THE COURSE OF CORONARY HEART DISEASE: FACTORS RELATING TO PROGNOSIS*

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CORONARY heart disease is the leading cause of death and is currently responsible for approximately one-half million deaths per year in the United States. These figures highlight the importance of this disease even without consideration of the magnitude of personal distress, disability, loss of work, and periods of hospitalization. In the present decade since the last clinical conference of the New York Heart Association was devoted to this subject, a number of studies have been undertaken which have produced important new information about this disease, its prevention, and control. The data which I am to report are derived from a study which has been in progress since 1961 and is being conducted by the Health Insurance Plan of Greater New York (HIP) with the support of the National Institutes of Health.

The HIP study was designed to place its major emphasis on a description of the course of the disease after the initial clinical diagnosis, and to examine those factors—personal, demographic, and medical—which are related to prognosis. In view of the great variability of the course of clinical coronary heart disease and the multiplicity of factors which may be relevant, a large number of patients must be followed; the group should be as inclusive as possible of all coronary heart disease cases arising in a general population of defined characteristics. The HIP study population consists of 110,000 men and women aged 25 to 64 who are insured for their health care by the HIP. Special circumstances in the HIP setting permit an alternative approach to the repetitive examination of sick and well persons to identify patients with clinical signs of coronary heart disease.[1] Patients suspected of having developed a

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clinical manifestation of coronary heart disease in the course of their normal health care are invited to attend a special study examination conducted at HIP's participating medical groups by internists on the study staff. The cooperation of both physicians and patients has been excellent; approximately 90 per cent of the invited patients have appeared for these special examinations. Cardiac and medical histories are obtained and certain standardized observations are made. The study record includes an abstract of all pertinent prior medical care, and information concerning an extensive list of personal and demographic characteristics. Diagnosis and classification are made in the central office in accordance with criteria which were developed for this study.[2] Eligible patients who satisfy those criteria enter one of the several cohorts which are being followed prospectively. Patients are reexamined six months after baseline examination and then at two-year intervals. Patients who succumb before their baseline examination are classified on the basis of all available information, which includes interviews with the next of kin or witnesses to the death, autopsy data, and other medical records.

A study of this size and complexity requires the cooperative effort of a dedicated staff, a team of examining physicians, and the consent of hundreds of practicing physicians who have made their patients and records available. I am reporting for this entire group and for the coinvestigators, Sam Shapiro, director, and Mrs. Eve Weinblatt, assistant director for research, Division of Research and Statistics, HIP of Greater New York. Robert Sager of HIP's central office and George Seiden, the study's electrocardiographer, have made significant contributions.

In the four-year period of case finding, 881 men suffered their initial myocardial infarction. This disease continues to exact a very high early mortality (Table I); more than one third of these men succumbed in the first month of illness, a case fatality rate similar to that reported from other populations. Most of this mortality occurred shortly after the onset of the illness; only 601 of the men survived long enough to be hospitalized. Among men hospitalized for their initial infarction, the mortality in the first month was 16.5 per cent, a value less than half of that for the entire cohort. Eighty-five per cent of all deaths occurred on the first day; more than two thirds of all deaths occurred before hospitalization was possible. This pattern of rapid death limits the

TABLE I.—MORTALITY AMONG MEN IN THE MONTH AFTER FIRST MYOCARDIAL INFARCTION BY AGE AND HOSPITALIZATION

Age	Total cohort	Died within 1 month		Died within 24 hours		Hospitalized patients		
		No.	%	No.	%	No.	Deaths No.	%
All ages	881	317	36.0	271	30.8	601	99	16.5
Under 45	99	25	25.3	21	21.2	74	7	9.5
45-54	334	103	30.8	93	27.8	238	27	11.3
55-64	448	189	42.2	157	35.0	289	65	22.5

