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The goals of genetic counselling are to mitigate the adverse effects, and to reduce the possible recurrence, of genetically influenced disorders. Its scope and consequences depend upon the degree to which the genetic mechanisms underlying the disease are understood, but they can include medical interventions, reproductive choices or prenatal or presymptomatic diagnoses. For the majority of psychiatric disorders at the present time, most counselees will be concerned either with the potential risk to children or, in the case of unaffected relatives of patients, with their probability of developing the disorder. However, future advances in molecular genetics can be expected to alter this picture and may allow presymptomatic and prenatal diagnoses at least in some families, as well as other possibilities of medical intervention. Clearly, these developments raise a number of important ethical issues which we shall also discuss.

Genetic counselling

It needs to be said at the outset that there is no place for public health campaigns persuading people with psychiatric disorder or a strong family history of psychiatric disorder not to have children. Still less is there a place for any attempts to legislate on this matter. However, an informed and responsible genetic counselling service has a small but definite current role, and this is likely to increase in the future. Most genetic counsellors in current practice adopt a non-directive, educational approach (Harper, 1988). Appropriate emphasis is therefore given to the personal autonomy of counselees. In practice, much of the work of a genetic counsellor is to allay anxiety and to dispel mistaken beliefs, for example that all the offspring of a parent with serious mental illness necessarily have the same 'hereditary taint' or that all disorders with a genetic component are necessarily untreatable. However, it may be legitimate not only to lessen anxiety by providing information and reassurance, but also to raise the awareness of potential problems where this appropriate. The counsellor needs to help the counsellee assess the risk as accurately as possible and to understand the potential burdens. However, finally, after assessing the risk/burden ratio, the ultimate decision must be that of the counsellee.

Murphy & Chase (1975) have pointed out that the assessment of risk in genetic counselling can be derived from three sources:

- (1) *empirical* information, consisting of estimates based on available research data
- (2) *modular* information, which depends upon a clear understanding of the mode of inheritance of the disorder
- (3) *particular* information, which is a compilation of all the data that can be used in assessing the risks to a particular family.

For the majority of common psychiatric disorders, most of the information imparted in genetic counselling should derive from empirical sources. A clear understanding of the mode of inheritance of psychiatric disorders is usually lacking, and it is important for anyone attempting genetic counselling not to confuse tentative hypothesis with proven fact. For example, as we have seen, it is possible to identify families in which functional psychosis appears to be segregating in a Mendelian fashion. However, such families could also occur as a result of multifactorial/polygenic transmission. While it may be perfectly valid to postulate the operation of genes of major effect for the purpose of linkage studies, it would be unwise, indeed unethical to do so for the purposes of risk prediction. However, in such highly loaded families one may wish to take account of particular information, bearing in mind that the risk to relatives increases according to the numbers of relatives already affected and decreases with the number of healthy relatives (Gottesman, 1991).

Whatever the type of information available, the role of the genetic counsellor is to educate and inform rather than to direct or advise. For example, a couple planning a family, one of whom has a schizophrenic parent, might beneficially be told that the average risk for each of their children displaying the disorder is about 3%, which although small is three times the rate in the general population. It must then be their decision rather than the counsellor's whether this low risk is acceptable.

Using knowledge of genetics

Other than informing potential parents about the risks to their offspring, how might empirical knowledge about genetics be used in counselling individuals or families about prevention? One obvious answer is that for most psychiatric disorders it is a diathesis that is inherited and environmental stresses are necessary before the disorder becomes manifest. Sometimes, as in schizophrenia, the nature of the relevant stresses are controversial or unknown. Alternatively, as in depression, relevant environmental insults have been defined with some certainty. However, it is of little use advising someone with familial diathesis to depression to avoid threatening life events! On the other hand, it may be quite legitimate and useful to advise an individual with a strong family history of alcoholism that he may be more than usually susceptible to moderate use becoming

immoderate. Similarly, the close relatives of patients suffering from schizophrenia should be informed that they especially should not 'experiment' with such street drugs as LSD, PCP and cocaine, because clinical evidence suggests that these substances can precipitate psychoses in those with a high genetic loading.

In the future, advances in molecular genetics should lead to greater accuracy in prediction. At present, Huntington's disease provides the best prototype. As we have seen presymptomatic and prenatal testing are available for Huntington's disease, allowing quite extensive risk prediction. These tests have been available in specialised centres for some years now, and there has been careful research and evaluation from which important results have been obtained (Morris *et al*, 1989; Morris & Harper, 1991).

