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Report on Genetic Screening and Testing

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1. This Report has been prepared on behalf of a Subcommittee established by the International Bioethics Committee of UNESCO (IBC). It has been amended in the light of discussion both by the Subcommittee and by the full IBC at its September 1994 meeting. The Subcommittee's members are listed in Annex C. The Subcommittee's Rapporteur, Mr D. Shapiro, had the benefit of written contributions and of responses to a brief questionnaire by his Subcommittee colleagues; he also received copies of papers by some other members of the IBC. These are acknowledged here. He also had the benefit of discussions at several meetings with members of the IBC's Bureau.

2. The structure of the Report is as follows:

- What are the problems and why are these problems pressing? (paragraphs 3-14)
- The ethical issues to be faced (paragraphs 15-19)
- Contribution to a possible declaration (paragraphs 20 - 30)
- Contribution to a possible convention (paragraphs 31 - 33)

I. WHAT ARE THE PROBLEMS?

3. The problems that have been identified fall under five very general heads:

1. Ethical limits to genetic screening and testing.
2. Public policy in genetic screening.
3. Genetic information and privacy.
4. Education and civic freedom.
5. Accuracy and quality control.

Three reports published since the first meeting of the IBC have demonstrated wide agreement on the nature of the problems, and also on how to resolve them. These reports are:

- Institute of Medicine (USA)
  Assessing Genetic Risks: Implications for Health and Social Policy
- Ministry of Health and Social Affairs (Norway)
  Biotechnology related to Human Beings
- Nuffield Council on Bioethics (UK)
  Genetic Screening: Ethical Issues

A list of some 30 reports issued between 1989 and 1993 can be found in the *Nuffield Council*'s Report, which has been distributed to all members of the IBC, at pages 100-102.

4. It should be emphasised that these problems are the product of the success of medical and scientific research. As Professor J. Dausset has noted(1) medicine, which historically has been preoccupied with curing, has now achieved the power to predict. This is the first step on the road to effective preventive medicine. Thus, the successes of medical research can with care be translated into real benefits for human health(2). Care will need to be that these biomedical advances benefit the whole of the population and that access should not be confined to the more affluent strata in the societies of the developed countries(3). Some estimate of the possibilities of preventive medicine can be seen in this account of genetic disease:

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(1) Jean DAUSSET, *Report to the IBC on predictive medicine*.

(2) For an appreciation of the positive benefits to be gained see also Rev. Jean-Marie MPENDAWATOU, *Remarques complémentaires* ..., paragraph 1.

(3) Laila EL-HAMAMSY, *Issues relevant to genetics of populations*, Section III.

"*With the increasingly successful control of environmental diseases in the developed world, disorders that are either wholly or in part genetically determined have assumed an increasingly prominent role in childhood illness and mortality. It is estimated that these conditions account for about a third of admissions to paediatric wards and are a significant cause of childhood deaths. Many of them are associated with chronic and distressing mental or physical handicap, or both. Hence genetic disease poses a considerable burden on health, social, and educational services. In addition, it causes immense stress and misery for the families of affected children. But this is not all. It is now clear that many of the major diseases of unknown cause that afflict western societies - stroke, coronary artery disease, mental illness, and diabetes, for example - have an important genetic component, and that many forms of cancer are due to inherited or acquired changes in the genetic make-up of cells. Clearly, the totality of genetic disease, or disorders in which changes in our genes play a major role, are of great importance in current clinical practice in the developed countries*."(4)

The author goes on to note the importance of genetic disease in the developing world.

II. WHY ARE THESE PROBLEMS PRESSING?

Common Diseases

5. Genetic screening to date has been applied to relatively rare conditions. The relative rarity of the diseases for which there are screening programmes can be judged by the annexed Tables I and II (see p. 22 and 23). Table I summarises the state of genetic screening in a country where research is relatively advanced, the United Kingdom, in the middle of 1993. It should be noted that, apart from the neonatal testing of all new-born infants for phenylketonuria and hypothyroidism, the pilot programmes of genetic screening, mainly for cystic fibrosis, were used to detect diseases with a frequency of under 1 : 2.000.

6. Nevertheless, in two societies, Sardinia and Cyprus, genetic screening has been applied to beta-thalassaemia, which is a commonly prevalent disease in these two societies. In Cyprus as many as 1 : 7 is a carrier of the disorder and thus both members of 1 : 49 couples are carriers.