TABLE II.—FREQUENCY OF SEVERAL CHARACTERISTICS PRIOR TO ONSET OF THE INITIAL MYOCARDIAL INFARCTION IN MEN

	Total cohort (881 men)		Men who died in 1st month (317)	
	No.	%	No.	%
Angina	155	17.6	82	25.9
Elevated blood pressure	223	25.3	97	30.6
Congestive failure	35	4.0	29	9.1
Diabetes	105	11.9	37	11.7
Other cardiovascular disease	68	7.7	31	9.8

over-all influence of efforts to improve the treatment of patients in the hospital. Clearly some therapeutic or preventive measures ought be instituted *before* the first infarction occurs. Nor is it safe to wait until angina pectoris or some other clinical manifestation of coronary heart disease appears. Table II indicates that only a minority of the men who suffered a first myocardial infarction—even rapidly fatal attacks—had earlier clinical evidence of angina, hypertension, congestive failure, diabetes, or other cardiovascular diseases.

Thus for the majority of men who suffer their initial myocardial infarction there has been no earlier clinical diagnosis of coronary disease or even of hypertension. One third die of this attack—most with such suddenness that the benefits of hospital care are not available.

These facts indicate the desirability of so-called primary prevention measures, or at least of efforts to induce some change in the biological characteristics of the men subject to this disease. Other studies have produced information on a wide range of conditions that are associated

with an increased risk of the disease in a general population. One of the factors examined in the HIP population was the relation of a man's habitual physical activities to his subsequent experience with his initial myocardial infarction.[3] Some years ago J. N. Morris[4] reported that the conductors in the London double-decker buses were less likely to incur and to die from a myocardial infarction than the drivers. The conclusion was drawn that these differences in coronary heart disease experiences were related to the differences in physical activities required by men in the two occupations. Subsequently a number of other studies in this country and abroad also attempted to determine whether the pattern of coronary heart disease was related to an occupational category. Most of these studies can be interpreted to support the hypothesis that men in occupations requiring less activity are more apt to suffer from coronary disease than men in occupations calling for heavier expenditures of energy. However, the lack of uniformity in these findings, the possibility of differences among the men in other traits, as well as the possibility of the selection of occupation because of preexisting disease, have restricted the validity of the conclusions. Further, studies which base their classification upon occupational categories ignore entirely the differences in physical activities that might be related to nonoccupational pursuits.

A questionnaire was developed for use in the HIP study which inquired into certain specific aspects of the job-connected and off-job activities. There were six areas of questioning in relation to job-connected activities. The men were requested to indicate the proportion of time at work spent in sitting and walking, and the amount of walking in going to and from work was estimated, as well as the frequency of lifting or carrying heavy objects, and the hours worked per week.

Four areas of off-job activity were also recorded. These included recreational walking, participation in sports (with an indication of the type of sport), the frequency of working around the house or apartment, and gardening. Scores were assigned to these responses and a scheme was developed which permitted classification of the population into three levels of habitual physical activity.[5] Similar information was obtained for the general population at risk by a survey questionnaire mailed to a random nonrepetitive 4 per cent sample of the population each year. Information for men who did not survive until the baseline examination was obtained by personal interviews with the next-of-kin.

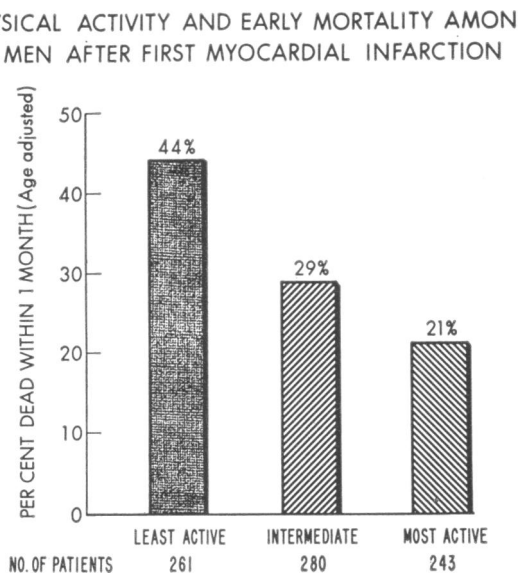

Fig. 1

Figure 1 depicts the early mortality experience in relation to the habitual physical activity classification prior to the onset of the initial myocardial infarction. The mortality experience of the least active men was more than twice as great as that of the most active men. It is proper to question whether this significant and important difference in mortality might be due to factors other than physical activity. The data are presented as age-adjusted rates—to account for differences in the age composition among the three physical-activity classes. The association of physical inactivity with an increased early mortality remains even when religion, color, broad occupational category, and smoking habits are taken into account.

