Nature, nurture and eugenics

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EUGENICS was defined by Francis Galton, in 1883, as the study of the means of increasing the fitness of the race, or of avoiding *dysgenic* changes (negative eugenics). That is, eugenic measures are ways of breeding selectively for improved human characteristics. This does not seem to be a particularly favourable moment in history to discuss this subject, since our major problem is the quantity, not the quality, of mankind so I broadened my title by prefacing it with a little jingle, 'nature and nurture', also invented by Galton. Nature here means only genetic inheritance, and nurture the total environment, everything other than genetic which contributes to the phenotype of the organism. Probably there has been more argument around this short phrase than around any other three words used in genetics, usually centring on debates about the 'primacy of nature over nurture', and the like. These have been mostly mistaken arguments in my view, and I have used the words only because I want to relate the three subjects of my title to one another, which is something Galton never quite got around to doing.

What I want to do, very briefly, is to try to put some of the problems of eugenics, the problems of maintaining or of improving human fitness, in their general context, and then look particularly at such of these problems as may seem of some relevance to you. Counselling is obviously an exercise in preventing dysgenic change. But we rightly think of counselling in the context of individuals and rarely relate it to eugenics, as Galton would have us do. I shall not try to press the Galtonian case (for reasons which I hope will become obvious). At the very most, my objective is the much more modest one of trying to give you some sort of terms of reference for thinking about this problem if, and when, it confronts you.

Man came into existence, distinct from his ape-like relatives, something like 1 million years ago. That is, 30,000 generations ago. For most of that time he has lived in a state of nature, and his genetic complement has been subject to selection which, we must assume, has adapted his fitness to this natural environment. This environment has not been homogeneous, either in time or place, nor did the various sub-populations stay in a particular environment. So we should expect to find, as we do indeed similarly find with snails, or butterflies etc. (Ford, 1964), that there is a

considerable genetic variability within the species as a whole, related basically to geographical differences, i.e. to environmental differences. There are many such known situations in man, often related to what we call racial differences, but not necessarily so. The well known example of sickle cell anaemia and its correlation with malaria distribution is sufficient to make the point. Wherever malaria was endemic the Hb^s gene was preserved, from S.E. Asia across Africa and Europe to the fenlands of England, i.e. across racial and national boundaries. Thus, the environment that concerns us is more easily comprehended as Galton's 'nurture' than in simple climatic terms.

Proponents of eugenics, like Julian Huxley (1963) in this country and the late H. J. Muller (1935) in the U.S., tend to talk about modern man, subject to this selection and adaptation, as 'the heir of all the ages', and about his 'priceless genetic heritage'. Indeed, both statements are true in a general sense, but we have to be careful not to assume that 'genetic heritage' defines something even as exact as that other omnibus term 'cultural heritage', and still less must we assume that we can specify our genetic heritage in any qualitative or quantitative terms. What Huxley and Muller are saying is that man, as a species, has been subject to natural selection over so many generations that his genotypes are now well adapted to his environments. Or, put conversely, mutations are now likely to be detrimental to that total genotype since most will be recurrences of mutations which have previously been tried out, found faulty, and eliminated by natural selection. This is why mutations are detrimental: the useful genes are already incorporated in the genotype; changes in these genes are likely to be disadvantageous just as are random modifications of any complex machine. I want to suggest that the eugenics proposition is not now true for two reasons: first, the environment has been changing, and recently it has been changing dramatically; and, second, breeding isolates are also breaking down. Members of a group which has lived and reproduced in a particular area ($\equiv$ environment) are now mixing with members of quite unrelated groups. Both these changes affect what one means with respect to genetic heritage adapted to survival in a particular environment. There is a third point which is whether or not our genetic heritage ever was really as homogeneous an

entity as was once thought, and this is worth spending a moment on.

In 1966, Hubby & Lewontin in the U.S.A. used electrophoresis to look at the enzyme complement of a wild population of *Drosophila*. This technique separates proteins of different charge, and will thus separate the wildtype (or standard) from a mutant gene product, if the two differ in charge. To everyone's surprise they found that about one-fifth of the enzymes they identified were polymorphic; that is to say, different forms of the same enzyme existed together in the population. Since genes determine enzymes there must be the equivalent number of mutant genes in the population. About the same time, and subsequently, Professor Harry Harris (1969) looked at human populations and found that of eighteen randomly selected enzymes six were polymorphic. Both results probably underestimate the extent of polymorphism since the technique depends only on differences in the electrical charge on the proteins, and there may be other kinds of differences not affecting charge. Consequently, both groups of workers estimate that about one-third of all genes in a population may be polymorphic. Not only does a particular gene exist in more than one form, but in some cases as many as ten different phenotypes can be identified for one locus. Indeed, Aarskog & Fagerhol (1970) have now identified seventeen phenotypes of human serum α_1 -antitrypsin. We have no satisfactory explanation of this heterogeneity at the present time. However, the point is that wherever we look, and there is much other such evidence, *natural* populations are found to be genetically more heterogeneous than we expected as recently as 5 years ago.

