BAR-CODING BABIES:

Good for Health?

GeneWatch UK

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Last year, in its White Paper on genetics in the National Health Service (NHS)[1] the Government included the idea of screening babies at birth "*to produce a comprehensive map of their key genetic markers, or even their entire genome.*" The Government has asked the Human Genetics Commission (HGC) and the National Screening Committee (NSC) to conduct an initial analysis of the ethical, social, scientific, economic and practical considerations of genetic profiling at birth. They will report by the end of 2004.

This proposal is already controversial[2]. Some issues that it raises are:

- How useful is genetic screening for an individual's health?
- Is genetic screening a cost-effective way to tackle disease?
- Should children have a say in the genetic tests they have?
- Will genetic screening lead to stigma and discrimination?
- What are the implications of a large-scale genetic database for privacy and human rights?

What is genetic screening?

"*For a genetic screening programme to be justified, good quality research studies, taking account of genetic and ethnic variability, must first have demonstrated that the benefits are likely to outweigh the harms and that the programme is likely to be effective.*" British Medical Association, 1998[3].

The Government proposal would involve identifying the genetic sequence of part or all of every baby's DNA. The idea is that each baby's genetic information could be stored and used throughout their lifetime. In theory, disease prevention and treatment regimes would be tailored to individual needs as further information becomes available about how genes affect risk of disease and response to medicines.

Although the Government recognises that its proposal raises ethical and social concerns which need to be discussed, the claimed health benefits of this approach are also questionable, and need full consideration.

The proposal would change current practice in three important ways.

- The existing system of separately assessing the pros, cons and alternatives of screening for each genetic variation would have to be abandoned, because many different genetic variations would be included in the sequence.
- The principle of informed consent would be undermined. Some genetic differences relate to the risk of diseases which do not start until adulthood and currently such tests are not done until the person is old enough to decide whether to have the test.
- DNA sequence information, and possibly samples, would be stored in a large database, linked with each person's medical records.

There are important differences between what is meant by 'genetic screening' and 'genetic testing', and between genetic disorders and other types of disease. Genetic testing usually involves testing children who are thought to have symptoms of a particular genetic disorder (such as cystic fibrosis or sickle cell disease). Adults who have a family history of a particular condition are also sometimes tested if they wish to find out whether they are at risk of developing this disorder in the future. They may also want a test to find out if they are a 'carrier' (which means some of their children may develop the disorder).

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In contrast to genetic testing, genetic screening involves testing *everyone in a given population*, whether or not they have any symptoms or a family history of a particular disease. Although people can opt out of a screening programme, the aim is to include as many people as possible. When newborn babies are screened, parents can decide to opt out on their child's behalf, since the baby can obviously not make his or her own decision.

In Britain there is a screening programme which involves taking a blood spot (heel prick) from every newborn baby. Currently no DNA-based tests to determine the gene sequence are made of this blood, but a biochemical test is made to detect the genetic condition phenylketonuria (PKU), which can be treated with a special diet. A test is also carried out for congenital hypothyroidism (in which the thyroid gland does not function properly). The tests made using the blood spot are currently being expanded to include a biochemical test for sickle cell disease and a biochemical test followed by a DNA-based, genetic test, for cystic fibrosis[4, 5].

Concerns about screening

The main advantage of screening is that it can detect some cases of disease that otherwise would not be diagnosed. This may be particularly important if early treatment is essential. Hence, including the PKU test in the current new-born screening programme is clearly beneficial[6]. However, using any test in a screening programme will also increase the number of false positive results (people wrongly reported as at risk) and false negative results (people wrongly reported as not at risk).