7. Recent research has begun to clarify the genetic basis of many cancers and heart diseases. Events have confirmed an estimate, given in 1990, that by the year 2000 genetic factors would have been uncovered for roughly one-quarter of cancers and heart diseases. This decade therefore presents us with the challenge of facing the implications of genetic screening for common diseases. Just how much of a challenge this may be can be judged by a recent specification of what doctors in the United Kingdom responsible for primary care will need to know about genetic testing for cancer(5). The specification is as follows:

- The risks, benefits, and limitations of genetic testing
- What pre-test counselling will be required
- What constitutes a significant family history
- How to assess risk in those at perceived high risk
- How to explain the consequent risks to the individual
- The implications of testing positive
- The implications of testing negative
- The implications for other family members
- Who should be referred for a specialist opinion
- Where patients should be referred - for example, family cancer genetics clinic

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(4) WEATHERALL, D.J. *The New Genetics and Clinical Practice*, 3rd ed., 1991 (page 1).

(5) AUSTOKER J., British Medical Journal, 1994, 309, pp 517-20 reviews the implications of genetic testing for cancer prevention in primary care.

- The effectiveness of current methods of screening and surveillance for those at high risk - that is, their limitations
- What post-test counselling will be required
- What advice can be offered to those not requiring referral for testing.

Multifactorial Disorders and Predisposition

8. The second facet of recent research developments is that our knowledge, hitherto confined to some 4.000 monogenic diseases, is now expanding to include multigenic and, more importantly, multifactorial conditions. Multifactorial conditions are those where the genetic element shows as a predisposition: that predisposition may depend on all sorts of "environmental" conditions to produce the expression of the disorder. The notion of a predisposition may be difficult for the general public and even for the legislator to grasp at first. In this respect the 1970s US campaign to combat sickle cell anaemia has become notorious, possible unfairly so[(6)]. To the pessimist a predisposition might be misinterpreted as condemning the carrier to the disorder. In fact, however, knowledge of a predisposition may give a powerful opportunity for the effective practice of preventive medicine.

Late-onset Diseases

9. The third issue that must be tackled is how late-onset diseases are to be treated. To date the paradigm case has been Huntington's Disease. This disease typically hits adults in their 40s. There is no treatment available. Typically it leads over a period of some years to a lingering death that can make huge demands on the family and other carers of the victim in the period of the illness. Most examination of the ethics of genetic screening on late-onset disease has hitherto been conducted in the context of Huntington's Disease[(7)].

10. The task now is to see if other late-onset conditions produce similar attitudes to genetic testing. Experience with Huntington's Disease has shown that very few of those potentially at risk wish to be tested. Genes potentially leading to a predisposition to Alzheimer's Disease have recently been identified. Should we expect the same reaction? The gene, BRCA-1, that predisposes severely to breast and ovarian cancer[(8)], has recently been identified and is estimated to produce roughly 80 per cent morbidity by the age of 70[(9)]. Preventive treatment for this condition is available. Mastectomy and removal of the ovaries after childbearing is currently recommended. Current experience suggests that women who are aware of familial predisposition to breast and ovarian cancer are quite anxious to be tested. This suggests that there are likely to be varying attitudes to screening for late-onset diseases depending on the nature of the condition and the availability of treatment.

Research in the Neurosciences[(10)]

11. New findings in the genetics of psychiatric and brain disorders are being rapidly developed. Researchers promise insight into the biological origins of human behaviour. Already genetic factors are being discussed for a wide range of behavioural problems such as substance abuse and sleep disorders as well as more clinically defined conditions such as schizophrenia. The centrality of the brain to notions of human consciousness, personality and dignity requires urgent discussion of guidelines to govern both research and its application in this area.

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(6) OFFICE OF TECHNOLOGY ASSESSMENT, *Genetic Monitoring and Screening in the Workplace*, 1990, pp 41-45.

(7) TIBBEN, A. *What is knowledge but Grieving? On psychological effects of presymptomatic DNA testing for Huntington's disease*, 1993.

(8) ALBERTSEN, H. et al., Nature Genetics, 1994, 7, 472-79.

(9) FORD, D. et al., Lancet, 1994, 343, 692-5.

(10) Prof. N. FUJIKI & D. MACER, *Intractable Neurological Disorders, Human Genome Research and Society*.

"Enhancement" and the Range of "Normal" Human Traits

12. Recent claims for the existence of "a gene for homosexuality" have made headlines around the world. Research into an apparent genetic component to violent behaviour has also raised the question of how far genetic screening should be permitted, either for so-called "enhancement" or to rule out human traits within the normal range of human variation. Biotechnology firms in the USA appear ready to contemplate the prospect that "*within a handful of years we will be able to do preimplantation embryo screening for traits such as height, hair pattern, hair colour, eye colour and the like*"(11).

