The Danish Twin Register, Copenhagen

Coronary Occlusion in Twins

B. Harvald, M. Hauge

It seems to be generally accepted that genetic factors take a place among the causes of coronary heart disease. Careful and extensive family studies, among others by workers in Carter's group, have shown that the risk to close relatives of patients with coronary heart disease is significantly increased. This may, however, be an effect of the common social background in families. Systematic twin investigations have been needed, which could distinguish between the effects of common environment and common genes, and allow an estimate of the relative importance of genetic and environmental factors.

The present study is an approach to this problem by using twins with coronary heart disease in the Danish Twin Register (Hauge et al, 1968). This was founded in 1954 and has been developed ever since. It now contains total medical information on about 10 000 unselected pairs of twins born in Denmark in the period 1870-1910, where both partners have survived the age of five. On January 1, 1968, coronary occlusion had been registered in a total of 352 twins.

The results are given in Tab. I. In the calculations the twin proband method has been used (Allen et al, 1967); i.e., concordant pairs are counted twice, as both partners are considered probands. Thus, among 77 MZ male probands, 30 had

Tab. I. Coronary occlusion in twins

Sex	Zygosity	Concordance rate	
		N.	%
♂♂	MZ	30/77	0.39
	DZ	32/122	0.26
♀♀	MZ	12/27	0.44
	DZ	8/54	0.14
♂♀	DZ, ♂ probands	7/53	0.13
	DZ, ♀ probands	8/19	0.42

cotwins, who were equally affected. The concordance rate of 0.39 differs significantly ($P < 0.05$) from that of 0.26 in same-sexed DZ male pairs. The difference is, however, not very impressive.

In females, the difference between MZ and DZ same-sexed pairs is much more pronounced and significant at a higher level ($P < 0.01$). A remarkably high concordance rate is found in DZ different-sexed pairs with female probands.

These findings are further illustrated in Fig. 1. Here, the first affected twin in a pair is considered as proband; in the present case, only such individuals who have died from their coronary occlusion. The curves then indicate the risk for cotwins of

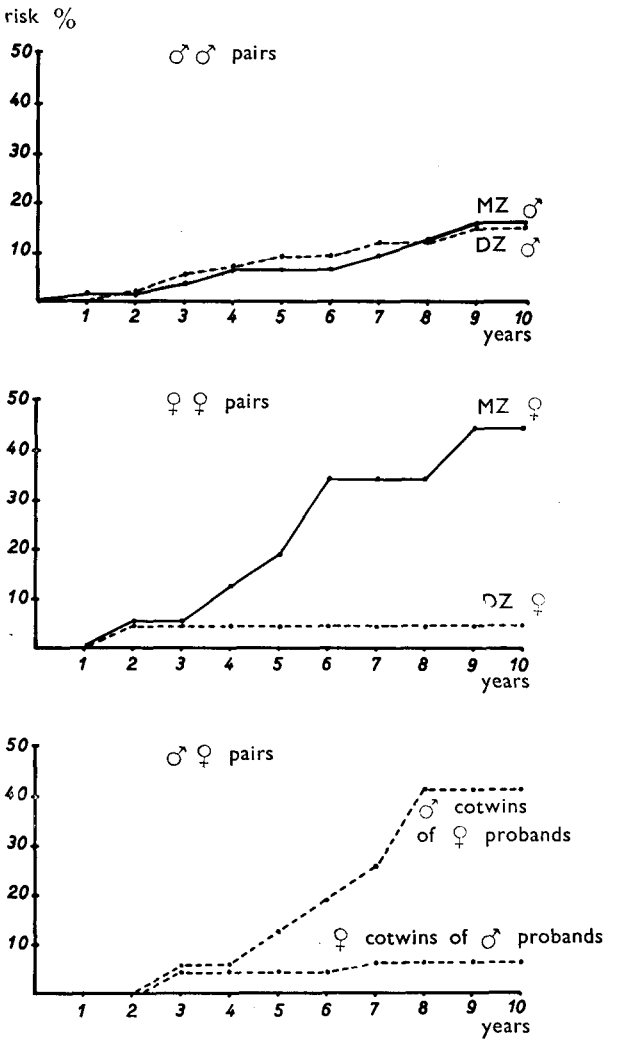

Fig. 1

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dying from coronary occlusion in the first 10 years after the proband's death. The risk curves for cotwins in MZ and same-sexed DZ male pairs follow each other very tightly. On the other hand, the curves for female pairs deviate from the very beginning. Thus, the risk for female MZ cotwins of dying from coronary occlusion is over 40% in the first 10 years after the proband's death. The corresponding risk for female cotwins of same-sexed DZ pairs only reaches a level of about 4%.

The interpretation of these findings should be that the occurrence or nonoccurrence of fatal coronary occlusion is genetically determined to a very limited extent in males, and to a much larger extent in females.

This finding is not very far from what should be expected. In a society where environmental factors known to influence the occurrence of coronary occlusion are more or less restricted to the male sex, the importance of these factors will outweigh the importance of the genetic set-up. Therefore, the risk curves for cotwins of MZ and DZ same-sexed male pairs will be very nearly the same, in spite of the difference of genetic predisposition in the two groups of individuals. In females, on the other hand, only those who are heavily genetically predisposed will be clinically affected. This explains the steep risk curve for MZ cotwins, who are genetically predisposed as the probands, whereas DZ cotwins fail to show the same high degree of predisposition. That this interpretation is correct, is confirmed by the risk curve for male cotwins of female probands in DZ different-sexed pairs, as compared with the risk curve for male cotwins of DZ same-sexed pairs. The former curve is much steeper, indicating that genetic predisposition is much higher in families where a female is clinically affected.

Most family studies leave the impression of an overwhelming accumulation of secondary cases among close relatives of patients with coronary occlusion. The present study seems to show that the overall genetic influence is rather limited in males but more pronounced in females. Twin studies, however, do not allow a formal analysis. The difference of manifestation between males and females advocates a multifactorial determination of genetic predisposition. A few mutant genes are known, however, which highly influence the predisposition of the carrier, such as the genes for hypertriglyceridemia and for hyper-β-lipoproteinemia, but the relative share of these specific genes for the occurrence or nonoccurrence of coronary occlusion in the general population should be estimated to be rather low.

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Dr. B. Harvald, Medical Department B, Odense Amts. og Bys Sygehus, 5000 Odense, Denmark.