Wrong or misleading results can harm health by leading to unnecessary treatment or worry

For many medical tests, the number of false positives is much larger than the number of true positives, so the balance of benefit and harm must be carefully assessed when deciding who to screen and when[7]. For example, for each death prevented by the UK cervical cancer screening programme, at least 150 women have abnormal results and at least 50 are treated. Cervical screening is not offered to women under 25, because tens of thousands of women would then get abnormal results for each woman helped[8]. Increasing the number of tests included in a screening programme rapidly increases the proportion of the healthy population who will get at least one abnormal result. Wrong or misleading results can harm health by leading to unnecessary treatment or worry[9, 10]. False negative results can cause false reassurance. Therefore, many 'screening' programmes are targeted to groups at greater risk. This would not be the case with genetic screening of all babies at birth.

The National Screening Committee (NSC) is responsible for ensuring that screening programmes meet certain criteria before they are implemented in the National Health Service (NHS). The 22 criteria include the validity of the test, its acceptability to the population being screened and evidence that the screening programme is effective[11]. This type of assessment is currently made for each disease or disorder individually.

One concern about the Government proposal is that this could not be done if substantial parts or all of a baby's genome were sequenced to be used in future. This means that the programme is likely to be 'technology-led' (testing for genetic variations because the technology exists to find them), rather than 'health-led' (testing for genetic variations that give accurate and useful information about a baby's health). The European Society of Human Genetics has warned that screening large numbers of genetic traits or disorders simultaneously would make it "*difficult if not impossible to provide proper information about each of the traits screened*[12]. Because knowledge about the

health implications of genetic differences is still poor and changing, tests could easily be included that do more harm than good, by misleading people about their baby's future health and perhaps leading to unnecessary treatment.

An important issue for the NSC is what type of test to use in a screening programme. DNA-based tests are not always the best option: for some types of genetic disorder biochemical testing may be better and/or cheaper. This is why alternatives to a DNA-based test are currently considered whenever a screening programme is assessed. Again, the Government's proposal is based on the assumption that using DNA technology is more important than checking which is the best option for a baby's health.

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Genetic health predictions: reality or hype?

"*[The Director of the US National Human Genome Research Institute] and many others have outlined scenarios where all individuals have a battery of genetic tests early in life so that the knowledge of 'susceptibility' can be used to avoid development of disease. Biomedical sectors would profit from acceptance of the above approach, but it is doubtful whether it is the approach most likely to increase the health of populations.*" Professor Patricia Baird, Department of Medical Genetics, University of British Columbia, Canada[13].

Very few genetic variations have yet been identified that are useful to an individual or their doctor to make decisions about their future health. Although a few predictive genetic tests are used in some adults now, none of them are suitable for inclusion in a newborn screening programme:

- Mutations in the BRCA1 and BRCA2 genes significantly increase the risk of familial breast cancer. However, most cases of breast cancer are not caused by mutations in these genes. In Britain, the National Institute for Clinical Excellence (NICE) has recently issued a new guideline which recognises that genetic testing for BRCA1 and BRCA2 is only appropriate for a small proportion of women who are from high-risk families[14]. Genetic screening is not recommended because mutations are rare; the risk associated with them is uncertain in the absence of a strong family history; and the options to reduce risk are limited and certainly not applicable to children (the main one is to have both breasts surgically removed while they are still healthy).

- Familial hypercholesterolaemia (FH) is an inherited condition leading to high blood cholesterol levels. It is under-diagnosed and can be treated with cholesterol-lowering drugs, but genetic screening is not practical because of the large number of possible mutations involved (over 350)[15]. Diagnosis is normally made by measuring cholesterol levels and checking family history, although genetic testing can be useful if the mutation in an affected family member is known. Screening only adult relatives of patients with FH is recommended by the NSC[16, 17].

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- Genetic screening has in the past been advocated for an inherited risk of blood clots and the blood condition haemochromatosis, but studies have now shown that genetic screening for these conditions is not useful because of the low predictive value of these tests[18, 19]. The NSC has concluded in both cases that there is no evidence to support a screening programme, even in relatives of patients.

No other genetic screening programmes for future disease risk have yet been proposed. There are no pharmacogenetic tests (genetic tests used to predict response to medicines) that would be suitable either[20].

The limitations of existing genetic tests are clear but what are the prospects for genetic screening in the future?