Another important consideration is whether men *became* "least active" because of some disease or condition that also increases the early mortality rate. Prior angina pectoris, for example, might act in this fashion.

This possibility is examined in Figure 2, which is restricted to men free of any prior indication of coronary heart disease, free even of prior elevated blood pressure and, finally, free of both of these factors. In each comparison, the least active class exhibited a significantly higher

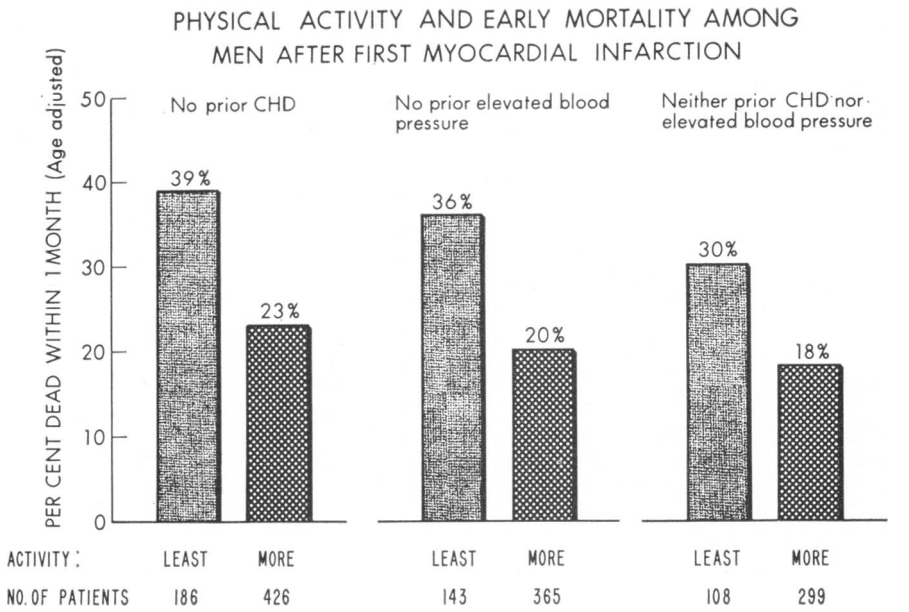

Fig. 2

early mortality in comparison with the two classes of greater activity combined. Finally the question was examined in men who stated that they had not reduced their physical activities for any health reason prior to their initial myocardial infarction; the association of physical inactivity with an excess early mortality rate remained.

Exercise induces a number of acute and persisting changes in the cardiovascular system of man and experimental animals. It would appear reasonable to suggest that the physical activities of the more active men in the HIP population had induced some biological influence which was protective against the development of a lethal myocardial infarction.

Interest naturally arises as to how these findings relate to the history of smoking cigarettes. Table III presents these interrelations. Men who smoke cigarettes are at considerably higher risk for suffering their initial myocardial infarction than men of the same age who do not smoke cigarettes. This increased risk for cigarette smokers occurs among men of each physical activity class. Conversely, men who are habitually least active have an increased incidence of myocardial infarction in

TABLE III.—INITIAL MYOCARDIAL INFARCTION AMONG MEN UNDER 65: INCIDENCE AND EARLY MORTALITY IN RELATION TO PHYSICAL ACTIVITY AND SMOKING HABITS*

