PHILOSOPHICAL TRANSACTIONS OF THE ROYAL SOCIETY B BIOLOGICAL SCIENCES

Conclusions and Summary

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XIII. Conclusions and summary

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The various studies of the Yemenite and Kurdish Jews which have been described in the previous papers were designed to assess the relative significance of genetic and environmental factors in relation to physiological characteristics. The results of the genetic study confirmed and extended previous observations (Goldschmidt 1963; Mourant 1959) and showed there were very considerable differences between the Yemenite and Kurdish Jews, so much so that genetically they could be considered as utterly dissimilar. The main points of difference are summarized in table 1.

Table 1. Genetic contrasts between Kurdish and Yemenite Jews

		percentage gene frequencies	
system	gene	Kurdish Jews	Yemenite Jews
ABO	*A*	27	16
	B	21	5
	O	52	79
MNSs	*M*	52	87
	S	31	55
Rh	*CDe*	52	44
	cDE	22	18
	cDe	0	14
	cde	21	24
	V	0	10
Duffy	Fy^a	48	17
	Fy^b	35	7
	Fy	17	77
Kidd	Jk^a	41	67
Gm	Gm^1	13	29
	Gm^1, 5	8	8
	Gm^5	78	63
haptoglobin	Hp^1	25	32
acid phosphatase	P^a	35	14
	P^b	60	74
	P^c	5	11
glucose 6-phosphate dehydrogenase	deficient genes	42†	8
haemoglobin A_2 percentage of subjects with Hb-A_2 over 3.5% of total Hb	—	24	9

† Considerably higher frequencies have been recorded in other population samples of Kurdish Jews.

One of the most striking differences was in the incidence of G6PD deficiency, very high in the Kurdish Jews, very low in the Yemenite Jews. Lehmann *et al.* (1973, this volume) have shown that there is only a low level of G6PD deficiency in Kurds (Moslems) living in the same region of Kurdistan as the parents of the Kurdish Jews studied in Israel. This finding raises the problem of the origin of high levels of G6PD deficiency. Many population studies suggest that high frequencies of such a deficiency are the result of natural selection favouring the deficient gene under conditions of malarial endemicity, and this is supported by a few studies showing reduced parasite counts in deficient individuals. However, Kurdistan is mountainous and the parents of the present subjects lived in towns and villages at altitudes of 1000 m or higher where the anopheles mosquito would not, in general, survive. There has been, and still is, malaria in the low altitude country of, and immediately adjacent to Kurdistan, close to Mosul, for example, but in most of Kurdistan itself malaria does not appear to be endemic. The low level of G6PD deficiency in Moslem Kurds rules out the hypothesis that the high incidence of this deficiency in Jewish Kurds is due to endemic malaria in Kurdistan. It may be possible that the original ancestors of the Kurdish Jews who migrated to this region already had this deficiency of G6PD but one difficulty in accepting this explanation is that the Babylonian Jews from Iraq are much less deficient and it has hitherto been assumed that the ancestors of the Kurdish Jews participated in that Babylonian exile. Lehmann *et al.* (1973, this volume) have suggested an alternative explanation. Some 140 years before the fall of Judea and the Babylonian exile (586 B.C.), the people of the northern Kingdom (Israel) were conquered by the Assyrians (722 B.C.) and deported to Assyria, which included this area or part of the area called Kurdistan today. This would explain the presence of genetic differences between the Kurdish and Babylonian Jews but it may further be noted that amongst the people of the northern Kingdom were those living in the upper Jordan valley, particularly the region of the Hula marshes. In this area, malaria was endemic until the marshes were drained in recent years. A deficiency of G6PD could have conferred a considerable selective advantage on people living in this area, and it may be that the ancestors of the Kurdish Jews examined in this study were those exiled from this notoriously malarial district. However, none of these hypotheses explains the co-existence for over 2000 years, in a common environment, of two populations with widely differing gene frequencies in a system which, according to other evidence, is in labile equilibrium with the malarial environment. There is, however, a partial parallel in the Shi'a Moslems of the formerly malarial eastern oases of Arabia. They are the only other known population with 50% or more of G6PD deficient genes. Their ancestors have probably lived in the oases for at least 1400 years, whereas the more recent Sunnite Moslem immigrants have considerably lower frequencies.

The anthropometric study showed that there were many highly significant differences between the two communities. The Kurdish Jews were heavier and bigger and had a lighter skin colour than the Yemenite Jews. Some of these differences were probably genetically determined, although the effects of disease and poor nutrition in early childhood before migration to Israel could have affected adult body size.

These genetically and anthropometrically contrasted communities have been shown to live in identical climatic conditions, work in similar conditions, with corresponding patterns of activity, and almost identical levels of energy expenditure. The only difference of any significance that could be detected was a higher food intake by the Kurdish Jews than by the Yemenite Jews.

