PRINT: ISSN 0970-9274 ONLINE: 2456-6608

DOI: 10.31901/24566608.1990/01.02.01

JOURNAL OF
HUMAN ECOLOGY
Kamla-Raj 1990

J. Hum. Ecol. (1990) 1 (2): 77-80

# The Genetic Future of Man

W. Fuhrmann
*Institute for Human Genetics, Giessen University,*
*Am Steintorgraben 14, D-6300 Giessen, West Germany*

KEY WORDS Genetic Future. Genetic Load. Human Species. Mutation.

ABSTRACT True genetic equilibrium has probably never existed for any human population for any length of time. The conditions of selection have been changing constantly. Quantitative data on these processes are scarce. Available models are discussed. The conclusion is that, from the viewpoint of genetics, no imminent danger exists for the human species, but a slow increase of the genetic load can be expected.

The discussion about the genetic future of man has been dominated over the last few decades by pessimistic projections of a steadily increasing genetic load. This view has been repeatedly expounded particularly by H.J. Muller. A few statistics available on the increase of hereditary diseases among hospital and doctors' patients already seem, at least at first glance, to confirm Muller's vision. Quite apart from the dubiousness of these estimates, however, there must, of course, be another explanation for these figures: due to the control of many acute ailments and infectious diseases, but also to an improvement in the methods of treating hereditary diseases, doctors have shifted their treatment priorities without there being an actual increase in the frequency of unfavourable genes.

Genetic equilibrium between mutation and selection has probably never existed for the human race. The slightest progress, even in primeval times, led to a change in the conditions of selection, although changes then were certainly slower and less extensive than today. Many early achievements of civilization have very probably influenced mutation frequency, too, but we are not in a position to assess them quantitatively.

In more recent times, the application of ionizing rays in medicine and technology has resulted in an increase in the mutation rate, but despite almost 50 years' research in the field of radiation genetics there is still no general agreement as to the scale of the additional mutation load caused in this way. In contrast to the older view of a linear cumulative effect of radiation doses, we assume today that a substantial proportion of mutations produced by radiation are corrected by the cells themselves in repair processes. We are particualrly uncertain in our estimates of the mutagenic effect of radioactive isotopes, especially those like $C^{14}$ or $P^{32}$ which can be integrated into the DNA. Even more uncertain is the quantitative assessment of the increase in mutation rates caused by chemical mutagenes. Due to the great variety of metabolic conditions, even greater differences in the mutagenicity between various species can be expected for chemical agents than for ionizing rays. These differences become all the more probable if, instead of dealing with the powerfully effective cytostatics, which are presently being extensively studied, we turn our attention to less effective substances. These are much more interesting, because they are also absorbed by young people at reproduction age, whereas only a few patients treated with cytostatics produced offspring. Little is known about the significance of repair processes in conjunction with chemical mutagenes.

The consequence is general anxiety about an

undesired increase of the mutation rate in our population without our being able to make a quantitative assessment of it. One can only hope-and there are indications of this-that today the dangers of chemical substances are as exaggerated as they were for some time in the case of X-rays.

Even when selection pressure remains constant, an increase in the mutation rate results in a higher frequency of mutatively altered genes for the human gene pool. The frequency of highly detrimental genes can increase until a new equilibrium establishes itself at a higher frequency level. However, a realistic quantitative assessment is thwarted by the fact that we only have a relatively efficient estimate of the spontaneous mutation rate for but a few human gene loci. The idea is complicated even further by the concept "neutral mutations". These can occur much more frequently than deleterious mutations. It remains open to question here, whether in fact, strictly speaking, there is such a thing as neutral mutations or whether the term "quasi-neutral mutants" preferred by Morton would not be more correct.

On the other hand, the selection factor has been crucially influenced by general factors of our technical civilization, by our way of life and by the consequences of modern medicine. Conditioned by civilization, the selection pressure against numerous defects has been reduced, as was exemplified, for instance, by Post on the subject of colour vision defects. Findings on the subject of myopia and numerous other less obvious defects are similar. The deliberate elimination of selection through the humanitarian protection of the handicapped must have genetically detrimental consequences everywhere where the original impediment is due wholly, or at least to a large extent, to a hereditary disposition. The effects of our social structure on the diffusion of dispositions which condition inaptitude and lack of mental endowments are not as easy to analyse. Although behaviour and endowment patterns of this nature have a very clear genetic foundation, it is highly complex and its realisation is heavily dependent on the influence of environmental factors.