This natural heterogeneity of man is being greatly, and additionally, increased by the breakdown of isolates, of breeding groups within populations, and by migration between nations, as Dahlberg (1942) pointed out 30 years ago or more. Genetic mixing is dependent on mobility, and I am sure I need not stress that point further. Changes in social custom also have their effects. In France, consanguineous marriages (taking relations up to second cousin) have declined from about 5% at the turn of the century to below 0.5% today. Obviously migration in all its forms has been encouraged by the steam and internal combustion engines, and made our population units more heterogeneous genetically in ways no one anticipated. Because other aspects of environment have also changed we cannot say if this heterogeneity has been good or bad *in itself* but obviously by increasing outbreeding it has reduced the *incidence* of recessive disease, as Dr Whittle pointed out. And it will continue to do so for some hundreds of years to come.

So much then for the 'nature' of my title. There is

much more that one could say, but it all merely adds to the fact that human populations are at a stage of development, of evolution, where their genetic heterogeneity is at least as important a characteristic as their homogeneity was once thought to be. Inevitably this means that our basic terms of reference to Galton's proposition, that we can select for improved genetic fitness in man, are vague. Do we want more heterogeneity or homogeneity for particular genes? In any event, have we any control over the large-scale social changes now occurring? In my view, no geneticist can give us answers, except for the extreme genetic variants discussed here with respect to genetic counselling. In short, we cannot readily define the 'better genes for tomorrow' (Muller, 1964).

But in addition to these changes in nature, we also have to cope with striking changes in nurture. Many of these have occurred since man became a settled agriculturist some 10,000 years ago (i.e. 300 generations), and have become increasingly important since the Industrial Revolution (i.e. about six to seven generations ago). It is hard to get good figures to indicate what this has meant. One general index is the expectation of life. Prior to the industrial revolution this was between 32 and 37 years in W. Europe (including Britain) and in the U.S. In short, it was about the same as that of an Indian living in a central Indian village today. By contrast, in the industrialized west, we now have problems in dealing with our aged; problems which are more familiar to you than to me. There is no need for me to emphasize this further, particularly since we all have experience of these changes in our own lifetime. What we call 'nurture' or total environment has now changed radically, and what we call natural selection must also have changed. To be specific, the culling role of infectious disease (for example) is now quite different from what it was a generation ago, just as the culling role of the motor car is quite different. Further, the number of generations exposed to selection is so small that selection can have had virtually no effect, i.e. brought about no genetic adaptation. Consequently, we have (a) no basis for assessing how far western man is genetically adapted to his *current* environment and (b) no way of thinking about selecting artificially for adaptation to a progressively changing, and essentially unpredictable, *future* environment. Galton's proposition that we should selectively breed for fitness implied fitness in an environment. This way of thinking may have made some kind of sense in a leisurely Victorian era; it makes less obvious sense now. For this reason there seems no point in going through some of the old arguments of how one might choose parents with the fine characteristics of high intelligence, altruism, courage, and physical

wellbeing, although it is worth noting the Oneida religious colony in the U.S.A. actually did do this, and did limit its breeding for about a decade to parents selected by a committee for just these attributes. But this was a freak experiment, too small to be significant. Changes of nurture are thus now so rapid, and our knowledge of human genetics so scanty, that it seems to me that the eugenic proposition falls to the ground. I hope this is a moral relief to you all!

Yet medicine does affect man's genotype, and I want to look at one or two issues which arise from this.

The first is the dysgenic action which permits the survival of those who would have died without medical assistance. This obvious consequence of normal medical practice is often held against medicine, as you know. I think it is largely mistaken. A great many such actions which preserve the individual in a healthy state make no difference to the number of children he (or she) has, and are therefore without genetic significance. Some do permit improved reproductive performance, and the classic example is insulin and the diabetic. Let me beg the question whether diabetes is due to a single gene of low penetrance or is multifactorial: the fact is that the heritability of this complaint is about 35% (Falconer, 1967) and it is argued that preserving diabetics will therefore increase the incidence of the gene in the population. Assuming everything else to be equal, it will. However, this omits the nurture half of the equation, for the environment now includes insulin, and has done so since Banting, Best and McLeod. As far as we can see into the future there always will be insulin; or if my colleague Dr Taylor's or Dr Shall's work is successful, there will in fact be improved insulins.

