SCREENING FOR FETAL AND GENETIC ABNORMALITY

KING'S FUND FORUM CONSENSUS STATEMENT

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The fourth King's Fund Forum was held in London from November 30 to December 2 1987. A panel of twelve listened to evidence from experts in public sessions attended by 250 people - including professionals from many fields as well as public and press. After closed sessions the panel discussed their report with the audience and the panel's consensus statement was then presented at a press conference.

The panel comprised: J. Grimley Evans (chairman), Eva Alberman, Ruth Ashton, Martin Bobrow, Peter Coe, Anthony Culyer, Marion Hall, Roger Higgs, Marianne Rigge, Hilary Rose, Alwyn Smith, Albert Weale.

Invited experts presenting evidence were: Ms E Anionwu, Professor D Brock, Dr H Cuckle, Professor G Dunstan, Professor M Ferguson Smith, Dr A Harding, Professor R Harris, Mr J Henderson, Professor B Hibbard, Mrs C Lavery, Dr S Macintyre, Ms M McTair, Dr B Modell, Dr M Pembrey, Dr M Richards, Professor C Rodeck, Mr S Thomas, Professor N Wald, Professor Sir David Weatherall.

Three factors have contributed to a growth in interest in the management of genetic and congenital impairments. First, the continued decline in mortality and morbidity due to other causes has increased the proportion due to genetic and congenital abnormality and led to demand for improved management of these conditions. Second the rapid advances in molecular biology provide radically new means for identifying the carriers of deleterious genes. Third, the Health for All initiative by the World Health Organisation has included a focus on disabled people.

A number of concerns have been expressed about the development of screening programmes and particularly those in which termination of pregnancy is an option. There is fear that a *de facto* programme of crude eugenics might be introduced. The claims of the fetus and the principle of the sanctity of life have been urged as

constraints on the mother's freedom of choice. There are concerns that the diversion of resources to screening may impair other services, including those for disabled people; that screening of high risk ethnic subgroups may foster racist attitudes; and that screening may lead to over-medicalisation of the process of child-bearing. There has also been fear that there might be increased stigmatisation of disabled people and their families particularly those who opted out of a screening programme.

A goal of our society is to promote the autonomy of its citizens and health services should contribute towards this goal. Although economic considerations are proper determinants of choice between different ways of attaining a goal, economic arguments should not in themselves determine what goals are to be sought.

Screening is only one possible approach to reducing disability. The primary prevention of environmentally determined congenital impairments, and improvement of the facilities and attitudes of society to physically or mentally impaired people, must be components of a comprehensive approach.

Screening should be seen as a means of acquiring information that increases the scope for choice by participants. While selective termination of pregnancy is one option to which this may lead, the success of a screening programme should not be judged only by its effect on the prevalence at birth of impairments, but by its total effect on the wellbeing of women and their families.

The purposes of screening for genetic and congenital disorders are:

a) to assist in informed decision-making before pregnancy. Accurate information on possible risks may allow some couples to avoid high-risk pregnancies, while other couples may elect to embark upon pregnancies that they would, without this knowledge, have avoided

b) to provide the option of not continuing with an abnormal pregnancy or to enable the mother and her family to prepare for the care of a disabled child

c) where fetal abnormality has been identified to allow optimal management of delivery and postnatal treatment.

Question 1

What kind of screening and diagnostic tests are possible for genetic and congenital disorders?

The disorders with which we are concerned include:

a) the 'single-gene' disorders, eg. haemophilia, muscular dystrophy and thalassaemia

b) the chromosome disorders, eg. Down's syndrome

c) congenital malformations eg. neural tube defects (NTD)

There are two broad but overlapping categories of procedures:

1) those which are cheap and safe, and therefore suitable for *screening* total populations

2) those which are expensive and/or invasive, suitable only for groups already known to be at high risk.

Multi-stage screening to define a high-risk population may begin simply by ascertaining age, family history and ethnic origin - eg. cystic fibrosis is common in Caucasian populations, sickle cell disease in those of Afro-Caribbean ancestry and Tay-Sachs disease in Ashkenazi Jews. *Tests for carrier status* of inherited disorders, such as the haemoglobinopathies and mucopolysaccharide disorders, can identify couples at high risk of having affected children. The techniques of the 'new genetics' will soon include detection of

the cystic fibrosis gene carried by about 5% of the UK population.

The level of risk at which a *diagnostic* test should be offered will depend on the natural history and severity of the condition screened for and the test's validity, safety, acceptability, availability and cost. Gene markers for many of the common disorders, including haemophilia, sickle cell disease, muscular dystrophy, cystic fibrosis, and Huntington's Chorea, are already available, and have reduced the numbers of unaffected male fetuses being aborted in the sex linked disorders.

Current techniques based largely on gene tracking require a prior detailed family study. More specific mutation site assays will circumvent this for many disorders, but not necessarily those caused by a variety of mutations eg. Duchenne muscular dystrophy.