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The physiological characteristics were just as strikingly similar so the obvious deduction would be that the environmental factors of climate and activity are prepotent and the genetic factors which might affect physical work capacity and the response to a raised body temperature are of little effect. Such a far-reaching conclusion cannot be accepted without qualification.

If the conclusion is correct, then it should apply to individuals as well as to the communities as a whole. Energy expenditure and climatic exposure time were both significantly related to sweat rates recorded during the summer. Work capacity was not related to daily energy expenditure. The examination of individual results showed that the sweating response to a raised body temperature was significantly affected by environmental conditions, but the scatter of the individual results was such that the particular conditions examined could not account for more than 50 % of the variance. Other unidentified environmental factors could be involved but genetic factors certainly cannot be excluded.

The failure to find a relationship between daily energy expenditure and work capacity was unexpected. Andersen (1966), in a review of the subject, considered that maximum oxygen consumption must be related to habitual activity. Other environmental factors may be involved or differences between individuals could be due primarily to inherited characteristics.

Consideration of individual results shows that the original conclusion cannot be supported but the original finding remains, namely the close physiological similarity of the Kurdish and Yemenite Jews as a whole, in spite of their genetic differences.

The original question concerning the role of genetic and environmental factors in determining physiological characteristics needs to be re-examined. It has been assumed, for example, that the large differences between the Kurdish and Yemenite Jews in the genetic factors examined implied that there would be many other genetic differences, including those which could affect work capacity or sweat rate. The assumption is supported to some extent by the anthropometric differences, reported by Lourie (1973, this volume), which may be as he suggests due to genetic factors. Nevertheless, the number of known genetic factors represents such a tiny fraction of all those possible it is hard to be confident that there would be substantial contrasts in the presumably multifactorial genes concerned with either temperature regulation or work capacity. With the possible exception of G6PD deficiency or a high level of haemoglobin A_2, none of the factors examined in the present study appears to be related to any physiological function concerned either with oxygen consumption or with sweat rate. There was no evidence of a reduced work capacity in those subjects with G6PD deficiency or with high levels of haemoglobin A_2 or in those subjects with both these features. More work is needed to identify genetic factors affecting physiological function; it should be possible, for example, to examine enzyme systems in muscle biopsy material.

The similarity in physiological function between the two communities implies either the genetic factors responsible were alike or that environmental influences were prepotent. It was expected that each of the two communities would be relatively homogenous in their physiological responses but, on the contrary, there were large individual variations which could not be explained by environmental factors. It is therefore probable that there are genetic factors affecting both sweat rate and oxygen consumption, but the distribution of the variable factors could have been comparable in the two communities. There is also the possibility that the methods used in this study were not sufficiently accurate or reliable, and hence real differences between the two communities might not have been detected. The assessments of energy expenditure and of climatic exposure were probably of sufficient accuracy for determining similarity

or difference between the two communities, although there could have been considerable errors in the case of individual subjects. The laboratory techniques for determining sweat rate and maximum oxygen consumption could be considered reliable and accurate for individual subjects. Nevertheless, with the numbers of subjects studied and the wide individual variation, differences of the order of 5% between the communities could not have been detected. The practical difficulties of studying much larger numbers with present techniques are considerable. There is a need, as Harrison (personal communication) has stressed, for physiologists to develop simple and reliable methods for assessing physiological functions in large numbers of subjects, or techniques must be so improved that small differences can be reliably detected.

The first and apparently obvious conclusion from these studies has to be restated. Two ethnic groups, genetically different but living in virtually identical conditions, were physiologically indistinguishable. Environmental factors therefore play a large part in determining physiological characteristics but the role of genetic factors could not be definitely identified.

This detailed study has shown the value and feasibility of linking a number of disciplines and could open a very wide field of investigation. The exploration of factors influencing individual variation could lead not only to a better understanding of human heredity but also to practical applications in medicine.

The formulation of the problem of this investigation was achieved after discussion and criticism with many colleagues. Although plans were initiated at an earlier date, it was the establishment of the International Biological Programme which made this study feasible. The problems of planning and executing a multidisciplinary study are considerable and could not have been overcome without the development of the I.B.P. and the establishment of concepts as well as the methods to be used.

It will be obvious that the success of the whole study depended on help and assistance from many organizations and individuals. In Israel, the organizations and institutions included: the Hebrew University Hadassah Medical School, Jerusalem; the National Council for Research and Development; the Central Bureau of Statistics; the Meteorological Office and the Ministry of Health; and the Negev Institute for Arid Zone Research in Beer Sheva. Professor J. Magnes of the Department of Physiology, Hadassah Medical School, not only played a large part in the initiation of the scheme but has also, throughout, provided valuable guidance and help.

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