	No. 1st MI's per 1,000 men at risk per year	*Per cent of men with 1st MI dying within 1 month*	*No. deaths within 1 mo. of 1st MI per 1,000 men at risk per year*
Total	5.20	36.0	1.87
Under 45	1.42	25.3	0.36
45-54	5.54	30.8	1.71
55-64	9.39	42.2	3.96
		Age-adjusted rates	
Physical activity			
Least active	8.52	43.6	3.71
Other levels	4.20	24.6	1.03
Intermediate	4.19	28.6	1.20
Most active	4.20	20.5	0.86
Smoking			
Cigaret smokers	7.01	32.6	2.29
Not cigaret smokers	3.82	32.8	1.25
Physical activity and smoking			
Least active			
Cigaret smokers	10.89	44.0	4.79
Not cigaret smokers	6.33	42.1	2.67
Other levels			
Cigaret smokers	5.78	22.3	1.29
Not cigaret smokers	3.04	28.6	0.87
Intermediate			
Cigaret smokers	5.80	26.6	1.54
Not cigaret smokers	3.07	31.1	0.95
Most active			
Cigaret smokers	5.77	17.8	1.03
Not cigaret smokers	3.01	24.7	0.74

*Source: final data, HIP CHD study. Numerators for the final incidence rates are derived from all first MI's identified in the male population at risk aged 35-64 in the 3 years 11/1/61-10/31/64. Denominators consist of men at risk, aged 35-64, in 3 annual mail surveys of 4 per cent random samples of the population, carried out in the spring of the years 1962, 1963, and 1964. Early mortality rates (per cent dead within 1 month of first MI) are based on the total 4 years of case finding—all first MI's identified in the population at risk aged 25-64 in the 4 years 11/1/61-10/31/65. The early mortality of men 35-44 is practically the same as that for men 25-44 (24.4 and 25.3 per cent, respectively).

comparison with men of the same age who are more active, and this increased risk is observed both among men who smoke and men who do not smoke cigarettes.

The increased early mortality rate of the least active men is exhibited both among cigarette smokers and noncigarette smokers. However, the

converse is not true. Within each category of physical activity, men who smoked cigarettes prior to their initial infarction have the same likelihood of dying within one month of onset as men who did not smoke cigarettes prior to their initial infarction. Thus, although each of these risk factors is associated with an increased incidence of initial myocardial infarction, an increased early mortality is associated with physical inactivity but not with cigarette smoking.

The last column of Table III shows the combined effect of the incidence and early mortality rates, and presents the annual incidence rate of rapidly fatal first myocardial infarctions in men. The least active men in the study population have nearly four times the likelihood of incurring a rapidly fatal infarction in comparison with men of the same age who had been habitually more active. This reflects both the increased incidence and the increased early mortality experience associated with habitual physical inactivity. If the men in the two extreme risk groups are contrasted, a profound difference is observed. Men who smoke cigarettes and are habitually "least active" have a chance of incurring a rapidly fatal myocardial infarction which is more than five times that of men of the same age who are habitually more active, and who do not smoke.

Men who have stopped smoking for one or another reason assume the lower risk of men who have never smoked at all, suggesting that the adverse influence of smoking may be reversible. Unfortunately, a similar experience is not available for analysis in relation to inactive men who have increased their physical activity. It remains to be seen whether inactive men can be induced to increase their activities and, if so, whether they will improve their experience with relation to coronary heart disease. The magnitude of the differential risk related to these two personal habits at least encourages inquiry into the possibility of reducing the incidence and mortality of coronary heart disease by altering these habits.

