Ischaemic heart disease

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There can be no truly objective frequency estimate of the susceptibility of the population to ischaemic heart disease: everybody has some degree of susceptibility. The disease kills 1 in 4 of the population, and 1 man in 10 dies of ischaemic heart disease before 65 years of age. The major burden is mortality, though there is often some degree of impairment among survivors of acute attacks. It is in fact mainly a problem of sudden death: as many as 50% of deaths occur within an hour of onset of the attack.

Table 1 Familial resemblances in serum cholesterol levels

	No. of pairs	r
Sib/sib	123	0.37
Mother/child	373	0.36
Father/child	373	0.21
Husband/wife	201	0.006

(Adlersberg *et al.*, 1957)

The disease has a large genetic component, probably involving multiple genes. Raised serum cholesterol levels have been implicated in ischaemic heart disease. Correlations in these levels have been noted between sibs and child/parent pairs, but not between mother/father pairs (Table 1). Studies comparing monozygotic with dizygotic twins have confirmed the presence of a genetic component controlling both serum cholesterol level (Table 2) and susceptibility to ischaemic heart disease (Table 3). National death rates from ischaemic heart disease have been correlated with population frequencies of histocompatibility antigen, HLA-8 (Fig. 1) and haplotype 1-8 (Fig. 2) (Mathews, 1975). It has, therefore, been suggested that HLA-8 is linked to genes which

Table 2 Resemblance between twins in serum cholesterol levels

	No. of pairs	Concordance
MZ	65	0.56
DZ	54	0.37

Heritability = $2(r_{MZ} - r_{DZ}) = 0.38$
(Pikkarainen *et al.*, 1966)

Table 3 Prevalence of IHD in surviving members of 197 same sex death-discordant twin pairs

	Prevalence of ischaemic heart disease in survivors	
	MZ	DZ
Index dead of ischaemic heart disease	17/18 (94%)	25/34 (74%)
Index dead, other causes	38/55 (69%)	56/90 (62%)

(De Faire, 1974)

predispose to hypercholesterolaemia and ischaemic heart disease.

The genetic component in ischaemic heart disease is certainly affected by environmental factors. Radiation, because it is mutagenic, may therefore affect the incidence but since the disease is so common it is

Fig. 1 Correlation of death rate from ischaemic heart disease for men aged 55 to 64 in 1970 with population frequency of antigen HLA-8. 19 Caucasian populations (France, Italy, Yugoslavia, Switzerland, Hungary, Austria, Germany, Sweden, Denmark, Netherlands, Iceland, Czechoslovakia, Norway, England and Wales, Canada, Scotland, Australia, USA, Finland); 3 non-Caucasian populations (Japan, Mexicans in USA, and Blacks in USA). For Caucasian populations: Rank correlation coefficient: $r = 0.64$, $P < 0.01$.

Fig. 2 Correlation of death rate from ischaemic heart disease for men aged 55-64 in 1970 with population frequency of HLA haplotype 1-8. 7 Caucasian populations (France, Italy, Iceland, Denmark, West Germany, England and Wales, USA, Scotland); 2 non-Caucasian populations (Japan and Blacks in USA). For the Caucasian populations regression is given by: $\text{Death rate} = 12.02 + 74.206 \times \text{frequency of HLA 1-8}$. Normal correlation coefficient: $r = 0.84$, $P < 0.01$ Rank correlation coefficient: $r = 0.81$, $P < 0.03$.

difficult to say whether it would increase or reduce the incidence. A 1% change in the genetic susceptibility

could increase or reduce the mortality by a factor of 1 to 2 deaths per thousand and because the condition is so common this would be a large effect. In this context it is interesting that incidence of this disease among radiologists is not found to be exceptional.

There are several indications of environmental factors, the most notable of which are the studies of migrants from low incidence areas to high incidence areas. After 2 to 3 generations these migrants show the same incidence as that in their new country.

It can be concluded that there is an important degree of genetic susceptibility but this does not act alone and it is modified strongly by environmental factors. Without a better control for environmental factors it is difficult to identify the high risk group genetically.

References

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