Quantitiatively, the influence of reduced selection on the diffusion of a detrimental, dominant gene has to remain limited as long as there are still remnants of selection pressure against that gene. A new equilibrium between mutation rate and continuing selection will always establish itself. Restoration of the original selection pressure would, in the short term, result in the death of a large number of people and thus rapidly restore the situation which prevailed before treatment began. In the case of autosomal-recessive hereditary ailments, changes can be expected to be much slower. Even radical successes in the treatment of such ailments would only raise the gene frequency very slowly. On the other hand, once the gene frequency has increased, even restoration of the original selection conditions would only cause it to decrease very slowly. Possibly a more powerful influence on the frequency of autosomal-recessive genes in the population than that exercised by the limited successes of medical treatment emanated from sociological changes which received little attention in the last century. Increasing settlement density and mobility in the population together with fewer children have resulted in a reduction in marriages between relatives. However, a falling inbreeding coefficient must result in a temporary decrease in the frequency of homozygotes and, hence, in a reduction of selection pressure. In the short term, this causes a fall in frequency of hereditary diseases but a simultaneous increase in the gene frequency. This continues until, even at a lower rate of inbreeding, homozygotes occur again in the same frequency as before and in every generation many genes are eliminated in accordance with the mutation rate.

It is practically impossible to make a quantitative assessment of possible dysgenic effects resulting from the successful therapy of multifactorially conditioned diseases. The number of genes involved and the relative shares of inheritance and environment in modelling character-

istics are unknown to us. It is certain that successful therapy which endows the bearer of certain characteristics with an improved reproduction potential must lead to an increased frequency of such characteristics. This would be most visible in the first generation after the introduction of some outstanding new therapy. It would make further progress under constant conditions only at an extremely slow pace. The simultaneous change in gene frequency, however, would be much slower because the bulk of the genes is widely spread across the whole population. In the end, a new equilibrium would be reached here, too.

In contrast to the classical mutation selection equilibrium, the example of interaction between malaria tropica and the haemoglobin-S gene has clearly demonstrated that selection favouring heterozygotes can have considerable consequences for the distribution and frequency of genes in the case of humans, too. Our knowledge is limited here to a few good examples because only relatively powerful effects can be elicited. Extremely complex, but of great general interest, is the case of frequently occurring ailments with a multifactorial hereditary base. The well-known model of diabetes mellitus is representative of many. Its frequency seems to originate from an early, no longer effective, selective advantage. Under changed nutritional and environmental conditions the same dispositions result more and more frequently in the disease "diabetes mellitus" and, hence, in the elimination of the genes. Successful treatment can delay this process of gene elimination but can hardly lead to a higher frequency of the genes involved.

Nothing certain can yet be said about the genetic consequences of family planning. Critical studies on differential fertility under the new conditions, the consequences of fewer children and the shift in reproduction age are not yet available. The consequences of a genetic counselling service and, possibly, the widespread application of heterozygote tests, have hitherto mere theoretical significance and certainly little influence. Neither is their effect uniform with regard to direction. As for the possibility of selective alteration of the human gene substance, debated with enthusiasm by many, even the greatest optimists expect at the most an aid in the treatment of isolated hereditary diseases or individual defects, but not a correction in the sense that the patient's children no longer inherit the disposition. The long-term genetic effect would be the same as that of another successful conventional form of treatment. Moreover, there would be the risk of unintentional damage to the genetic material.

The tendencies which are important for our genetic future cannot be compressed into a single short formula. Almost all the hiterto identifiable influences of civilization and medicine are instrumental in changing the gene pool in an undesirable direction, *i.e.* an increase in detrimental genes. The development is characterized by an increased rate of mutation and a simultaneously diminishing selection, but both are probably often exaggerated with regard to their scale and their consequence. The simple black-and white pattern of eugenic and dysgenic influences has given way to a colourful spectrum. There are only a few cases where the signficance of polymorphisms and heterosis have been analysed better. In order to provide extrapolations into the future with a firmer basis, it is necessary to secure documentary information on developments which have already reached their conclusion. The opportunities to carry out such comparative studies on a closed population, still under primitive conditions, are diminishing rapidly. The considerable cost and effort involved in such studies make it imperative to set one's sights on testing certain working hypotheses instead of limiting oneself to merely collecting data.

## REFERENCES

Carter, C.O.: Changing patterns in the causes of death at the hospital for sick children. *Great Ormond Street J., 11:* 65 (1965).

Edwards, J. H.: Advantageous detrimentals and the neutral gene. *Nature, 236:* 250 (1972).

Falconer, D.S., Duncan, L.J.P. and Smith, C.: A statistical and genetical study of diabetes. *Ann. Hum. Genet., 34:* 347-369 (1971).

Falek, A.: Differential fertility and intelligence: Current status of the problem. *Soc. Biol., 18:* 50-59 (1971).

Fuhrmann, W.: Die Auswirkung der modern Medizin auf die Zukunft des Menschen in genetischer Hinsicht. *Naturwissenschaftl. Rundschau, 21:* 414-418 (1968).

Fuhrmann, W.: Aktuelle Selektionsmechanismen. *Studium Generale, Heidelberg, 24:* 246-263 (1971).

Fuhrmann W.: *Genetik-moderne Medizin und Zukunft des Menschen.* Wissenschaftl. Taschenbuch, Mannheim (1970).

Fuhrmann, W.: Fuhrt die erfolgreiche operative Behandlung angeborener Herzfehler zu einer Zunahme solcher Fehlbildungen in kommenden Generationen? *Mschr. Kinderheilkunde, 123:* 368-371 (1975)

Fuhrmann, W., Koch F. und Schweckendiek, W.: Autosomal dominante Vererbung von Gaumenspalte und Lippenspalte zwischen Gauman and Mundboden oder Zunge. *Humangenetik, 14:* 196-203 (1972).