Blood Pressure

I should like to turn now to blood pressure as a parameter in coronary heart disease. It has been well known for some years that hypertensive individuals develop atherosclerosis prematurely and that they have a higher risk of incurring coronary heart disease than normotensives of the same age. I should like to present data from the HIP

TABLE IV.—MORTALITY AMONG MEN IN THE MONTH AFTER FIRST MYOCARDIAL INFARCTION, BY AGE AND BLOOD PRESSURE CATEGORY—MEN FOLLOWED FROM DIAGNOSIS OF FIRST MI

Blood pressure category	Number of patients				Per cent dead in one month				
	All ages	Age at diagnosis <45	45-54	55-64	All ages	Age-adj.	Age at diagnosis <45	45-54	55-64
Total	881	99	334	448	36.0		25.3	30.8	42.2
*Blood pressure**									
Elevated	223	13	79	131	43.5	42.5 ‡	30.8	40.5	46.6
Other known	551	73	208	270	27.8	28.1 ‡	17.8	19.7	36.7
Borderline	268	26	96	146	36.2	35.5	26.9	25.0	45.2
Normal	283	47	112	124	19.8	20.7	12.8	15.2	26.6

*Omitted from the table are 107 men with first MI for whom there was insufficient information to categorize blood pressure as of date of MI. The most common situation in which the blood pressure could not be classified arose from men who died suddenly under circumstances meeting the study criteria for 'new coronary events leading to death' for whom no prior medical records containing blood pressure information could be located. Thus 67 of the 107 men were dead within one month of their first MI.

‡Confidence level in test of statistical significance between the two rates is 0.99.

study that demonstrate the extent to which "hypertensives" continue to exhibit a more unfavorable course in comparison with "normotensives" of the same age after onset of the initial myocardial infarction (MI).[6] Blood pressure information on all of the patients who incurred a myocardial infarction was abstracted from the HIP medical records which existed prior to the onset of the first illness. Patients for whom three or more casual blood pressure determinations were recorded with systolic levels of 160 or greater or diastolic levels of 95 or greater were classified as having elevated blood pressure.*

Evidence of hypertension prior to the onset of the initial myocardial infarction carries with it a markedly increased risk of death during the acute episode.

Table IV presents the mortality experience in the first month following onset of the initial myocardial infarction in relation to the blood pressure classification. For each age group the early mortality is roughly double for men who had been hypertensive prior to onset.

*If only one or two elevated readings were noted, the blood pressure was classified as elevated only if, in addition, a diagnosis of hypertension was indicated on the medical record or if left ventricular hypertrophy was in evidence on the ECG. Patients were classified as *normal* with respect to blood pressure if the systolic pressure was recorded as under 140 and the diastolic as under 90 on one or more occasions, provided no higher levels of blood pressure were recorded, and no history of hypertension was noted in the chart. For patients with no blood pressure readings recorded prior to the MI, a classification of normal blood pressure was made if there was a denial of hypertension by history and the baseline reading was under 160 systolic and under 95 diastolic. Patients with blood pressure findings not meeting the definition of "elevated" or "normal" were classified as *borderline*.

TABLE V.—PROBABILITY OF FIRST RECURRENT MYOCARDIAL INFARCTION AND OF CARDIAC DEATH WITHIN 4.5 YEARS OF INITIAL MI, BY AGE AND BLOOD PRESSURE CATEGORY—MEN FOLLOWED FROM ONE MONTH AFTER FIRST MI

	Number alive one month post MI	*Number experiencing given event within 4.5 years per 100 men alive one month after 1st MI*	
		1st recurrent MI	*Cardiac death*
Total cohort	564	25.0	15.9
Age at 1st MI			
Under 45	74	19.6	11.7
45-54	231	23.1	15.5
55-64	259	28.2	17.4
*Blood pressure as of time of MI**			
Elevated	126	44.2 ‡	35.9 ‡
Other†	438	19.7 ‡	10.5 ‡
Borderline	171	20.1	14.3
Normal	227	19.1	6.5

*The blood pressure classification is described under *Methods*.
†Included are 40 men whose blood pressure as of time of MI was unclassified.
‡Confidence level in test of statistical significance between the two rates is 0.99.

Moreover, this sizeable disadvantage of the hypertensive population continued well beyond this early mortality period.

Table V presents the probability of the first recurrence and of cardiac death in the four and one half years after onset for all men alive one month after their initial myocardial infarction. Those with an elevated blood pressure are more than twice as likely to suffer a recurrence in comparison with men of the same age who have lower levels of blood pressure. The probability of death shows an even steeper gradient in relation to blood pressure.

