease - aims to increase public awareness of the broad scope of pathology and its role in saving and protecting lives.

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For more information about ACGT see the Department of Health Homepage:

http://www.open.gov.uk/doh/genetics.htm

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