13. These considerations raise the spectre of a renewed eugenics movement. Public opinion is understandably concerned to avoid any return to the eugenics policies pursued in some democratic states, let alone to the horrors of the Nazi regime.

Genetic "Fingerprinting" and Its Forensic Use

14. The technique known as genetic fingerprinting has been rapidly seized on for forensic use by police forces in the First World. There are three technical points about this use. First, can adequate quality control be assured? Second, there are very serious debates continuing about the statistical validity of the techniques currently being employed(12). Third, there are also problems about how to present these statistics in an appropriate manner for courtroom use(13). Questions of the liberty of the individual may arise with the introduction of widespread use of the technique and with the retention of DNA records on a large scale.

III. THE ETHICAL ISSUES TO BE FACED

15. The IBC may have to accept that it will be unable to resolve at least one of the ethical issues raised by genetic screening. There are such divergences on the issue of the termination of pregnancies because of severe genetic disorders that the IBC can aspire only to the calm discussion of the differences of opinion. It is noteworthy that the Council of Europe (see below, paragraph 31) has found it necessary to side-step that issue. It is even less likely that UNESCO or its IBC could attempt a resolution on a world-wide scale. This may be a disappointment to some. Three points need to be stressed. First, alternatives to diagnosis at the prenatal stage (see Annex B) need to be encouraged. Second, that particular debate may affect an increasingly small proportion of genetic tests performed in the future. Hitherto genetic screening has been applied in the main to single-gene, life-threatening disorders. Genetic screening will concentrate increasingly on multifactorial disorders where the genetic component may indicate a predisposition to the disorder. Third, the genetic screening programmes in Sardinia and Cyprus (see paragraph 6) have demonstrated that success does not require termination of pregnancies. Finally, societies must take heed of the side effects of genetic screening. Such programmes must not stigmatise those who suffer from genetic disorders nor detract from the provision of services and support to enable them to live as equal members of society.

16. The IBC might usefully concentrate on seeing if a consensus can be reached that termination of pregnancy is out of the question in cases where the aim is:

1. "enhancement" of human characteristics;
2. avoidance of particular human traits within the range of human normality;
3. avoidance of predisposition to treatable diseases.

17. The IBC might wish to heed the advice of our colleague Dr Qiu Renzong on addressing possible conflicts between different cultures(14), (15):

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(11) Hastings Report, Vol. 24, N° 4 (July-August 1994), p. 3.
(12) BALDING, D.J. & DONNELLY, P., Nature, 1994, 368, pp. 285-6.
(13) MATTHEWS, R., New Scientist, 16 April 1994, pp. 12-13.
(14) *Ethical issues ... in a multicultural context*, pp. 4-5.
(15) See also on Africa Rev. J.-M. MPENDAWATOU, *Remarques complémentaires* ..., paragraph 10 ff.

"*(1)* ***Respect and tolerance***

Respect for the culture of the other side, especially respect for the feelings the other side cherishes for its culture. and also respect for its change. Culture is a set of belief and value systems, some beliefs or values will change, some not, but deposited in people's deep mind. Actually, each system is reinterpreted again and again, and some practices based on this system rejected, the others kept intact. This may explain why old traditions can survive to nowadays. Respect entails tolerance. We think that some practices in other cultures are definitely wrong, but we have to be tolerant of them. Otherwise, what can we do? When Westerners came to China one century ago, they would think binding women's feet was an ugly practice. But what could they do then? Then even Chinese women themselves thought that there was nothing wrong in it, even that it was a symbol of women's social status, because it was not permitted for workers or peasants' daughters with lower social status. But gradually, the Chinese rejected this practice by themselves. In a multi-cultural society or world we have to be tolerant of what others do which we think to be wrong.

"*(2)* ***Dialogue and negotiation***

The only solution or resolution of differences or conflicts between cultures is dialogue and negotiation. (...)

"*(3)* ***Seek common ground while reserving differences***

During dialogue participants from different cultures can negotiate to identify their similarities and differences, and to see if these similarities can form a common ground or framework and which differences can be compromised, can be put aside, and discussed again at an appropriate time.

"*(4)* ***Patience***

Different cultures overlap. The overlapping area will be widened after each negotiation and mutual learning. But it is hardly possible to melt all different cultures into one. Even if we share some values, the priority will be different. That each culture reserves its particularities will not jeopardise working together to build up a common framework and take common action based on this framework. But the change or evolution of a traditional culture takes time because the change or evolution has to take place within. Any step imposed from outside will jeopardise the change, the evolution and the progress or spoil it, resulting into chaos."