The recurrence rate is particularly high in the first half year following onset. Table VI examines the probability of first recurrence in three sequential portions of the four and one half years of observation: the first half year, the next two years, and the final two years. The data are presented as annualized, age-adjusted rates of first recurrence for all men alive one month after the initial infarction. In each of these time intervals the men with elevated blood pressure prior to their initial myocardial infarction showed distinctly higher rates of recurrence and cardiac death than the men with lower levels of blood pressure.

These data do not indicate whether lowering of the blood pressure

TABLE VI.—ANNUALIZED AGE-ADJUSTED RATES OF FIRST RECURRENCE AND CARDIAC DEATH IN THREE SPECIFIED TIME INTERVALS AFTER FIRST MYOCARDIAL INFARCTION, BY BLOOD PRESSURE CATEGORY AS OF THE TIME OF INITIAL MI (MEN FOLLOWED FROM ONE MONTH AFTER FIRST MI)

	*Number alive at start of interval Time interval**			*Per cent with 1st recurrence per year Time interval**			*Per cent dying cardiac death per year Time interval**		
	I (5 mos.)	*II (24 mos.)*	*III (24 mos.)*	*I (5 mos.)*	*II (24 mos.)*	*III (24 mos.)*	*I (5 mos.)*	*II (24 mos.)*	*III (24 mos.)*
All men	564	543	404	9.4	6.2	5.4	8.5	3.7	2.9
Blood pressure‡									
Elevated	126	117	78	15.7	10.0	12.7	15.6	7.4	9.8
Other†	438	426	367	7.2	5.2	3.9	6.1	2.8	1.4

*Definition of time intervals: I—from 2d month after MI through 6th month after MI (5 months); II—from 7th month after MI through 30th month after MI (24 months); and III—from 31st month after MI through 54th month after MI (24 months).

‡The blood pressure classification is described under *Methods*.

†See corresponding footnote, Table V.

would reduce these adverse influences and, if so, how soon and how effectively. They do add support to the suggestion that the level of arterial blood pressure is a major factor in the development of generalized and coronary atherosclerosis in American men. They add urgency to the proposal that suitable clinical trials be conducted to test the hypothesis that reduction of elevated blood pressure levels in men apparently free of coronary heart disease will reduce their risk of incurring and dying from this condition.

ANGINA PECTORIS

The final observations that I bring to your attention from the HIP study concern the prognosis of men whose coronary symptoms begin as recurrent angina pectoris. One of the well-recognized characteristics of patients with this syndrome is their propensity for sudden death, and yet most cardiologists can recall patients who have had classical angina of effort for 20 or 30 years without ever suffering a myocardial infarction in that time. The prediction of the prognosis of an individual patient with this syndrome is most hazardous. Yet with the cardiac surgeon beckoning to revascularize the ischemic myocardium the question must now be squarely faced: can we define a *group* of men with

TABLE VII.—SCORING OF ELEMENTS OF THE ANGINA HISTORY

Location			
Substernal	+3	Localized to apex	—1
Precordial	+2		
Left chest, base of neck, lower jaw, epigastrium	+1		
Radiation			
Either arm	+2		
Shoulder, back, neck, lower jaw (arm not mentioned)	+1		
Character			
Crushing, pressing, squeezing	+3	Sticking, stabbing, pinprick, catching	—1
Heaviness or tightness	+2		
Severity			
Severe	+2*		
Moderate	+1*		
Relation to effort			
Precipitated by effort and response is consistent	+5	Not related to effort	—5
Usually but not always related to effort	+3		
Other Precipitants			
Emotion	+1	Bodily movement, specified, or interpreted by examining MD as musculoskeletal	—5
Cold weather	+1	Musculoskeletal etiology suggested to MD by other findings	—3
		Bodily movement, not specified and uninterpreted by examining MD	—2
		Breathing	—5
		Meals and GI pathology is suspected by examining MD	—3
Usual Duration			
1-4 min.	+3†	More than ½ hour	—5‡
5-10 min.	+2		
Relief by Rest			
Yes, in 5 min. or less	+2	Yes, but takes more than ½ hr.	—5‡
		No, no further information	—3‡§
Relief by NTG			
Yes, in less than 5 min.	+5	NTG tried, effective dose, no relief or only after > ½ hr.	—5
Yes, in 5-10 min.	+3	NTG tried, unknown if effective dose, no relief or only after > ½ hr.	—2
Relief by Other			
Improved with long-acting nitrites	+1	No improvement with long-acting nitrites	—1
		Relieved by antacids	—5

