For Debate

Screening and the new genetics; a public health perspective on the ethical debate

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Summary

Advances in the diagnostic applications of molecular genetics have made possible the identification of recessive carrier states in the population. The debate surrounding screening for cystic fibrosis therefore has a public health significance which transcends that specific disorder. The two most frequently cited objectives of screening for a recessive carrier state are to reduce the prevalence of the disorder and to inform the reproductive choices of individuals and couples at risk. The latter aim represents a paradigm shift in the philosophy of screening in that no preventive principle is involved. Instead, information is regarded as worth while in itself, regardless of outcome. The authors argue that the benefits arising from the information generated in the course of genetic carrier screening cannot be presumed merely by asserting a ‘right to know’ ethical imperative, and draw attention to the danger that a combination of technical capability, professional zeal and consumer demand will override currently accepted screening principles. In this event, future efforts to subject screening programmes to rational evaluation could be undermined.

A recent report on screening in Scotland has reiterated an earlier call for the establishment of a national strategic working group or task force comprising individuals with expertise in and knowledge of screening. Its remit would be twofold: to identify those screening procedures and programmes which should be incorporated into routine health care, and to assume responsibility for the development, implementation and audit of screening policy and practice. Such a group would have no shortage of agenda items. A strong contender to head the list would be community genetics.

The diagnostic potential of molecular genetics is formidable. Recent advances have made possible the identification of several recessive carrier states in the population and it has been widely predicted that the mapping of the entire human genome is in sight. So far, attention has focused on a small number of such disorders, most notably cystic fibrosis, where the prospect of mass screening is imminent, although it is certain that many more will follow. The debate surrounding cystic fibrosis therefore has a significance which transcends that specific disorder.

Cystic fibrosis (CF) is one of the commonest autosomal recessive disorders found in populations of northern European descent. Despite therapeutic advances, it remains a distressing and debilitating disease which substantially reduces life expectancy. The CF gene (cystic fibrosis transmembrane conductance regulator) was cloned and the major mutation in Caucasians characterized in 1989. The incidence of CF in white populations is about 1 in 2500 live births and the prevalence of asymptomatic heterozygote carriers is estimated at around 4 per cent. Technically, the 2–3 million carriers of the gene in the UK population can now be identified by testing mouthwash samples. There are no false positives but 15 per cent of carriers give a negative result on screening. In 1 in 12 couples one partner is a carrier, and in 1 in 540 couples both partners are carriers and have a 1 in 4 chance in each pregnancy of having an affected child. Of the various screening strategies, probably the optimum means of identifying a high proportion of carrier couples before the birth of an affected child is by offering screening to the total population combined with testing of the relatives of carriers (‘cascade screening’). This approach is not currently regarded as realistic. An alternative approach is ‘couple screening’ during pregnancy in which both partners are screened and are offered prenatal diagnosis if both are found to be carriers. It appears that little lasting anxiety or stress is caused to participants, whether the results are positive or negative, although the long-term psychological...

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consequences are less clear.\textsuperscript{10} The public uptake of screening is highly variable depending on the setting and method of invitation.\textsuperscript{11} Experience of screening for other recessive disorders suggests that both patients and professionals are reasonably comfortable with the idea of screening in pregnancy.\textsuperscript{12} Much of the argument about CF screening has centred on technical and practical issues. In the United States, two policy statements\textsuperscript{13,14} dampened the initial enthusiasm for CF carrier screening on that side of the Atlantic. Both recommended a moratorium on routine screening and agreed on the following four points: the results of pilot studies should be awaited; if the test has a detection rate close to 100 per cent, mass population screening should be considered; carrier testing should be offered to couples in which either partner has a close relative with CF; the optimal setting for carrier testing is primary care.

Wilfond and Fost,\textsuperscript{15} in a detailed critique of these recommendations, questioned whether the detection rate is really a decisive issue as 'even with 100% detection of carriers, the personnel and logistic resources needed to meet educational and counselling needs must be developed and evaluated'. They also queried whether primary care was the ideal setting, and drew a fine distinction between informing patients about the test and actually providing it.