Testing for fetal chromosome abnormalities is commonly undertaken at relatively advanced maternal ages, since the birth prevalence of Down's syndrome is strongly age dependent. Recent evidence shows that low maternal serum level of alpha fetoprotein (AFP)at 16 to 20 weeks of pregnancy is an important independent predictor of Down's syndrome, which may increase the efficiency of detection of this disorder.

Fetal material for laboratory analysis may be obtained by chorion villus sampling (CVS), by amniocentesis or by sampling fetal blood or other tissues in the second trimester. Only CVS is useful much before the 16th week of gestation, but it is not applicable to the detection of NTD. Neither the risks of CVS nor the error rates in subsequent chromosome analysis have yet been fully evaluated, but the procedure is thought to cause more miscarriages than amniocentesis.

Screening for NTDs is widely practised by maternal serum AFP mesurement at 16-20 weeks gestation as estimated by ultrasonic scan. The diagnostic procedure may be an amniocentesis to obtain

fluid for measurement of AFP and acetyl-cholinesterase, with extremely high accuracy rates (but with a small additional risk of miscarriage) or ultrasonic scanning, which is not invasive, but seems to have higher false negative and false positive rates. The widespread replacement of AFP screening by ultrasound scanning would be premature until better data are available.

Routine ultrasound scanning performed at early gestation for confirmation of gestational age and presence of a heart beat, will sometimes incidentally detect fetal malformations. In contrast, detailed anomaly scanning at 18-20 weeks is, in experienced hands, highly effective in the detection of many malformations.

Identification by ultrasound in late pregnancy of conditions such as diaphragmatic hernia or exomphalos allows delivery at an appropriate time in a hospital with immediately available paediatric surgery.

Neonatal screening to detect treatable conditions (P.K.U., sickle cell disease, hypothyroidism) is widely practised, whereas screening for cystic fibrosis and muscular dystrophies have not come into common use.

Question 2

What are the benefits and costs of these tests?

There is evidence that some programmes pay for themselves from the resources saved by having fewer disabled people. If the condition is relatively common and causes serious disability, these savings can be substantial. Even if this were not so, such programmes might be justifiable by their social and clinical outcomes. At least 6,000 (one in every hundred) babies born alive each year in the UK are seriously impaired in spite of nearly 2,000 planned terminations for fetal and genetic abnormalities.

In the past new procedures have not been subjected to scrutiny of cost and benefit but evaluation research of this type is necessary, given competing claims on resources. A characteristic of such research is that costs in the sense of value of resources used are generally presented as quantitative and monetary. The outcomes, whether positive or negative, are descriptive and qualitative, and are often taken as no more than points for consideration. The principal justification for providing screening programmes lies in such currently unquantified effects. Examples of benefits are: the provision of authoritative information, relief from uncertainty, support during a period of crisis and the expansion of an individual's scope for exercising choice. Examples of potential harms are: the introduction of worrying delays while confirmatory tests are conducted, the distress that may result from false positives and the illusory reassurance given by false negatives. Another set of considerations concerns long term social effects such as changes in the status and integration of disabled people.

If only monetary information is considered there is a danger that the quantified may drive out the important in a kind of Gresham's Law of screening.

This is a particular danger when the quantified costs of a service exceed the subsequent financial savings. A further difficulty occurs when the costs of the tests are borne by one sector of the community and the savings are found in another. This may happen when a preventive programme funded by the NHS reduces costs later for a family or a social services department (eg. screening for Down's syndrome).

The only secure way to avoid biased appraisals is to attempt to account comprehensively and imaginatively for all possible costs and benefits. The weights attached to the components may differ according to the level at which a decision is being made. Those used in determining a budget for a population would not necessarily correspond to those used in a clinical encounter.

Question 3

What social and ethical issues arise?

The development and improvement of screening services should not be seen as an alternative to improving services for people who have impairments. A woman's informed and considered decision not to participate in a screening programme should be respected and appropriate care and support offered to her, her baby and her family. Decisions require the free and informed participation of the woman: where there is a conflict of interest between parents it must be the woman who ultimately decides. She should however be entitled to involve her partner as much as she wishes, in particular to support her during the course of a termination. If it is desirable to include relatives and partners in screening, this must also be based upon informed consent.

A woman's access to a screening or diagnostic test should be independent of any decision she may make about the continuation of the pregnancy.

Genetic tests bring particular problems of confidentiality. Providers must take adequate steps to safeguard the interest of the screened individual. The woman should have access to information about herself and the pregnancy. Some parents prefer not to be told the sex of the fetus, and this wish should be respected. Where the sex is revealed, that fact alone should not be a reason for termination.

The early stages of pregnancy are not the best time to inform and educate people about the types, extent and purposes of screening. Education should start in schools; health, including basic genetics, should be in the core curriculum.

Government and health authorities have an ethical responsibility to ensure that screening services are provided equitably. The quality of, and access to these services, should meet the reasonable expectations of an informed public. Doctors and other professionals

have a duty to provide services that are both technically competent and sensitive to the personal dilemmas that screening involves.