In the light of the analysis set out above, we can see how far the international community has already moved by way of dialogue and negotiation. The Universal Declaration of Human Rights and the two International Covenants on Human Rights demonstrate that from certain internationally accepted principles we can derive those that apply to genetic screening:

- the respect for human dignity and worth;
- the right to equality before the law;
- the protection of rights of vulnerable individuals;
- the right not to be subjected without free consent to medical or scientific experimentation;
- the right to the highest attainable standard of physical and mental health;
- the right to protection against arbitrary interference with privacy or with the family.

In what follows, we have attempted to apply these general principles to genetic screening.

Ethical Limits to Genetic Screening and Testing

18. Should it be generally accepted that the introduction of screening programmes must be carefully monitored? The case for doing so rests on the following propositions:

- screening for some genetic disorders has become a practical possibility;
- medical knowledge about genetic susceptibility to common multifactorial conditions (for example, some heart diseases and some cancers) is still developing. Even with increased medical knowledge, the individual's risk may be difficult to evaluate;
- many of the ethical issues associated with genetic screening arise from the inescapable involvement of families (both blood relations and spouses);
- the benefits and disadvantages of screening programmes - for individuals, families and society in general - will need to be carefully assessed for each proposed screening programme. Factors to be taken into account include:
  - (a) the predictive power and accuracy of the genetic test;
  - (b) the benefits of informed personal choice in reproductive decisions and their consequences;
  - (c) the psychological impact of the outcome of screening for both individuals and families;
  - (d) therapeutic possibilities;
  - (e) possible social and economic disadvantages relating for example, to insurance and stigma;
  - (f) the resource costs and the relative priority, in view of limited resources, of establishing a screening programme; and,
  - (g) the alternative means of aiding individuals and families afflicted by the disorder.

19. Since the regulation of genetic screening programmes raises questions of such importance to society as a whole, the body responsible for the introduction of new genetic screening programmes should pay heed to the following considerations:

1 the gravity of the disorder: it will be necessary to assess how far the expression of the disorder varies between severe and light, and how far the varying severity is predictable from the genetic test. Such predictions are proving difficult for cystic fibrosis[16]. For Huntington's Disease (HD) some progress has been made in correlating age of onset and the number of CAG repeats[17]. (The gene for the protein in question normally contains between 6 and 37 repeats of the nucleotide sequence CAG - which codes for the amino-acid, glutamine - but those who inherit a chromosome 4 in which the number of CAG repeats lies above that range are at risk of developing HD);

2 what is the age of onset of the disease? As far as possible, policy should discriminate between the different late-onset disorders on the basis of the known expression of wish to be screened by those at risk from the disorder. It may be difficult at the start of a screening programme to estimate likely take-up. As soon as significant statistics on the take-up become available, these need to be taken into account in the management of the programme of the particular disorder. There must be for each programme the necessary mechanisms both for audit and review and for the feeding into the programme of the results of that review;

3 the availability of treatment. The greater the availability of treatment and the greater its effectiveness, the more substantial is the case for introducing screening for that disorder. Genetic predisposition to cancers or heart diseases in principle and in practice offer considerable scope for preventive medicine;

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(16) ROSENSTEIN, B.J., Lancet, 1994, 343, pp. 746-7.

(17) KREMER, B., New England Journal of Medicine, 1994, 330, pp. 1401-6, and material cited in refs. 24, 28 and 29.

4 what boundary should be placed on genetic screening and testing? At what point does the potential screen for human traits lead to the undesirable practice of eugenics? For example, can the screening of embryos for gender choice be considered acceptable outside the therapeutic avoidance of severe X-linked disorders?

IV. CONTRIBUTION TO A POSSIBLE DECLARATION

Ethical Limits to Genetic Screening and Testing

20. Genetic screening and testing should be restricted to conditions that seriously affect the health of the individual. Genetic screening and testing may be particularly appropriate to those conditions that result in early death.

21. It is inappropriate to screen for conditions that do not seriously affect health and/or which fall within the normal range of human traits.

22. Great care must be exercised in initiating screening programmes and testing for late-onset diseases. It will usually be appropriate to screen for those late-onset diseases for which preventive treatment is available. For late-onset diseases where treatment is not available, great care must be taken before initiating any screening or testing. In most such cases, it is unlikely to be appropriate for any testing to be done before adulthood.

