CORONARY HEART DISEASE IN MALE TWINS
Seven-Year Follow-up of Discordant Pairs

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In an investigation in 1967 of about 100 male twin pairs collected from the Swedish Twin Register, discordance with respect to the presence of CHD was found in 37 pairs of which 19 were MZ. The investigation included physical examination, cholesterol measurements, and an interview regarding, among other things, smoking habits. In a follow-up study in 1974 — seven years after the original investigation — all but one of the 37 twins regarded in 1967 as free from overt CHD could be traced. Ten of the 36 twins had developed symptoms of overt CHD (angina pectoris or infarction); 18 twins were still healthy, 2 had died from other causes, and 6 had questionable complaints of breast pains. In a comparison of the two groups of twins with and without symptoms of overt CHD, no differences were found with respect to blood pressure, serum cholesterol, or smoking habits, as presented at the 1967 investigation. It is concluded that none of these factors seemed to influence the future development of CHD in twins apparently tainted with a heredity for this disease.

INTRODUCTION

As one of the leading causes of death and disablement, cardiac disease due to impaired coronary blood flow has long been in the focus for clinical research the world over. Great efforts have been made trying to prevent or delay phases of the disease that lead to circulatory malfunction. The etiology, however, as well as the pathophysiology is still uncelar and as yet certain factors can be identified which characterize people who are likely to become affected. The most important so called *risk factors* seem to be high cholesterol, high blood pressure and some behavioral characteristics of which smoking is one of those most discussed. A genetic dispostion for the disease has been claimed whether carried by the factors mentioned or by yet unidentified factors. From the present knowledge, however, it seems to be a multifactorial etiology and the main issue from a therapeutic point of view would be to discriminate between factors of mainly genetic and environmental origin.
Family studies have the disadvantage of not being able to separate genetic traits from family habits, while twin studies offer better opportunities in that respect. The previously described Swedish twin register (Cederlöf et al. 1966) has been compiled to provide opportunities for the study of chronic diseases such as coronary heart disease (CHD) with an epidemiologic approach.

1967 CHD TWIN STUDY

In 1967 a subsample of 91 male twin pairs from the Swedish twin register was clinically examined for the presence of overt CHD (Liljefors 1970). The twins had entered the study in accordance with a positive answer to a mailed questionnaire regarding, among other things, the presence of symptoms of CHD (Fig. 1).
The material was purposely limited to men aged 42 to 67 and the DZ twins were taken from a restricted geographical area.

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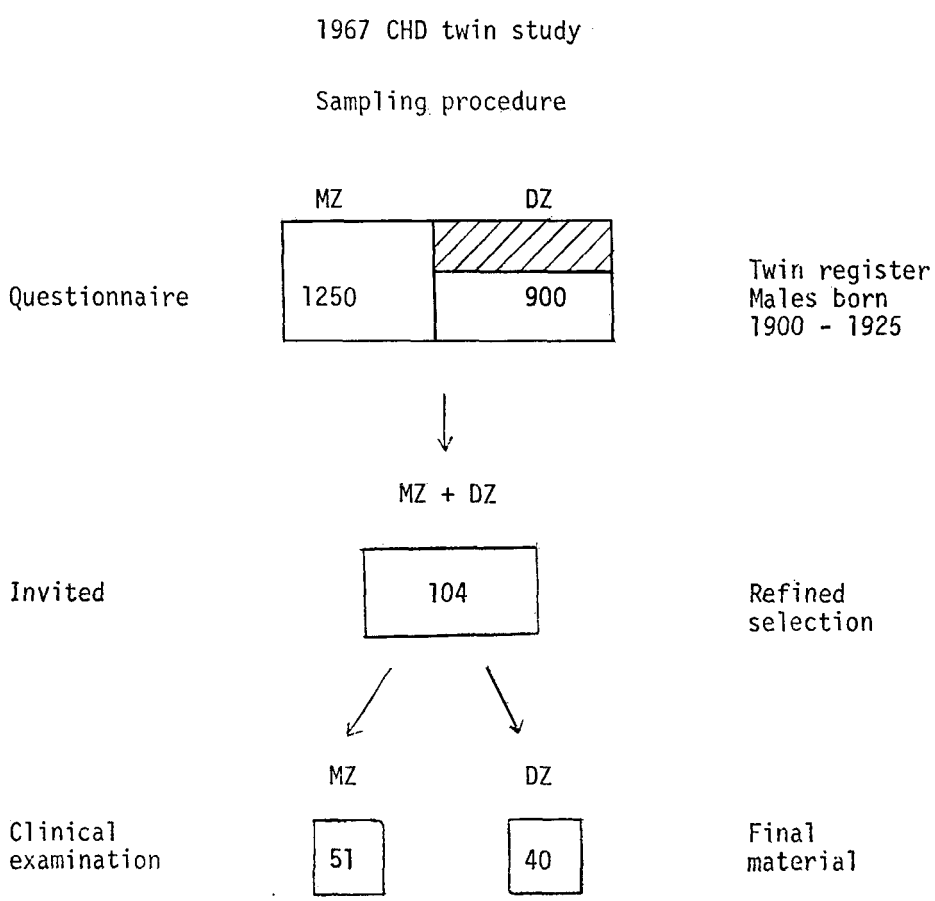