In addition to expected problems such as reaction to adverse test results, with suicides having been recorded, many other difficulties have emerged. These include unintentional risk alteration, in which an individual who participates in a linkage study aimed at determining risk in a relative but who has not volunteered for predictive testing unintentionally has his/her perceived risk altered by testing. One of the most common problems is in fact inappropriate referral (Morris & Harper, 1991), which indicates that much more professional and family education is necessary. In some cases, adult patients at risk were referred by doctors without being told. It has been argued that this is inappropriate on two grounds (Morris & Harper, 1991). First, patients have a legitimate right to know what use will be made of their blood samples. Secondly, and more generally, it is a mistake to regard presymptomatic testing in the same way as other medical investigations, since the applicants are not generally medically ill and samples are required not only from the applicants but from key relatives. It is generally agreed that people should not be tested without their knowledge. There is international agreement that the testing of children, not uncommonly requested by parents or adoption agencies, is an inappropriate use of the test.

It is unlikely that future research with genetic markers will allow similar levels of predictive certainty for common disorders such as schizophrenia and affective disorders. However, predictive tests may soon have a place in subforms of early-onset Alzheimer's disease and in prion diseases, and here the ethical and psychological issues are similar to those in Huntington's disease. This work should not be attempted by centres without specialised expertise. In particular, such testing should only be offered in centres that can precede the test with expert counselling and can provide facilities for psychological support when the outcome is adverse.

The need and demand for expert psychiatric genetic counselling is likely to increase as the accuracy and value of such counselling increases. The rudiments of genetic counselling could usefully be covered in general professional psychiatric training. It might also be prudent to plan for the development of psychiatric genetic counselling services which could be set up on a regional basis within the next 5–10 years. Until this is achieved,

genetic counselling for psychiatric disorders is likely to be carried out by general psychiatrists or geneticists. Since misinformation may be more damaging to the counsellee than no information at all, the main message for both groups is to be frank and open about the inherent complexities and ambiguities of psychiatric genetic counselling, and to be prepared to seek advice from colleagues with specialist knowledge.

Ethical issues

We can consider ethical issues in psychiatric genetics under two broad headings relating first to research and second to clinical practice.

Is research into psychiatric genetics unethical?

As we hope has been shown in the earlier chapters of this book, study of the genetics of psychiatric disorders currently offers one of the most exciting approaches to understanding causes and discovering cures for these common diseases. However, the concern persists that there is something slightly sinister about investigating the inheritance of abnormal behaviours.

It is not difficult to trace the historical roots of this disquiet. The first of these probably stems from a reaction to the eugenics movement in the early part of the century. Eugenics was based upon the optimistic notion that a knowledge of genetics could not only enable the abolition of certain diseases but could lead to improvements of human stock in general (Carlson, 1987; Roll-Hanssen, 1988). Some believed that this could be implemented on a national basis, and invalid beliefs about genetic and racial influences on IQ and other behavioural characteristics played a part in a way immigration policies were carried out in the USA (Kamin, 1974). However, as is well known, there was much worse to come. Eugenic arguments were commandeered by the German Third Reich in a way that blended an astonishing mixture of scientific *naïveté* and evil intent (Müller-Hill, 1988). Despite the fact that such policies were seen by most of the scientific community as not just morally repugnant but intellectually bankrupt, psychiatric genetics acquired a sort of guilt by association. Perhaps not surprisingly, a reactive antagonism to psychiatric genetics among politicians is still more evident in Germany than in other parts of Europe.

A less tangible but still potent source of antipathy to psychiatric genetics is the view that genetic explanations of psychological disorders are unacceptably mechanistic and demeaningly simplistic, often allegedly ignoring the obvious influences of poverty, child abuse, poor education, interpersonal relationships, and so on. This argument is often allied with another which claims that not only do genetic theories reduce the richness and complexity of human experience, but also that they offer only the prospect of therapeutic nihilism because genetic mechanisms must be impossible to treat and are certainly unlikely to be susceptible to psychological interventions. A related concern is that interest in molecular

genetics could lead to neglect of non-biological, potentially remediable contributions to mental illness (Pelosi & David, 1989).

Fortunately, counterarguments are not too difficult to find. The main thrust of modern molecular medicine is towards precisely defining aetiology both at the molecular level and at the level of interplay between genes and environment. By so defining causes more precisely, we should be able in the long term to acquire knowledge which allows the development of rational therapies and preventative strategies. There are a number of examples already of genetic diseases where environmental manipulations form the basis of treatment such as phenylketonuria (see Chapter 4), and there is no necessary reason why finding that there are genetic influences on a disorder should rule out psychological or behavioural treatments. For example, two findings from the same unit at the Institute of Psychiatry, London, have shown that anorexia nervosa is substantially heritable (Treasure & Holland, 1991) (see also Chapter 7) but is responsive to psychotherapy (Russell *et al*, 1987). Other well known examples include the effectiveness of cognitive therapy in depression and the useful combination of drug plus family therapy in prolonging remissions in schizophrenia. However, it would be naïve to suppose that successful application of molecular genetics will not produce specific ethical problems relating to clinical practice, and it is to these that we shall now turn.