*Score is entered for severity only if some positive score has been entered for location, radiation, or character.
†Fleeting pain, characterized as lasting only for seconds, produces *no* score.
‡Only the *single* highest negative score from these items is tallied.
§If 'no relief by rest' seems clearly related to the fact that the patient always takes NTG, no negative score is applied here.

angina pectoris in whom the prognosis is so poor with medical management as to warrant a surgical attempt not only to relieve the symptoms but also to improve the prognosis? And, conversely, can we define a group of men with a prognosis so good that the risk of surgical intervention is unwarranted? Data from the HIP study suggest that such a prognostic classification can be made.

It is accepted that the syndrome of angina pectoris commonly occurs in the absence of any objective abnormalities on physical or electrocardiographic examination. It is by definition a subjective complaint which requires a careful and painstaking history to identify. In order to gain reliability and consistency in the weighing of the various elements of the history, a scoring system was devised (Table VII). Highest scores are assigned to episodes of severe crushing substernal pain, radiating to either arm, induced by effort, relieved by rest, or more promptly alleviated by nitroglycerine. Lower scores are cumulated from variations of this symptomatology. The data to be presented below are restricted to patients with pain patterns scoring high enough to be considered characteristic of angina pectoris.

In the four years of case finding 275 men were considered to have developed angina pectoris in the absence of historical or electrocardiographic evidence of a myocardial infarction. In order to permit sufficient time to characterize the syndrome and to avoid confusion with "pre-infarction angina" the cohort was further limited to men whose symptoms had persisted for more than two months. At the time of the baseline examination nearly half had been symptomatic for between two and six months and a great majority had been symptomatic for under one year.

Table VIII presents the probability of experiencing an initial myocardial infarction and the probability of a cardiac death in the two-and-one-half-year period following this baseline examination. Some 12.5 per cent of the entire group of men can be expected to experience a myocardial infarction in this time period. As a group they are four times as likely to die in the next 30 months as men of the same age without overt coronary heart disease.

The prognosis of the men with newly diagnosed angina was examined in relation to a number of personal characteristics and medical observations at the time of the baseline examination. No prognostic significance could be related to the frequency of occurence of the pain

TABLE VIII.—PROBABILITY OF DEATH AND OF FIRST MYOCARDIAL INFARCTION WITHIN 30 MONTHS OF BASELINE EXAMINATION—BLOOD PRESSURE AND ECG FINDINGS AT BASELINE (COHORT OF 275 MALES FOR PROGNOSIS OF ANGINA)

	Number examined at baseline	*No. dead within 30 mos. per 100 examined*		*No. who experienced 1st MI within 30 mos. per 100 examined*
		All causes	*Cardiac only*	
Total cohort	275	10.5	7.5	12.5
Blood pressure				
Elevated*	73	18.6 } †	15.0 } †	24.0 } *
Not elevated	202	7.9 }	5.0 }	8.7 }
ECG findings				
Specified abnormality‡	98	20.8 } ‡	16.6 } ‡	19.6 } *
Normal, or NS abnl.	177	5.0 }	2.7 }	8.8 }
Blood pressure and ECG				
BP elevated				
ECG specified abnl.	30	31.8 } †	28.9 } *	35.4
ECG normal or NS abnl.	43	9.9 }	6.2 }	16.8
BP not elevated				
ECG specified abnl.	68	16.6 } *	11.8 } *	13.6
ECG normal or NS abnl.	134	3.5 }	1.6 }	6.4
ECG specified abnormality				
BP elevated	30	31.8	28.9	35.4 } †
BP not elevated	68	16.6	11.8	13.6 }
ECG normal or NS abnl.				
BP elevated	43	9.9	6.2	16.8
BP not elevated	134	3.5	1.6	6.4