Public Policy and Genetic Screening

23. Genetic screening should be voluntary and without any element of compulsion. It may be appropriate for the state to emphasise the possible advantages of screening, in accordance with cultural traditions and medical capabilities.

24. In genetic screening programmes, as in all screening programmes, a balance has to be kept between the potential benefits of screening for a particular genetic disorder as against the potential harm, for example the creation of undue anxiety through the process of screening. The state should ensure that the appropriate body is created to consider that balance. The form of that body will naturally vary according to the traditions of the particular society. It should contain representation both of appropriate expertise and, more generally, of the community. Whatever its formal composition the body should review the empirical results of pilot programmes; another task is to monitor subsequent programmes.

25. Genetic screening may be regarded as a matter of public health policy. It follows that the state should assume certain responsibilities (the executive responsibility for these matters may, in some states, be delegated to professional bodies or to bodies with a high proportion of professional membership). These responsibilities include the following:

1 ensuring **adequate information** is available to the person being screened or tested;

2 provision of **appropriate support and/or counselling** for those being screened and tested and for their families, where this is appropriate;

3 ensuring the maintenance of **medical confidentiality**. This is no easy task in the face of the growing tendency to store medical information in computable form;

4 protection against the **misuse of genetic information by third parties**. Experience in some countries has already shown that problems may be raised in connection with **employment** and **insurance**;

5 ensuring **equitable access** to medical treatment.

Genetic Information and Privacy

26. The individual being screened or tested must be presumed to have a right to expect the information derived from the test to remain private. The concept of privacy varies between societies. In some societies privacy may be regarded as attaching to the individual; more

generally in other societies privacy may be seen as a family matter. It is, therefore, important to make it clear to the person being screened how far the information gained will be of use to other members of the family and how far it may be appropriate to assume that certain information should be passed on to the other members of the family.

27. The duty of the health professional is to secure the appropriate privacy for genetic information that is laid down by the norms of the particular society. The professional bodies charged with supervising the particular health professions involved in genetic screening therefore have a general duty to lay down guidelines on the handling of genetic information so that the individual being screened enjoys the degree of privacy appropriate to the given society.

Education and Civic Freedom

28. The threat of abuse of genetic screening requires safeguards. Public understanding of human genetics should create awareness of the dangers both of eugenics and of the possible stigmatisation of those carrying or suffering from genetic disorder. This need for an understanding of human genetics should be borne in mind by those responsible for the educational curriculum and for public health education(18).

29. It should be recognised, however, that there are limits to the effects of educational work, however good. Essential, therefore as safeguards against abuse are provisions for:

- adequately informed and free consent
- confidentiality of genetic information
- appropriate restrictions on third party use of genetic information, for example in respect of employment and insurance.

Accuracy and Quality Control

30. The safety and effectiveness of genetic tests should be established before they are used routinely and, even when that comes to pass, great care should be taken in performing the tests and interpreting the results. While the regulatory burden should not impede further development of tests or the offering of genetic testing services, nevertheless the nature of genetic tests and their interpretation and the magnitude of the personal and clinical decisions which may be made based on those results - including the abortion of affected foetuses - warrants a standard with close to "zero-error" chance of error for such tests. Consequently, laboratories and personnel performing these tests should participate in proficiency testing programmes, including review of the interpretation provided by the laboratory to referring doctors. (On communication to the person who has been screened, see paragraph 25(2).) It may be necessary to devise systems whereby laboratories with any error should be placed on probation and proficiency testing repeated, preferably using blinded methods. Unless the laboratory can attain this standard, its certification to perform this test should be removed.

V. CONTRIBUTION TO A POSSIBLE CONVENTION

31. It may be useful at this early stage of the IBC's work towards a possible legal instrument to take careful note of the work of the Council of Europe, which in July 1994 published a Draft Convention *for the protection of human rights and dignity of the human being with regard to the applications of biology and medicine: Bioethics Convention, and explanatory report*. The critical reading below of the draft articles on genetic screening is intended to demonstrate how difficult is the task imposed on the IBC. Can the IBC hope to improve on the diplomatic ambiguities in the Council of Europe's drafting?

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(18) This point is emphasized in Dr L. VIDAL-RIOJA’s contribution on genetics in Argentina, *Genetic screening and testing.*

32. The draft articles relevant to genetic screening and tests are as follows:

Article 16 (Human genome)

An intervention on the human genome may only be undertaken for preventive, therapeutic or diagnostic purposes and as long as the aim is not to interfere with the germ cell line.

Article 17 (Tests predictive of genetic disease)

Tests which are predictive of genetic diseases or that may identify a genetic predisposition to a disease may only be performed for health purposes or for scientific research linked to health purposes.