Groenberg, A., Larsson, T. and Jung, J. : Diabetes in Sweden. *Acta Med. Scand. Suppl.*, 477 (1962).

Haldane, J.B.S. : The spread of harmful autosomal recessive genes in human populations. *Ann. Eugen., 9:* 252-257 (1939)

Hollaender, A (Ed.): *Chemical Mutagenesis.* Plenum, New York (1971).

Jackson, W.P.U.: Racial and geographic factors in diabetes. *Lancet, 1:* 601 (1971).

Jackson, W.P.U., van Mieghem, W. and Keller, P. : Insulin excess as the initial lesion in diabetes. *Lancet, 1:* 1040 (1972).

Kidwell, J.F. and Hagy, G.W. : Selection against recessive deleterious and lethal alleles. *Hum. Hered., 21:* 320 (1971)

Lehmann, H. and Carrell, R.W. : Variations in the structure of human haemoglobin: with particular reference to the unstable haemoglobin. *Brit Med. Bull., 25:* 14(1969)

Matsunaga, E.: Possible genetic consequences of relaxed selection against common disorders with complex inheritance. *Hum. Genet., 31:* 53-57 (1976).

Morton, N.E. : Population genetics and disease control. *Soc. Biol., 18:* 243-251 (1971)

Morton, N.E.: The future of human population genetics. pp 103. In: *Progress in Medical Genetics, Vol. VIII,* A.G. Steinberg and A.G. Bearn (Eds.). New York, London (1971)

Motulsky, A.G., Fraser G.R. and Felsenstein, J. : Public health and long-term genetic implications of intrauterine diagnosis and selective abortion. *Birth Defects, Original Article Series, Vol. VII,* No. 5:22 (1971)

Muller H.J.: Strahleneinwirkung und Mutation beim Menschen. *Naturwissenschaftl. Rundschau, 9:* 127 (1956).

Neel J.V.: Diabetes mellitus: A << thrifty >> genotype rendered detrimental by << Progress >> *Am. J. Hum Genet., 14:* 353-362 (1962).

Neel, J.V.: Evaluation of the effects of chemical mutagens on man: The long road ahead. *Proc. Nat. Acad. Sci., 67:* 908 (1970).

Ohno, S.: *Evolution by Gene Duplication.* Springer-Verlag, Berlin, Heidelberg, New York (1970).

Poon King, T., Henry, M.V. and Rampersad, F. : Prevalence and natural history of diabetes in Trinidad. *Lancet, 1:* 155 (1968).

Post, R.H. : Possible cases of relaxed selection in civilized population. *Humangenetik, 13:* 253-284 (1971).

Reaven, G.M., Olefsky, J. and Farquhar, J.W.: Does hyperglycaemia or hyperinsulinaemia characterize the patient with chemical diabetes? *Lancet, 1:* 1247 (1972).

Roberts, D.F., Chavez, I. and Court, S.D.M. : The genetic component in child mortality. *Arch. Dis. Childhood, 45:* 33 (1970)

Smith, C., Falconer, D.S. and Duncan, J.P.: A statistical and genetical study of diabetes. II. Heritability of liability. *Ann. Hum. Genet., 35:* 281-299 (1972)

Stephens, F.E.: An achondroplastic mutation and the nature of its inheritance *J. Hered., 34:* 229 (1943)

Stern, C.: *Grundlagen der Humangenetik.* Jena (1968).

Stevenson, A.C.: The load of hereditary defects in human population. *Radiation Res. Suppl., 1:* 306 (1959).

Vogel, F.: ABO blood groups and disease. *Am. J. Hum. Genet., 22:* 464-475 (1970)

Vogel, F. and Rohrborn, G. (Eds.): *Chemical Mutagenesis in Mammals and Man.* Springer-Verlag, Berlin, Heidelberg, New York (1970)

Vogel, F. und Helmbold W.: Blutgruppen-Populations genetik und Statistik, 129-557, *In: Humanagenetik.* Band 1/4 P.E. Becker (Ed.). Gustav Fischer, Stuttgart (1972).

Whitfield, H.S., Martin R.G. and Ames, B.N.: Classification of aminotransferase (gene) mutants in the histidine operon. *J. Molec. Biol., 21:* 335 (1966).

Wiener, A.S.: Blood groups and disease. *Am J Hum.Genet., 22:* 476-483 (1970)

Woolf, L.I. and Goodwin, B.L.: Effect of dietary treatment on frequency of Phenylketonuria gene. *Lancet, 1:* 216 (1967).

---

This article was an adaption from Fuhrmann, W.: Über die genetische Zukunft des Menschen. pp. 686-700. In: *Bevölkerungsbiologie.* W. Berghard and A. Kandler (Eds.) F. Fischer, Stuttgart (1974) and published in the present form in *Journal of Human Evolution, 6:* 751-754 (1977). After seeking permission from Academic Press, London, this article is being reproduced here, although refereinces from its German publication have been included.