Note: Confidence levels in tests of statistical significance of the difference between two rates are noted by ‡ for 0.99, * for 0.95, and † for 0.90.

Casual reading of 160 systolic or 95* diastolic.

‡Criteria for 'specified' ECG abnormalities have been published.[3] The most common 'specified' abnormality noted was a horizontal depression of the ST segment of 0.5 mm. or greater. T-wave inversions, conduction defects, and certain QRS deformities were also included. By definition of the cohort, no ECG revealed Q waves and ST-T changes usually considered diagnostic of MI. 'Non-specified' abnormalities include such findings as flat T waves and junctional ST segment depressions.

syndrome or to the intensity of effort ordinarily required to induce the pain. Men with pain which radiated to the arm fared no worse than men whose pain did not radiate. Obesity had no apparent relation to the prognosis. The serum cholesterol levels in this population of men with angina had no relation to prognosis in the two-and-one-half-year period following baseline examination. Men with serum cholesterol levels in excess of 260 mg. per cent did not have a significantly higher rate of occurrence of infarction or death than men with cholesterol levels under 220 mg. per cent.

There were, however, two medical observations made at the baseline examination which proved to be most useful in discriminating

between men with a good prognosis and men with a poor prognosis: these were the blood pressure and the electrocardiographic findings obtained at rest.

Men who had a systolic blood pressure of 160+ or diastolic of 95+ at the baseline examination had three times the likelihood of incurring an infarction or cardiac death in comparison with men who had lower blood pressures. These differences could not be explained by any age differential.

The electrocardiograms obtained at the baseline examination were all coded according to criteria developed for and published from this study.[2] The angina cohort excluded men who already had electrocardiographic evidence of definite myocardial infarction by the baseline examination. The commonest abnormality detected was a horizontal ST segment depression of 0.5 mm. or more, the so-called ischemic ST segment, and abnormal T wave inversion across the left precordium. Lesser abnormalities such as junctional depression or flat T waves were coded as "nonspecified abnormalities," and were included with the normal records for this comparison. Men with the specified electrocardiographic abnormalities were much more apt to suffer infarction and to die, in comparison with men who had more normal electrocardiograms.

Cross classification of the angina cohort by blood pressure and ECG findings produced an even more dramatic separation of the patient population. Myocardial infarction and cardiac death can be expected within 30 months in approximately one third of the men with angina who have both an abnormal electrocardiogram and an elevated blood pressure. By contrast these probabilities are 6 per cent for infarction and under 2 per cent for death for men with similar anginal syndromes but with a normal electrocardiogram and a blood pressure which is not elevated. At the Albert Einstein College of Medicine we are currently employing this as yet unpublished information in a clinical trial of the Vineberg procedure. Since the probability of cardiac death over a two-and-a-half-year period observed for the HIP angina cohort with a normal blood pressure and normal ECG was less than the immediate mortality commonly associated with this operative procedure, we are not considering such patients for this trial. Rather, we are concentrating on gathering a cohort of men with characteristics similar to that of the HIP angina cohort with both an elevated blood pressure and an abnormal ECG. This group did so poorly with conventional medical treat-

ment that a therapeutic trial appears to be both reasonable and feasible.

The determination of the prognosis of an individual patient with coronary heart disease will undoubtedly remain less than precise. But the more clearly we can detail the course of illness for *groups* of patients with well-defined characteristics, the better our clinical judgments will become. I hope that the examples presented will help make the point that the disciplines of clinical and epidemiologic research have much to gain from and give to each other.

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