Curiously, there has been almost no discussion of the ideological or philosophical basis of the case for CF screening, the rationale for which is seldom challenged. The two most frequently cited objectives of screening are to reduce the incidence (or at least the birth prevalence) of CF in the population and to inform the reproductive choices of individuals and couples at risk.\textsuperscript{15} Neither explicitly accords with the conventional aim of prescriptive screening – to benefit the health of the screened individuals.\textsuperscript{16} It may be argued that the 'epidemiological' aim scarcely breaks new ground, given the well-established precedents of antenatal screening for conditions such as neural tube defects and Down's syndrome, the avoidance of which is generally regarded as a legitimate public health as well as clinical goal. The 'information' aim, however, is qualitatively different from that of most other forms of screening in that it encapsulates no preventive principle (except in a most tenuous and indirect fashion). Instead, the generation of information is regarded as a worthwhile aim in itself, regardless of outcome. This represents a paradigm shift in the philosophy of screening and deserves closer scrutiny.

Reflecting prevailing social attitudes to health care generally, the recognition of information as a 'right' is a recurrent theme of the advocates of the new genetics.\textsuperscript{17} Withholding information is viewed as an unjustifiable form of medical paternalism. Brock,\textsuperscript{18} for example, questioned 'whether we have the right to withhold, largely because of our own unresolved worries about the capacity to provide adequate counselling, screening for those who request it'. Clarke and Parsons,\textsuperscript{19} though writing in relation to another disease (Duchenne muscular dystrophy), took issue with the view that screening should meet the criterion that treatment at the pre-symptomatic stage need favourably influence outcome as 'families can be offered reproductive choice ... and practical and emotional planning for the future'.

Harper\textsuperscript{20} is one of the rare dissenting voices within the genetics fraternity. He has expressed profound unease about the risk that community genetics will result in the needs of individuals and families being rendered subservient to broader eugenic goals, and points to past abuses of genetics by racist regimes. Even Harper, however, appears to take for granted the underlying premise that genetic screening can benefit individuals and families provided an individualistic as well as a public health perspective is retained.

In fact, the benefits of large-scale genetic screening to individuals, families or society as a whole remain largely theoretical. There is scant evidence to support the view that the public at large perceives a need for carrier screening, despite the rhetoric of the self-appointed champions of the people's 'right to know'. This apathy may, of course, evaporate as public awareness increases. For the sake of argument, let us give the screening enthusiasts the benefit of the doubt and make two assumptions: first, that patient demand for carrier screening will grow, and second, that most of the technical and practical problems surrounding testing will be resolved in the near future. What other areas of uncertainty remain?

Here are a few. How well are people able to interpret information about their genetic status? What do people perceive to be the purpose and value of such information? How competent are health care professionals in explaining the nature of screening to their patients, and in responding to questions before and after the results are available? What counselling skills are required to support a screening programme, and are such skills likely to become available on a sufficient scale? Armed with genetic knowledge, do people actually use it in reproductive decision-making or in long-term planning? How can confidentiality be maintained given the large numbers of people who are carriers and the implications for other family members? What is the outcome, in terms of both general and reproductive health, of genetic screening for those who have been screened compared with those who have not?

Partial answers to these questions are beginning to
emerge as experience accumulates. Until more extensive and detailed information becomes available from controlled studies, the introduction of mass population screening for genetic carrier states is difficult to justify except on an experimental basis. The danger is that a combination of technical capability, professional zeal and consumer demand will lead to a 'right to know' imperative which will override currently accepted screening principles and marginalize empirical study. If this occurs, the fragile professional consensus endorsed by the World Health Organization in 1968 — that screening should be based on demonstrable evidence of benefit rather than assertion — will be shattered. This could undermine future efforts to subject screening programmes of all types to rational evaluation.

References


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