Clinical practice

As we have already seen, Huntington's disease provides the best prototype for considering some of the ethical problems that are likely to arise in psychiatric genetics. At the outset we should note that the 10-year gap between the identification of linkage to markers on chromosome 4 (Gusella *et al*, 1983) and the identification of the mutation responsible for the disease (Huntington's Disease Collaborative Research Group, 1993) has led to considerable experience being gained in the application of linkage markers to presymptomatic and prenatal diagnosis. Now that the pathogenic mutation has been identified, it should soon be possible to identify gene carriers directly and this will have a number of new ethical implications, which we shall also consider.

Presymptomatic diagnosis of Huntington's disease with linked markers is possible with a high degree of accuracy because these markers are tightly linked to the disease locus, there is apparently 100% penetrance, and the great majority if not all cases result from mutations in the same gene on the short arm of chromosome 4. However, there are a number of problems. First, the test cannot be applied to everyone at risk; at least one living, affected grandparent must be available. In one study this criterion was fulfilled by only 15% of individuals at risk (Harper, 1986). Secondly, because there is up to a 5% chance of recombination occurring between the markers and the disease locus, the test is not 100% accurate.

However, young adults at risk of developing Huntington's disease, providing they have an informative family structure and relatives available for testing, can be told that their probability of developing this fatal degenerative disease is either less than 5% or more than 95%. Given that there is no cure or treatment for Huntington's disease, it is a matter of debate how to provide such a predictive service and indeed whether such a service should be provided at all. We have already considered some of the useful guidelines that have emerged as a result of early experience in predictive testing and it seems strongly advisable that such testing should only be offered in certain specialised centres.

As long as inappropriate referrals are rejected, that testing is preceded with expert counselling, and the counsellee's autonomy to decide whether to continue with the test is respected, it would seem entirely reasonable to provide such a service. Out of 238 initial serious enquiries for testing in one published series (Tyler *et al*, 1992) only 40 final results were given. While in 43 cases testing proved impossible because of unsuitable pedigree structure or laboratory factors, a decision to withdraw from the programme by choice occurred in 46 of the 143 individuals who proceeded to the first interview. This suggests that patients in this series felt able to exercise their autonomy by declining to be tested. We also know that the majority of those at risk of developing Huntington's disease do not request testing. In large measure this probably reflects the fact that no effective treatment is available. However, further research is required to understand in how many instances this decision is based upon adequate factual understanding of the presymptomatic test and its consequences.

The marker test is likely to be more useful for prenatal diagnosis, where the foetus now represents the third generation. However, in most cases the parent will not have reached the age of risk and the test will therefore only determine whether or not the foetus has the same 50% risk as the parent. The availability of this test provokes an obvious moral dilemma. If the foetus' risk is close to zero, no difficulty arises. However, if the result is adverse, the counsellee must decide whether or not to continue with the pregnancy when the child's risk of illness is approximately the same as the counsellee's own risk. Moreover, carriers of the disease gene can be expected to live quite healthily for upwards of 30–40 years.

Concern has been expressed that prenatal diagnosis will be applied to more common psychiatric disorders, such as schizophrenia and bipolar disorder. As we have pointed out, the complexity of the genetics in these disorders is such that it is unlikely that it will be possible to attain similar levels of predictive certainty. It is conceivable that rare families exist which represent single-gene subforms of these common disorders. If prenatal testing was possible in such families, we would suggest an extension of the approach that we have already advocated. This is based upon skilled counselling, consideration of the severity, age of onset and other aspects of the phenotype, allowing the counsellee to take a fully informed decision.

All experience relating to presymptomatic testing for Huntington's disease up until now has related to linked DNA markers. However, the identification of the pathogenic mutation now makes possible a specific test that will be largely independent of family structure, and it seems likely from consideration of other disorders that mutation testing will rapidly be brought into clinical practice and will become the principal basis for prediction. Mutational testing will have a number of advantages, including greater accuracy (it should be possible to assign risks of virtually 0 or 100% to individuals) and the feasibility of testing without the need to involve relatives, resulting in greater privacy. However, disadvantages can also be envisaged. These include inadvertent prediction (e.g. a parent being shown to have the mutation with the testing of their offspring), and pressure for testing without appropriate counselling due to the relative simplicity of the test. With regard to this latter point, it may be necessary for guidelines to restrict the availability of mutational testing to those centres with the ability to offer appropriate counselling. Greater accuracy may also prove to be a double-edged sword, and the psychological consequences of an adverse result be much greater.