Fig. 1

The examination included ECG during exercise, analysis of serum lipids and a sociologic interview. CHD diagnosis was made according to the following criteria: (1) Myocardial infarction; (2) Angina pectoris *and* pathologic ECG at rest or during exercise; (3) Angina pectoris *or* pathologic ECG at rest or during exercise; (4) Suspected angina pectoris or suspected pathologic ECG; (5) No such findings.

The CHD groups 1, 2 and 3 were decided to represent clinically overt CHD; the groups 4 and 5 probably no CHD.

The examination of the 91 pairs revealed concordance with respect to various criteria of CHD according to Table 1.

Each one of the MZ and DZ pairs was concordant with respect to myocardial infarction (MI) (represented as group 1); 4 of the MZ and 3 of the DZ pairs were concordant with respect to MI or angina pectoris (AP) (group 1 and 2); 16 of the MZ and 7 of the DZ pairs were concordant if the CHD criteria also included group 3.

Thus, including less serious manifestations of CHD, the concordance ratio of MZ vs. DZ rose, but not however to reach statistical significance.

A total of 19 MZ and 18 DZ pairs were discordant with respect to the presence of clinically overt CHD (group 1-3).

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Table 1. *1967 CHD twin study; cumulative concordance for various CHD groups*

CHD groups	Concordance ratio		
	MZ	DZ	MZ/DZ
1	1/17	1/12	0.71
1-2	4/25	3/18	0.96
1-3	16/33	7/25	1.73
1-4	25/41	16/35	1.33

Table 2. *1967 CHD twin study; serum cholesterol mean values in CHD discordant pairs*

	MZ twins		DZ twins	
	CHD	No CHD	CHD	No CHD
N	10	10	8	8
Cholesterol (mg/100 ml)	283.4	299.0	294.3	294.5

Table 3. *1967 CHD study; serum cholesterol mean values in concordant pairs (CHD and no CHD)*

	CHD concordant	No CHD
N	28	24
Cholesterol (mg/100 ml)	313.9	257,5

Table 4. *1967 CHD twin study. Diagnosis in discordant pairs*

			Partners		
Group			4	5	N
Index twins	1 (MI)	MZ	5	4	9
		DZ	3	5	8
	2, 3 (AP)	MZ	5	5	10
		DZ	4	6*	10

* 1 partner no follow-up.

Analysis of the aforementioned risk factors (high serum lipids, high blood pressure, smoking) showed no difference within these pairs between the twin with and without CHD. As an example, Table 2 presents the mean values of serum cholesterol in the discordant MZ and DZ pairs. A comparison was also made between the serum cholesterol value in the total group of CHD concordant twins and an agematched group of twin pairs in which neither twin had presented significant symptoms or signs of CHD (Table 3). Only the difference between the twins with and without CHD in the concordant pairs was significant. Moreover, the level of the serum cholesterol in the discordant pairs was nearly as high as in the CHD concordant pairs.

FOLLOW-UP STUDY

The intention of the present study was to follow up the 37 pairs of CHD discordant twins 7 years after the original examination in order to see to what extent they had become concordant with respect to symptoms of CHD, and to investigate the prognostic value of the risk factors analysed in 1967. Table 4 shows the 37 partners who in 1967 were found to have no (group 5) of minor (group 4) signs of CHD distributed on the diagnosis of cotwin and zygosity.