Article 18 (Communication of results)

The communication of results of genetic testing outside the health field may only be allowed in accordance with the provisions of Article 2 paragraph 2 of this Convention.

[Paragraph 2 of Article 2 is as follows:

"*No restrictions shall be placed on the exercise of the rights contained in this Convention other than such as are prescribed by law and are necessary in a democratic society in the interest of public safety, for the prevention of disorder or crime, for the protection of public health or for the protection of the rights and freedoms of others*".]

33. The IBC should note how relatively brief are the provisions tentatively agreed by the governments represented in the Council of Europe. Even so, those brief provisions may not necessarily be acceptable outside Europe. Points to note about the provisions include the following:

(1) Article 17 limits tests to "*health purposes or for scientific research linked to health purposes*". The commentary at paragraph 117 states:

"*Therefore, predictive genetic testing as part of pre-employment medical examinations, is excluded whenever it does not serve a health purpose. However national law may allow for the performance of a test predictive of a genetic disease outside the health field for one of the reasons and under the conditions provided for in Article 2 paragraph 2 of the Convention.*"

Paragraph 2 of Article 2 might appear to give much leeway for testing other than for health purposes.

(2) How tightly does Article 17 circumscribe the potential activity of insurance companies? The commentary at paragraph 118 states:

"Article 17 prohibits predictive tests for reasons other that health or health-related research, even with the assent of the person concerned. This covers the field of insurance, for example. An insurance company will not be entitled to subject the conclusion or modification of an insurance policy to the holding of a predictive genetic test. Nor will it be able to refuse the conclusion or modification of such a policy on the ground that the applicant has not submitted to a test, as the conclusion of a policy cannot reasonable be made conditional on the performance of an illegal act."

It might be argued, however, that Article 2 paragraph 2 would allow use of tests to guard against what might be defined in some states as attempts to defraud insurance companies. This is explicitly recognised in the commentary at paragraph 123:

"*Furthermore, the individual who has knowledge of his or her genetic constitution could try to use this unduly, in particular in the case of private insurance contracts. It is left to national law, taking into account especially the notion of good faith and the general principle forbidding the abuse of law, to specify the appropriate solutions.*"

(3) How far would Article 18 constrain those states that might wish to ban eugenic or "enhancement" uses of genetic tests? The commentary at paragraph 121 states:

> "*People should have unhindered access to genetic testing which may serve their health purposes. In order to be able to take advantage of these techniques in the health care setting, external factors which might interfere with people's free choice to use genetic services in health care should be barred. It must be noted that the scope of Article 18 which deals with the results of any genetic test is broader than that of Article 17 which only concerns predictive test of genetic diseases or of a genetic predisposition to a disease.*"

(4) Does Article 18, when taken in conjunction with Article 2 paragraph 2, provide an adequate basis for the preservation of the confidentiality of the results of genetic testing? The commentary at paragraph 122 seems decidedly ambiguous:

> "*Therefore it is important to prevent third parties from making use of genetic information which the individual has acquired by making use of genetic services in health care. This holds in particular when the attainment of social goods is involved (for instance, employment, life, health and disability insurance). Therefore, the communication of results of genetic testing acquired in the framework of health care for other purposes is forbidden, notwithstanding the free contractual relationship. Otherwise, the individual could refuse to undergo a test and obtain essential information about his or her health because of the fear of consequences. However the article states that national law may allow for communication of the results of a genetic test outside the health [sic] in certain cases under the conditions provided for in Article 2 paragraph 2. Such communication should thus be a necessary measure in a democratic society and serve one of the purposes referred to in this article.*"

VI. CONCLUSIONS

34. The IBC is invited to consider how far Paragraphs 20 to 30 might form a suitable background for the proposed declaration.

35. The IBC is invited to take note of the Council of Europe's Draft Convention insofar as it relates to genetic screening (Paragraphs 31 to 33). In the light of these draft articles it may wish to frame further guidance for a possible UNESCO legal instrument.