The limitations of existing genetic tests are clear but what are the prospects for genetic screening in the future? The Government's policy paper includes numerous claims that future genetic tests will predict adverse drug reactions; the risk of common diseases; and susceptibility to exposures such as foods, chemicals and smoking.

Unfortunately, the Government did not make any assessment of the claims it makes about the benefits of genetic testing, which are based on an out-dated view of genetic science. There is growing evidence that genetic tests, whilst useful in research, will not be useful for making medical decisions for most people[21, 22]. Although it may be possible to identify genetic factors in disease, thereby improving understanding, it will not usually be possible to quantify the effects of these genetic risk factors on an individual's risk[23]. The European Society of Human Genetics has stated that testing for genetic influences in common diseases "*is likely to be of limited utility*"[24]. Concerns include: the low predictive value of genetic tests; the greater importance of lifestyle and environment; psychological reactions to and social consequences of genetic tests; and costs.

For common diseases, genetic testing may divert resources from other more useful interventions. Widespread genetic testing may even undermine the public health measures needed to tackle problems such as obesity, smoking, poverty and pollution[25]. These problems are not limited to a minority of people who are 'genetically susceptible'. For example, testing smokers for "genetic susceptibility" to smoking-related diseases could mislead them about the risk of smoking and convince some people that they do not need to quit[26, 27,].

Many academic scientists believe that pharmacogenetic testing has been oversold and that tests already available have dubious utility[28]. It is at best premature to propose pharmacogenetic screening in babies when no genetic tests to predict medicine response are yet in routine use. Even if pharmacogenetic tests are useful in some cases in the future, there is no obvious benefit to including them in a screening programme rather than offering them only to those individuals who are about to take the medicine.

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The cost of genetic screening

"*The ability to screen for genetic susceptibility to common diseases provides new opportunities for disease prevention. However, with the entire population potentially eligible for genetic screening, the cost implications are staggering*." Dr Nananda Col, Harvard Medical School[29].

Testing a single gene typically costs around £50 to £150[30]. Costs are expected to decrease as technology improves. However, genetic risk assessments also require other information (such as family history) and professional judgement for the test result to be properly interpreted. The cost of interpreting and explaining the results may be higher than the test itself. Each risk category (low, medium, high genetic risk) then needs management within the NHS. This process may or may not compare favourably with other strategies for reducing risk.

One study of genetic screening to try to predict the risk of blood clots in women taking oral contraceptives estimated that the cost to prevent one death would exceed £165 million, far higher than the £30,000 cost that is usually considered cost-effective[32]. If the predictive value of future genetic tests is also low or their utility is similarly limited the benefits will also be too small to justify the costs. It is hard to see how cost-effectiveness will be evaluated if it takes place without a full, prior assessment of the benefits and harms of screening each genetic variation.

Requirements for informed consent and counselling

"*Genetic screening can be of benefit but can also do harm. The availability of genetic tests at low cost may lead to the systematic offer of screening tests without the appropriate medical environment for providing information prior to testing and counselling afterwards*." European Society of Human Genetics, 2003[33].

Testing babies for genetic markers that relate to adult-onset disorders would breach existing guidelines for seeking informed consent and for genetic counselling[21]. Although the White Paper states that participation in the screening programme would be voluntary, people cannot make choices about which genetic tests to have if they are scanned at birth. Parents may feel obliged to agree to the whole screen because a small number of the tests may be relevant to their baby's health.

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When a baby needs a test to diagnose a genetic disorder and aid treatment, it is obvious that the parents should be able to agree to such a test on a child's behalf. But this does not apply to genetic variations that are not relevant to treatment until the child becomes an adult: for example, tests that indicate a risk of breast cancer or Alzheimer's disease. In such cases, the test is not medically necessary for children and they should be allowed to make their own decisions later on. Many adults decide they do not want to have a genetic test and many risk-reducing options (such as cancer screening, medication or surgery) will not be appropriate for children. Genetic screening at birth removes children's rights to make their own decisions[34].