Another problem arises once specific mutations are identified in Mendelian disorders. This occurs when clinicians wish to use genetic tests for diagnostic purposes, and this is relevant not only in Huntington's disease but also in some forms of early-onset Alzheimer's disease and in prion dementia. Clearly, tests for genetic mutations are not the same as many other diagnostic tests, in that their results have implications for other members of the family. Of course, it can be argued that the same is true for any other type of test that allows diagnosis of a Mendelian disorder. However, inadvertent risk alteration is a particular problem in diseases of late onset. We should therefore ensure that families are adequately counselled before genetic tests are used in diagnostic settings, and that clinicians are dissuaded from including genetic tests as part of 'routine' diagnostic screens.

Another general area of ethical concern relates to the question of availability of genetic information to third parties such as relatives, employers, and insurance companies. These issues may not be areas of immediate concern, but are likely to pose problems in the future, particularly as we identify susceptibility genes to common disorders such as cardiovascular disease, cancers, and mental illness. Areas that are already of relevance to some disorders such as Huntington's disease include the use of genetic testing in relation to life and health insurance (Harper, 1993) and the related issue of possible testing by employers. These issues are complex, but future developments need to be discussed and debated openly, not only by professionals but also by the public (Harper, 1992a, 1993). This will require an improvement in public education about science in general and genetics in particular. We shall also need to pay particular attention to issues of confidentiality and to ensure that individuals and

families fully understand the implications of testing as well as retaining control over the disclosure of the results. Understanding the genetic basis of common disorders will have profound public health implications. Many of these relating to improvements in treatment and prevention will be beneficial. However, the excesses of the eugenics movement and the abuses of Nazi Germany are stark reminders of the dangerous consequences of individual interests becoming subordinated to broader, population-based goals, particularly in relation to mental illness (Holtzman, 1989; Harper, 1992b).

References

- Carlson, E. A. (1987) Eugenics and basic genetics. in H. J. Muller's *Approach to Human Genetics. History and Philosophy of the Life Sciences*, **3**, 57-78.
- Huntington's Disease Collaborative Research Group (1993) A novel gene containing a trinucleotide repeat that is expanded and unstable in Huntington's disease. *Cell*, **72**, 1-20.
- Gottesman, I. I. (1991) *Schizophrenia Genesis. Origins of Madness*. San Francisco: W. H. Freeman.
- Gusella, J. F., Wexler, N. S., Conneally, P. M., *et al* (1983) A polymorphic marker limited to Huntington's disease. *Nature*, **306**, 234-238.
- Harper, P. S. (1986) The prevention of Huntington's chorea. *Journal of the Royal College of Physicians*, **20**, 7-14.
- (1988) *Practical Genetic Counselling* (3rd edn). Bristol: Wright.
- (1992a) Genetics and public health. *British Medical Journal*, **304**, 721.
- (1992b) Insurance and genetic testing. *Lancet*, **341**, 224-227.
- (1993) Huntington's disease and the abuse of genetics. *American Journal of Human Genetics*, **50**, 460-464.
- Holtzman, N. A. (1989) *Proceed with Caution: Predicting Genetic Risks in the Recombinant DNA Era*. Baltimore: Johns Hopkins University Press.
- Kamin, L. J. (1974) *The Science and Politics of IQ*. Chichester: Wiley.
- Morris, M. J., Tyler, A., Lazarou, I., *et al* (1989) Problems in genetic prediction of Huntington's disease. *Lancet*, *i*, 601-603.
- & Harper, P. S. (1991) Prediction and prevention in Huntington's disease. In *The New Genetics and Mental Illness* (eds P. McGuffin & R. Murray), pp. 281-298. Oxford: Butterworth-Heinemann.
- Müller-Hill, B. (1988) *Murderous Science*. Oxford: Oxford University Press.
- Murphy, E. A. & Chase, G. A. (1975) *Principles of Genetic Counselling*. Chicago: Yearbook Publishers.
- Pelosi, A. J. & David, A. S. (1989) Ethical implication of the new genetics for psychiatry. *International Review of Psychiatry*, **1**, 315-320.
- Roll-Hanssen, N. (1988) The progress of eugenics: growth of knowledge and change in ideology. *History of Science*, **26**, 295-331.
- Russell, G., *et al* (1987) An evaluation of family therapy in anorexia nervosa and bulimia nervosa. *Archives of General Psychiatry*, **44**, 1047-1056.
- Treasure, J. L. & Holland, A. J. (1991) Genes and the aetiology of eating disorders. In *The New Genetics and Mental Illness* (eds P. McGuffin & R. Murray), pp. 198-211. Oxford: Butterworth-Heinemann.
- Tyler, A., Ball, D. & Crawford, D. (1992) Presymptomatic testing for Huntington's disease in the U.K. *British Medical Journal*, **304**, 1593-1596.