One of the DZ twins could not be traced for follow-up, giving 36 partners to report on.

The study was performed as an interview mainly by telephone regarding symptoms of CHD in the form of: (1) myocardial infarction; (2) angina pectoris according to the WHO criteria, and (3) other symptoms of CHD.

Table 5 shows that 3 of the partners had experienced MI all with a fatal outcome; 7 had developed angina pectoris, while 18 were still healthy. Two MZ partners had died from other causes (one in

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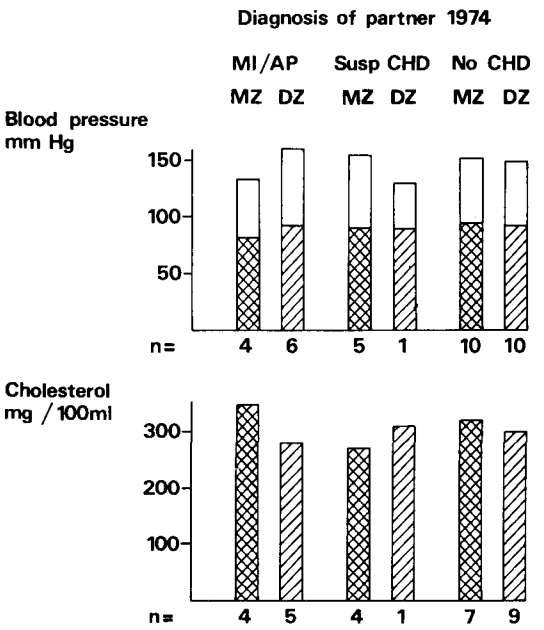

Fig. 2. CHD twin study follow-up; blood pressure and serum cholesterol in 1967; mean values.

a traffic accident and one from stroke); there was no information of any CHD symptoms in these cases. The 6 twins with suspected CHD all had uncharacteristic chest pains or other vague symptoms. An analysis was performed concerning the blood pressure and serum cholesterol mean values from the 1967 investigation in the partners according to the symptoms displayed in the follow-up study (Fig. 2).

Neither the blood pressure nor the serum cholesterol values was correlated with the CHD symptoms reported at the follow-up. However, the rather high cholesterol level (above 300 mg/100 ml) irrespec-

Table 5. *CHD twin study follow-up*

Diagnosis of		Partners 1974			
		MI	AP	Susp. CHD	No CHD
Index twins 1967	MI MZ	1	3	2	3
	MI DZ	2	—	1	5
	AP MZ	—	—	3	7*
	AP DZ	—	4	—	5
	Total	3	7	6	20
	Mean age	65	65	67	65

* 2 dead by other causes.

Table 6. *CHD twin study follow-up*

Smoking habits 1967	Diagnosis of partners 1974					
	MI/AP		Susp. CHD		No CHD	
	MZ	DZ	MZ	DZ	MZ	DZ
Cigarettes	1	1	2	–	3	3
No cigarettes	3	5	3	1	7	6
Total	4	6	5	1	10	9

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tive of the development of overt CHD or not, should be pointed out. Smoking habits presented as the number of cigarette smokers in 1967 (Table 6) were of no prognostic value in the partners.

DISCUSSION

Since MZ twins share all and DZ twins half of the genetic predisposition, any disease in which heredity were of importance would display a high intrapair concordance. This was also found in the present as in other twin studies of CHD (Liljefors 1970, de Faire 1974).

The 1967 CHD Twin Study showed the highest concordance in the MZ pairs when the CHD criteria also included discrete symptoms or signs of the disease. Irrespective of whether concordant or discordant with respect to CHD the cholesterol level in these pairs was higher than in pairs with no signs of CHD. These results of the 1967 study would indicate the presence of a genetic predisposition for the development of overt CHD. There is some evidence that this predisposition can be manipulated by environmental influence. Change of diet (Leren 1970, Miettinen et al. 1972) and lowering blood pressure (Vet. Adm. Coop. Study Grp 1970) has given some effects on cardiovascular mortality. Risk factors like smoking and other behavioral characteristics are far more difficult to influence and have for that reason not been studied in a proper controlled manner. Since, however, the genetic predisposition for CHD seems to be of great importance, the environmental variance of the clinical expression would be best studied in a genetic homogeneous population like MZ twin pairs.

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