Let me take another, but hypothetical, example. A paper by Karlsson (1971) concludes that 'close relatives of psychotic individuals have a significantly increased probability of being considered people of eminence' (i.e. of being in *'Who's Who'* in Iceland). Further, 'that the dominant principal gene for schizophrenia may, in the heterozygous state, lead to cerebral stimulation with improved performance in areas of giftedness and creativity'. Let us assume these statements to be correct. Then, if we can find the equivalent of an insulin for schizophrenia, which is by no means outside the bounds of possibility now that brain biochemistry is attracting Nobel prizes, the use of such a drug would be eugenic for we should have the advantage of the creative heterozygotes without the disadvantage of the disturbed homozygote, as a result of this one environmental change. Of course such environmental changes cost money (and this is always pointed out), but the decisions as to how society spends its wealth seems to me to be another and altogether different issue.

Population control is another area where medicine impinges on genetics, but we know regrettably little about the results. Simple reduction of family size will itself reduce consanguineous mating and the frequency of homozygosis, and has probably contributed to the decline in cousin marriage. Differences in family size between social groups of all kinds (geographical, religious, class, racial) will all contribute to changing gene frequencies, in addition to the mechanisms which I mentioned earlier. One population control is perhaps worth mentioning since it turned out to be eugenic. The Japanese used abortion as a major birth control measure after 1947, and at the peak about a third of all pregnancies were so terminated. As the abortion rate increased, deaths from congenital malformations decreased from 23.7 to 19/1000. There was also a 40% reduction of trisomy 21, and about 50% reduction of erythroblastosis (quoted by Lerner, 1968). The reason for this was easy to see since the proportion of live births not later than third in the family rose from sixty-four to ninety during this period. In short, the abortions were sought mainly by older mothers, and they eliminated later members of the sibship. The pill and intra-uterine coil are now used in Japan, as in the West, but are presumably altering family structure in the same way as abortion. And this is happening to us, too. With the improvement of techniques for typing the cells of the foetus, and I expect these to develop greatly, abortion will become increasingly important, and may become a very significant sector of the genetic counselling area.

The other side of this coin is AID. Certainly this is usually thought of as positive eugenics, although it is rather difficult to assess if donors are always superior to the population average. Where employed in agriculture, AI has been of enormous importance in upgrading stock, but only because the required characters are relatively easy to define, like milk yield, and AID practised on a wide scale and with a higher degree of inbreeding than we would tolerate. The advanced forms of AI involve sperm storage. Human sperm banks already exist in California and in Japan, and the Russian Serebrovsky's proposal (*euteleogenesis*) that we should preserve the genes of notable individuals (as sperm and eggs) in order to propagate their virtues is now a practical possibility. Future census takers might thus find themselves filling in forms which specify legal father and mother, genetic father and mother, and if Edwards' work in Cambridge is successful, incubator proxy mother as well. And there are other more dramatic possibilities like nuclear transplantation from somatic cells into ova to produce clones of genetically identical people (Gurdon, 1970) and from Harris' work (1971), the insertion of particular genes into defective genomes. (Hotchkiss has pointed out that insertion of a gene

which would allow us to digest cellulose, and therefore feed on grass, would solve the food problem. It would also permit you truly to say that you enjoyed this Journal!) Molecular genetics is now growing so fast that science fiction writers are out of date before their books are published! I shall not get caught on the same hook by speculating about the future. The point, and it is an important one, is that the eugenicist now has to face the fact that, if we survive to the end of this century, there will be so many new ways available for improving our genetic heritage that selective breeding is likely to be relegated to a minor role. The concepts of eugenics will therefore have to be rethought in a new environment.