VII. ACKNOWLEDGEMENTS

Due acknowledgement should be given to the contributions made by the following IBC members:

Professor A. Bompiani
Professor J. Dausset, see ref. 1
Mrs L. El-Hamamsy, see ref. 3
Dr J. Fleming, see ref. 6
Professor N. Fujiki, see ref. 10
Professor D. Macer, see ref. 10
Rev J.-M. Mpendawatu, see refs. 2 and 15
Dr Qiu Renzong, see ref. 14
Professor H.-M. Sass
Professor D. Serrao, see information summarised in Table II
Dr L. Vidal-Rioja, see ref. 18

TABLE I: CURRENT GENETIC SCREENING PROGRAMMES IN THE UNITED KINGDOM (September 1993)

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

Age Group	Disease	Population Screened	Type of Screening Test	Confirmation Required	Other Comments
Neonatal	Phenylketonuria	All new-born infants	Indirect	Yes	
	Hypothyroidism	All new-born infants	Indirect	Yes	
	Sickle cell disease	All new-born in some areas; confined to certain ethnic groups in others	Indirect	Yes	Also detects carriers
	Cystic fibrosis	Some areas only (still at pilot stage)	Indirect	Yes	
	Duchenne Muscular Dystrophy	Pilot studies	Indirect	Yes	
	Other rare metabolic disorders	Family testing	Usually indirect		
Later childhood	None in UK				
Pre-marital and pre-pregnancy	Cystic fibrosis	Pilot projects in general practice	Direct	No	Detects 85-90% of carriers
During pregnancy	Rhesus haemolytic disease	All mothers	Indirect		
	Diabetes mellitus	All mothers	Indirect		Foetuses have expert foetal anomaly scanning
	Congenital malformations	Most foetuses	Routine ultrasound	Yes. Foetal anomaly ultrasound	
	Down's syndrome	1) All mothers in some areas	Serum screening tests	Amniocentesis with chromosome tests on foetus required for confirmation	
		2) All mothers over 35-37	Chromosome tests on foetus	No	
	Neural tube defects (spina bifida and anencephaly)	All mothers in many areas	Indirect	Foetal anomaly ultrasound	
	Haemoglobin disorders	All mothers not of North European origin	Indirect		Detects carriers
	Cystic fibrosis	Pilot studies	Direct	No	Detects 85-90% of carriers

TABLE II

PORTUGAL

- Population screening at birth: the tests are free.
  PKU
  Hypothyroidism

  Test results in 1993:
  PKU 111,917 tests: 10 cases diagnosed
  Hypothyroidism 111,917 tests: 36 cases diagnosed

- For cystic fibrosis tests are still at the experimental stage

- Prenatal diagnosis is carried out at centres in Lisbon, Coimbra and Porto

- Between 1982 and 1993 the following cases have been diagnosed:

Lysosomal disorders		167
of which sphingolipid disorders	99	
of which Gaucher	33	
others	66	
Mucopolysaccharide disorders		46
of which Hunter	17	
Peroxysomal disorders		9
of which X-linked ALD	6	

UNITED STATES OF AMERICA

Genetic Disorders For Which New-borns Were Screened in the United States in 1990.

Disorder	Number of States That Provided Screening[a]
Phenylketonuria	52
Congenital hypothyroidism*	52
Hemoglobinopathy	42[b]
Galactosemia	38
Maple Syrup urine disorder	22
Homocysteinuria	21
Biotinidase deficiency	14
Adrenal hyperplasia	8
Tyrosinemia	5
Cystic fibrosis	3[c]

* Only a proportion of cases have a genetic aetiology.
a Includes District of Columbia, Puerto Rico, and US Virgin Islands.
b Utah's hemoglobinopathy pilot study (6-1-90 through 3-31-91) has been discontinued.
c Wisconsin's cystic fibrosis screening program is for research purposes only.

SOURCE: *Council of Regional Networks for Genetic Services*, 1992.

ANNEX A

TECHNIQUES OF GENETIC SCREENING AND PRENATAL DIAGNOSIS

1. The following techniques are in common use:

1 ultrasound scanning
2 amniocentesis
3 chorionic villus sampling (CVS)
4 foetal blood sampling
5 biochemical screening tests

Research is being vigorously pursued to find techniques that are less invasive and give results as early as possible in the course of pregnancy.

Ultrasound Scanning

2. The rapid development of obstetric ultrasound has greatly increased the feasibility of directly detecting congenital malformations. With an appropriately organised obstetric ultrasound service, most major structural malformations could be detected in the second trimester of pregnancy (at about 19 weeks gestation).

3. It has been argued that there is no evidence for a harmful effect of diagnostic obstetric ultrasound. Recently, however, it has been suggested that such use of ultrasound may result in an increased rate of left-handedness. Otherwise, the main limitations of the technique are its dependence on the skill of the operator and the quality of the equipment. Its main risk is misinterpretation of the image, leading to failure to detect abnormalities (false negatives) or to abortion of a healthy foetus (false positives).