Currently, adults offered genetic tests that indicate a risk of future disease, or a risk of passing a genetic disorder on to future children, are offered genetic counselling. Counselling involves explaining the implications of the test, both before and after someone takes it, and helping people to make their own decisions about what to do. Screening at birth means omitting counselling, with a danger that children are later given misleading or confusing information about their test results. Little is known about the psychological effects on children of predictive genetic test results, which can only give limited and uncertain information about conditions that they might develop when they are much older.

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It is unclear from the Government's proposal whether or not DNA samples and genetic data collected from babies will also be used for research. If so, the proposal may also breach the child's right to give (or refuse) informed consent for such research. Informed consent is one important safeguard that helps ensure that research is ethical and socially acceptable. The use of medical records, including children's records, for genetic research without seeking consent has caused considerable controversy in Iceland and this project now faces legal difficulties[35]. Some genetic research may be controversial (e.g. looking for the 'gene for criminality') or involve commercial practices that some people find unacceptable (such as patenting gene sequences identified in a sample of DNA)[36].

Genetic discrimination, stigma and social implications

Classifying everyone at birth according to their genes risks creating a society where some people's lives are valued less than others[37]. Choices (schooling, pensions, jobs) might become restricted for those thought to have a poor genetic make-up, creating a 'genetic underclass'; and stigma may be associated with some categories of genetic risk. Although it is not part of the Government proposal, the use of prenatal screening and abortion to eliminate those who are supposedly at 'high genetic risk' may then become more

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commonplace. There are also currently no laws in the UK to prevent insurers or employers from using genetic test results to deny insurance cover or refuse someone a job.

The Government's proposal would require details of each person's unique genetic make-up to be entered in a computer database at birth and linked to medical records. DNA samples might also be stored and linked to the database (making what is called a 'biobank'). Biobanks raise many important issues, including how consent is obtained for different uses of the information and how privacy can be guaranteed[38].

The police could seek access to such records under existing legislation and Government access might also be allowed under proposals to share databases between departments, or include data chips on identity cards. One concern is that a health service genetic database could become a back-door forensic database without proper public scrutiny or debate. Access by the police or Government to individual genome scans of the whole population could lead to the erosion of civil liberties[39]. Because DNA samples are left wherever a person goes, the Government could gain unprecedented powers to track the movements of every individual, as well as increasing the likelihood of access to private information about health or relationships (e.g. paternity).

Conclusions

"*Leaving aside the thorny issue of how a newborn can consent to genetic testing, one wonders why a DNA sample taken at birth is any more useful than one taken later in life*." Drs Kavalier and Kent, 2003[40].

The health claims made for predictive genetic testing in the White Paper are based on spin and not on substance. A prior assessment of such claims, including the predictive value and cost-effectiveness of currently available genetic tests, is urgently needed. Genetic profiling at birth would over-ride important safeguards such as the need for informed consent and genetic counselling. Genetic tests should be used only when they are useful for a child's diagnosis and treatment. Some genetic screening programmes (e.g. for PKU) are important and worthwhile, but other genetic tests may be better used only in specific circumstances. Genetically screening babies to seek to predict adult-onset disorders or 'susceptibilities' is neither necessary nor beneficial and much misinformation is likely to result.

The biotech and pharmaceutical industries have vested interests in promoting genetic testing for common diseases

'Bar-coding babies' is unlikely to be acceptable either to the public or to the health professionals who would be required to implement it. It is difficult to see why this proposal was included in the White Paper at all, except as a way for genetic testing companies to make a profit from a 'captive market' at taxpayers' expense[41].

The biotech and pharmaceutical industries have vested interests in promoting genetic testing for common diseases because it allows them to expand the market for both genetic tests and preventive medication ('pills for the healthy ill')[22]. There is a danger that genetic tests could drive a new wave of inappropriate medicalisation if they are not properly evaluated[42]. Because the predictive value of most genetic tests is very low, many children could end up taking medicines that they do not need.

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