While eugenic proposals are being reconsidered, we can, and must, concentrate on *euphenics*: improvement of the phenotype by environmental manipulation, leaving the genotype unchanged. In many respects this is just good medical practice: the reconstruction of skeletal or other defects, the provision of missing or defective hormones, enzymes, antigens, etc., and the restructuring of metabolism. Obviously euphenic measures have the advantage of operating on a short time-scale, and can be expected to improve as our knowledge of biochemistry and physiology advances. At the present we tend to replace and patch, but surely we can expect our manipulations to become more subtle and, eventually, to allow us to guide the (genetically defective) developing organism to a normal end. This does not mean that we must have full knowledge of every process, only empirical information about what works. For example, *Drosophila* has a melanotic tumour gene which is a recessive of variable penetrance. The so-called tumours derive from blood cells which transform precociously and aggregate to form the tumour mass, half-way through larval development. Homozygotes grown 'normally' average about 1.3 tumours per fly. Simple dietary manipulations during the first half of larval life can either 'cure' this genetic complaint, so that flies have no tumours, or raise tumour frequency to an average of about seven per fly (Sang, 1970). Yet we do not know what the primary genetic lesion is, although it has been worked on since 1918! Medical practice has always recognized the value of such empirical results, while pressing forward to a deeper understanding of their causes. However, I doubt if it has paid enough attention to applying euphenic measures to mutant genes of variable penetrance and expressivity. Yet these cause the genetic complaints most likely to be amenable to cure through nurture.

As an erstwhile animal breeder I am perhaps oversceptical of the eugenics proposition: but then I know how difficult it is for breeders with even nominally the same objectives to get down to defining them exactly, and agreeing what to do. I also know how

difficult it is to achieve these objectives if they are at all complex, even using organisms whose reproductive performance is entirely under the control of the experimenter. With man the objectives are more difficult to define, and the breeders' techniques of inbreeding, or of deliberate hybridization, socially unacceptable. But thinking about eugenics has this virtue: it makes us examine what is happening to our genes. The increase in heterozygosity of deleterious recessives, which I have mentioned, will lead to their spread through the population, and we may now be starting a phase of 'genetic pollution' roughly equivalent to the beginnings of environmental pollution a generation ago. Certainly the situation is similarly out of control, and beyond our immediate capabilities of predicting the consequences of present events. If these are dire consequences, the medical profession will be the first to see the danger signals. It should therefore give a passing thought to Galton's ideas. It may also find it consoling to realize that molecular biology may already know the answer to some of these future problems: DNA may be the ultimate drug (Aposhian, 1970).

References

- AARSKOG, D. & FAGERHOL, M.K. (1970) Protease inhibitor (*Pi*) phenotypes in chromosome aberrations. *Journal of Medical Genetics*, **7**, 367.
- APOSHIAN, H. VASKEN (1970) DNA for gene therapy. *Perspectives in Biology and Medicine*, **14**, 98.
- DAHLBERG, G. (1942) *Race, Reason and Rubbish*. Allen & Unwin, London.
- FALCONER, D.S. (1967) The inheritance of liability to disease with variable age of onset, with particular reference to diabetes mellitus. *Annals of Human Genetics*, **37**, 1.
- FORD, E.B. (1964) *Ecological Genetics*. Methuen, London.
- GALTON, F. (1883) *Inquiries into Human Faculty and its Development*. Macmillan, London. (Reprinted 1951 for the Eugenics Society by Dent, London.)
- GURDON, J.B. (1970) Nuclear transplantation and the control of gene activity in animal development. *Proceedings of the Royal Society of London*, **B176**, 303.
- HARRIS, H. (1969) Genes and isozymes. *Proceedings of the Royal Society of London*, **B174**, 1.
- HARRIS, H. (1971) Cell fusion and the analysis of malignancy. *Proceedings of the Royal Society of London*, **B179**, 1.
- HUBBY, J.L. & LEWONTIN, R.C. (1966) A molecular approach to the study of genic heterozygosity in natural populations. 1. The number of alleles at different loci in *Drosophila pseudoobscura*. *Genetics*, **54**, 577.
- HUXLEY, J.H. (1963) In: *Man and His Future* (Ed. by G. Wolstenholme). Churchill, London.
- KARLSSON, J.L. (1971) Genetic association of giftedness and creativity with schizophrenia. *Heredity*, **66**, 177.
- LERNER, I.M. (1968) *Heredity, Evolution and Society*. Freeman, San Francisco.
- MULLER, H.J. (1964) In: *The Population Crisis and the Use of World Resources*. Junk, The Hague.
- MULLER, H.J. (1935) *Out of the Night*. Gollancz, London.
- SANG, J.H. (1970) Biochemical basis of hereditary melanotic tumors in *Drosophila*. *National Cancer Institute Monograph*, **31**, 291.
- SCHWARTZ, A.G., COOK, P.R. & HARRIS, H. (1971) Correction of a genetic defect in a mammalian cell. *Nature New Biology*, **230**, 5.