Amniocentesis

4. Amniocentesis is a procedure for taking amniotic fluid through a needle from the amniotic cavity. The fluid and the cells that it contains can then be analysed to determine genetic abnormalities in the foetus.

5. Amniocentesis is usually carried out at around 16 weeks of pregnancy. There is still some uncertainty about its risk to the pregnancy, partly because the risk is so low as to be difficult to measure. Generally accepted studies suggest a 1 per cent excess risk of spontaneous abortion following amniocentesis and a slightly increased incidence of mild respiratory problems in the new-born. The main disadvantage of amniocentesis is the long delay before diagnosis, and the late stage at which abortion can be offered if the foetus is found to be affected.

Chorionic Villus Sampling

6. Chorionic villus sampling (CVS) is a relatively new procedure whereby a small sample of chorionic (placental) tissue is removed for prenatal diagnosis. CVS can be carried out in the first trimester of pregnancy, with only minimal discomfort, and often allows a diagnosis to be achieved before 12 weeks gestation. This means that termination of pregnancy, when required, can be carried out simply, painlessly and in privacy under general anaesthesia. A WHO-sponsored registry showed a total foetal loss rate of less than 4 per cent in over 10.000 cases reported between 1982 and 1986. Some large, expert centres reported a total foetal loss rate of 2 to 3 per cent estimated to be about 1 per cent in excess of expectation at this stage of pregnancy.

Foetal Blood Sampling

7. Foetal blood sampling is used for diagnosis of the haemoglobin disorders and haemophilia when DNA diagnosis is not possible, for immunological diagnosis of combined immune deficiency syndromes or intrauterine infections, and for rapid karyotyping of foetal lymphocytes when a malformation has been detected by ultrasound. It can be performed safely only after the seventeenth week of pregnancy and only by experts. Initially, foetal blood sampling was done by foetoscopy, a highly specialised procedure with 3 to 5 per cent risk of foetal loss. This is now being replaced by the safer and less specialised technique of ultrasound-guided transabdominal needle puncture of the foetal cord insertion.

Biochemical Screening Tests

8. Tests for the effects of genes do not detect the gene itself but some aspect of its function. The most direct of these tests are for the specific protein produced by the gene. In a genetic disorder such tests may show that the protein is not being made, or is present in reduced amount; or it may be altered so that it does not function adequately. Biochemical diagnosis requires that the relevant gene is expressed in an accessible source of foetal cells. As there is usually extensive overlap between normal and carrier ranges, biochemical methods can be used only rarely to identify carriers. Where the gene or its product cannot easily be tested, it may be possible to measure some other substance that is disturbed by the disease.

ANNEX B

ALTERNATIVES TO PRENATAL DIAGNOSIS

1. At present, screening for genetic and other reproductive risks is mainly concentrated on pregnant women. (For some conditions, for example PKU and hypothyroidism, new-born babies are screened in order to start immediate treatment).

2. There are strong arguments for genetic testing being carried out before pregnancy whenever possible. Prenatal diagnosis, when earlier testing would have been possible, seems particularly unsuitable for inherited diseases for a number of reasons, which include the following:

a prenatal diagnosis does not allow a choice among the full range of reproductive options;

b couples at risk are at present offered diagnosis too late for the option of first trimester abortion;

c some carrier tests (for Tay-Sachs Disease and haemophilia) are more difficult to interpret during pregnancy, and there is no chance to correct any laboratory mistake;

d couples at risk need months (not days) to adjust to their new knowledge and make fully informed choices. They should also have the opportunity to choose options other than prenatal diagnosis.

3. These arguments suggest that, in communities where the risk of serious genetic disorder is high (for example for beta-thalassaemia in Cyprus and Sardinia and for Tay-Sachs Disease in Ashkenazi Jewish communities) carrier screening of children in their later teens may be desirable.

Preimplantation Diagnosis

4. This technique is new and experimental, and should be regarded as being at the research stage. In the USA the most important centre has been in Chicago; in Europe, in Sardinia (in collaboration with Milan) and in the United Kingdom several centres have worked on a relatively few single-gene defects.

5. The technique requires stimulation of ovulation with expensive drugs, which can have very serious side-effects. The success rate is low. Egg collection is an invasive procedure; reimplantation somewhat less so.

6. The technique has the apparently great advantage of avoiding abortion. But undue hopes as yet should not be placed in this technique. It is difficult to ensure accurate diagnosis on one or two cells. It follows that the risk of misdiagnosis is higher than in prenatal screening. At present the technique seems suitable only for a limited number of cases of high carrier risk.

ANNEX C

UNESCO

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