There is no consensus about the meaningfulness or extent of any 'rights' of the early fetus. Some people have deeply held views against abortion, but while such a personal view should be respected people should be allowed to follow their own conscience in this matter. There is evidence that a conscientious objection to abortion on the grounds of fetal abnormality is the view only of a minority in our society.

The rapid pace of technical advance will open the prospect of prenatal testing for anomalies of a wide range of severity. Society may justifiably place limits on the types of conditions for which to provide testing.

Question 4 & 5

The criteria for provision of screening programmes; their organisation and monitoring

Screening for fetal and genetic disorders can be carried out on the fetus, on the newborn, or would be parents. A programme of screening should ensure that each screening test is offered at the optimal time.

While there should be a nationally agreed policy for the provision of screening programmes the pattern of screening required dictates a need for facilities to be organised at supraregional, regional and district levels depending on disease prevalence and the complexity of the investigational procedures.

A single person should have overall managerial responsibility for the entire process from public information and primary ascertainment to post-delivery care and support. This person would be responsible for quality assurance, and for co-ordinating

the relevant professionals, and fostering support networks with self-help groups within the community. Such people should be identified at regional and district level. There is disturbing evidence of current inadequacy in communication among professionals and between them and the users of the services.

Once decisions have been made about what screening procedures are to be offered it will be possible to decide on which aspects of the screening programme require to be associated with a specialised clinical genetics service and which can satisfactorily be carried out by hospital and community obstetric services. Basic pregnancy screening is best carried out as part of normal antenatal care.

The confirmation of dates and the screening procedures should be carried out as early in pregnancy as is possible, and delay will affect outcome.

The next stage of the screening programme involves the further investigation of those found positive to the screening tests. Further investigation may require referral to more specialised services. In a significant proportion of cases the necessary investigations will not be completed by the middle of the second trimester. Current proposals to remove the availability of abortion above 18 weeks would severely restrict the potential benefit of screening programmes and are opposed by the panel. Any reduction in the availability of abortion couched in terms of weeks and not in terms of viability will not deal adequately with this issue.

At present, the pregnancy screening techniques with general application are largely limited to those concerned with neural tube defects and Down's syndrome and to the haemoglobinopathies. In the future, screening for heterozygotes for the haemoglobinopathies and possibly for common recessively determined disorders such as cystic fibrosis will seek to identify carriers during their

pre-pregnancy period and this will require a different pattern of organisation.

Carrier testing for heterozygote status for those genes for which particular ethnic groups are at high risk must be sensitively performed to avoid any suggestion of racism, and must involve the full support and understanding of the individuals and community concerned.

A regional genetic service will require an effective database including some form of genetic register and a DNA bank.

Another essential requirement of a genetic and screening service is the provision of counselling. Experienced specialist counsellors should form part of a genetics service but training in counselling will also need to be more widely provided for health professionals in obstetric and community services. There should be specialised genetic counselling available to mothers at every stage of the screening programme. If a termination of pregnancy ensues, the mother should have access to a bereavement counselling service which should be available in every district to those who have undergone termination of pregnancy for whatever reason. An introduction to the appropriate support groups may be very helpful for mothers with affected fetuses whether terminated or not.

At a national level there will be a need to promote genetic services and initiatives from Royal Colleges, on post graduate training for this specialty are to be commended. There is evidence that basic education in modern genetics is deficient in the curriculum of medical students and other health professionals, and this should be remedied in basic and post basic training.

The Health Education Authority should initiate a specific programme to raise general public understanding of advances in genetics and of the developing services associated with them.

Monitoring and evaluation of screening services needs to be organised both in relation to process and to outcome. Definition of target groups makes it possible to assess the extent to which members of some groups have been offered screening, have taken it up, have been found to be positive and have taken up intervention options. Whenever possible confirmation of abnormality in terminated pregnancies should be sought. Simple systematic statistical monitoring along these lines is a logical extension of suitably devised recording procedures. Because of cross boundary flows for the services, district-based records systems are inadequate.

Outcome monitoring is essential despite the undoubted difficulties posed by the breadth of the objectives of screening. Monitoring of changes in birth prevalence of the disorders for which screening is carried out provides an assessment of only one legitimate objective. Facilitating access and choice in matters of reproduction are much more difficult to monitor and this may require specific research.

Research and development is required, not only for the technical advances of more effective screening but also for the identification and assessment of service innovation - especially in respect of the nature and adequacy of counselling services.

The complexity of these issues suggests a need for planning and co-ordination at national level with a remit to see that the good quality services at present deployed in some regions should be available throughout the country. Services should be able to respond appropriately to the opportunities to be expected from the new genetic technologies. These developments seem inevitably to require new monies not provided from within the national health service

For further copies of this statement please contact the King's Fund Centre, 126 Albert Street, London NW1 7NF.

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