PREDICTING CORONARY HEART DISEASE FROM MINOR SYMPTOMS AND ELECTROCARDIOGRAPHIC FINDINGS

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Many coronary heart disease (CHD) deaths and many attacks of myocardial infarction seem clinically to occur as unheralded catastrophes. This is surprising, considering that pathologically such events are preceded by years of progressive atherosclerosis and ischaemia. The present study estimates the frequency with which minor symptoms and electrocardiographic changes may occur in the years before these major 'unexpected' illnesses.

RESULTS

A group of 1,127 men, aged 35 to 59 and initially free of known CHD, have had annual examinations since 1961 (Rose, 1968), including a standard questionnaire on chest pain (Rose, 1962) and (on three occasions) an electrocardiogram. The ECGs were classified according to the Minnesota Code (Blackburn *et al.*, 1960). Subjects were classified according to their symptoms as having or not having (a) a defined syndrome of 'angina of effort', and (b) a history of 'possible infarction' (defined as an attack of severe central chest pain lasting for half an hour or more). Experience in applying this questionnaire to population samples has shown that the ascertained cases tend to be less severe than the more familiar cases of angina and suspect infarction in ordinary clinical practice. Generally, in fact, these symptoms attracted little attention, and often the affected individuals had not even reported to their doctors.

During the first seven years of follow-up, 79 men developed major coronary illnesses (37 deaths, 34 cases of non-fatal myocardial infarction, and 8 cases of major angina only). In 29 of these men (37%) the first major illness had been preceded by a positive questionnaire (i.e., angina or 'possible infarction' at any one or more of the interviews), and in 23 (29%) by a 'positive' ECG (Minnesota code 1.1-2 or 4.1-2 or 5.1-2 or 7.1). In 33 cases (42%) the major

illness occurred without any previous record of either kind of abnormality; 17% of these men had reported 'non-specific' types of chest pain or discomfort, whilst others had failed to attend for their examinations. In fact major CHD illnesses occurred in only seven individuals who had attended two or more prior examinations, all completely negative. Only two such cases were in men with four or more prior examinations, all negative.

Predictive power may be expressed in various ways: (1) the *actual risk (incidence)* in affected persons; (2) *relative risk*—the ratio of incidence rates in persons with and without the finding; (3) a finding may carry a high relative risk but still, if its prevalence is low, it may miss most of the subsequent cases. One therefore also wants to know the *proportion of cases predicted*.

Table I sets out these estimates of predictive power for major coronary illness in this study. In each of the classes the relative risk is about 3 and the seven-year incidence is around 20%. The proportion of CHD cases predicted ranges from about 10% for

TABLE I
SEVEN AND A HALF-YEAR RISK OF CHD ACCORDING TO INITIAL EXAMINATION FINDINGS IN 1,127 MEN

Initial Examination (1961)		Follow-up (1961-8)		
Positive Items	Prevalence %	% Developing CHD	Relative Risk of CHD	% of Total CHD Predicted
Symptoms				
Angina	3.6	20	3.0	10
'Possible infarction'	5.3	22	3.5	16
Angina or 'possible infarction'	8.0	17	2.7	19
ECG				
Major	3.5	17	2.7	9
Minor	6.8	17	2.7	16
Major or minor	10.4	18	3.1	27
Symptoms or ECG	16.4	16	3.0	37

TABLE II

RISK OF CHD IN 1,127 MEN ACCORDING TO INITIAL EXAMINATION FINDINGS IN (a) FIRST THREE YEARS, AND (b) ENSUING FOUR AND A HALF YEARS

Items Positive in 1961	Relative Risk of CHD		Proportion of Total CHD Predicted (as % of cases in period)	
	1961-4	1964-8	1961-4	1964-8
Symptoms				
Angina	5.0	2.1	16	7
'Possible infarction'	10.0	1.4	36	7
ECG 'positive'	9.3	1.5	52	15
Symptoms or ECG 'positive'	6.5	2.0	56	28

angina and major ECG findings up to 37% for all abnormalities combined. Symptoms taken as a whole predicted a somewhat lower proportion of cases than ECG findings as a whole. Due to the large measure of independence between the two sets of findings, however, a combination was much more effective than either taken alone.

Table II shows predictive power in relation to length of follow-up. All the relative risks are much higher in the first three years, especially for 'possible infarction' and the ECG. Relative risks in the second period are low but still above unity.

DISCUSSION

Similar evidence on the frequency of antecedent minor abnormalities has been reported from the Tecumseh study (Chiang *et al.*, 1970). In our study these early manifestations of CHD were often transient. Of men classed at the initial examination as having angina, less than 50% remained positive a year later (Rose, 1968). Many who lost their symptoms also seemed to lose even the memory of them. Of men answering 'yes' to the question on severe central chest pain, about half when questioned a year later denied ever having had such a pain. Similarly, it is known that minor ECG findings are often evanescent (Ostrander, 1966).

This variability in the early manifestations of CHD implies that the probability of detecting changes before a major attack will depend on the number of times that the individual has been examined. With annual examinations, many cases that would otherwise have been called 'unexpected' were in fact foreshadowed.

The data presented in Table II suggest that these minor premonitory findings are powerful risk predictors only in the short and medium term. More needs to be known about the corresponding changes in predictive power over time for risk

factors (such as blood pressure and blood cholesterol), which are not themselves manifestations of atherosclerotic disease: possibly the decline may be slower.

The ECG, like all methods of physical examination, has the limitation in mass population screening that it requires the actual presence of the subjects and the use of skilled staff. A symptom questionnaire has the potential advantage that it may be completed by the subjects themselves. In this study it was always administered by nurses. But when interviewer-administered and self-administered versions have been compared in random samples of the same population, we have found that the prevalence of positives is about twice as high with the self-administered version. Nevertheless the experience of the U.S./U.K./Norwegian Migrants Study (Krueger, Rogot, Blackwelder, and Reid, 1970) shows that its predictive power is still both high and also relatively specific (Table III), suggesting that in the hurried conditions of a conventional interview or consultation one perhaps tends to miss a history of minor symptoms; but these may nevertheless be of serious prognostic import.

There is unfortunately no possibility of direct validation of the diagnostic reliability of measures of CHD, since there is no reference test which would identify with certainty all the false positive and false negative cases. The most that can be done is to study the association between the various available measures—in this case between certain early and probably non-specific manifestations, and the subsequent incidence of major clinical disease. The finding that 80% of symptom-positive and ECG-positive patients were alive and well seven years later does not mean necessarily that they were false positives: they may have been true positive cases but with a benign course. Equally, the occurrence of major disease in 20% of those who had been identified by questionnaire or ECG does not prove that these were true positives: they may have included false positives who subsequently happened to become ill.

Nevertheless, despite these uncertainties in inter-

TABLE III

PREDICTION BY POSTAL QUESTIONNAIRE IN THE U.S./U.K./NORWEGIAN MIGRANTS STUDY: RELATIVE MORTALITY RISK IN A TWO-YEAR FOLLOW-UP OF SUBJECTS AGED UNDER 65 YEARS (KRUEGER *et al.*, 1970)

Symptom Group	Relative Mortality Risk			
	CHD		Other Causes	
	Male	Female	Male	Female
Angina	4.8	6.3	1.6	1.8
'Possible infarction'	3.0	6.8	1.1	1.0

pretation of individual cases, it is valuable to have available these simple techniques of mass examination: they permit identification of a high-risk group of persons who stand in special need of preventive care. Experience in their application gives added support to the view that in most cases major CHD is potentially predictable (Chiang *et al.*, 1970).

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