III. A Prospective Study of Degenerative Cardiovascular Disease in Albany: Report of Three Years' Experience— I. Ischemic Heart Disease

JOSEPH T. DOYLE, M.D.; A. SANDRA HESLIN; HERMAN E. HILLEBOE, M.D., F.A.P.H.A.; PAUL F. FORMEL; and ROBERT F. KORNS, M.D., F.A.P.H.A.

Early in 1953 the New York State Department of Health in contract with the Albany Medical College established the Cardiovascular Health Center.[1, 2] The primary objective of the Center was to detect the earliest manifestations of degenerative cardiovascular disease in an especially susceptible population. Voluntary participation in this study was solicited of male New York State Civil Service employees 39 through 55 years of age residing in the Albany area. This is a stable, intelligent, and cooperative group, almost exclusively white and of predominantly Northern European extraction with large Jewish and Italo-American minorities.

Methods

At the first examination a detailed medical history was obtained, based on a comprehensive, self-administered questionnaire supplemented by an interview with a physician. A complete physical examination was done. The laboratory studies included the measurement of the hemoglobin concentration and of the serum total cholesterol level,[3] a urinalysis; 14 by 17 inch roentgenograms of the heart and lungs in the postero-anterior and lateral projections during cardiac systole; skinfold measurements at standardized sites [4]; a 12-lead electrocardiogram; and a high-frequency (Starr) ballistocardiogram.[5] Unless physically impossible or contraindicated by a history strongly suggestive of ischemic heart disease, all participants were subjected to a stress test, after which selected electrocardiographic leads and the ballistocardiogram were repeated. The first 715 men examined performed a master double two-step test.[6] All subsequent stress tests have consisted of a 10-minute walk at three miles per hour against a 5 per cent grade on a motor-driven treadmill.

An interval history, based on a short self-administered questionnaire and supplemented by a physician interview, was obtained for the second and third examinations. A complete physical examination was again done. The same battery of laboratory tests was done with one exception. Because of the accelerated schedule of examinations it was possible to perform stress tests on only half of the eligible participants at the second examination, and on the other half at the third examination. Numerous specialized studies have been carried out incidental to the reexaminations, some of which will be reported later.

Diagnostic Criteria

The term ischemic heart disease has been used in preference to coronary artery disease, not only because it has no etiologic or pathogenetic implica-

The authors are associated with the Cardiovascular Health Center and Department of Medicine, Albany Medical College, and the New York State Department of Health, Albany, N. Y.

Table 1—Follow-Up of Initial Study Group After 31 Months' Observation (Cardiovascular Health Center)

Age	Total Eligible Population	Examined At		Lost		
		I	III	Total	I–II	II–III
Total	2,202	1,913	1,682	231	156	75
Under 40	89	84	76	8	5	3
40–44	760	665	605	60	41	19
45–49	775	675	591	84	55	29
50–54	567	481	406	75	53	22
55 and over	11	8	4	4	2	2

tions, but also because it is semantically more precise. The diagnosis of ischemic heart disease has been based on: (a) an unequivocal history, preferably supplemented by medical records and electrocardiograms, of an acute myocardial infarction or, uncommonly, the electrocardiographic stigmata of a healed myocardial infarction without an appropriate history; (b) classical Heberden's angina; (c) an abnormal electrocardiographic response to exercise. The criteria of an abnormal electrocardiographic response to exercise have been: (a) depression of J (the RS-T junction) of 1.0 mm or more in the axial and of 1.5 mm or more in the lateral precordial leads; (b) coving of ST segments; (c) frank inversion of T_I or of T waves in the lateral precordial leads. These empirical criteria have evolved from experience and coincide closely with those employed by Mattingly and Robb.[8] The nomenclature of the New York Heart Association with minor modifications has been used in formulating cardiac diagnoses.[9]

Results

From February, 1953, through September, 1954, 1,913 men were examined, 89 per cent of those eligible. At the completion of the first reexamination in September, 1955, 156 participants had been lost, of whom 102 refused to return; 45 had left state employment and for various reasons found it inconvenient to return; and nine had died. In September, 1956, at the completion of the second reexamination 1,670 individuals had returned and 75 had been lost. Of these 75 men, 42 refused to return; 24 had left Albany; and nine more had died (Table 1).

A summary of the results of each examination was sent to the personal physician designated by the patient, who was instructed to consult his physician for interpretation of the findings and for execution of any indicated diagnostic or therapeutic procedures. Although nearly all participants designated a physician, only 60 per cent consulted them for a report.

Prevalence

At the first examination 70 individuals were found to have ischemic heart disease, a prevalence rate of 36 per 1,000. Thirty-seven men had survived a myo-

NOTE: Abbreviations Used in Tables

ASHD	Arteriosclerotic Heart Disease
AP	Angina Pectoris
AX	Abnormal Electrocardiographic Response to Exercise
EH	Essential Hypertension
IHD	Ischemic Heart Disease
MI	Myocardial Infarction
RHD	Rheumatic Heart Disease
Tbc	Tuberculosis

Table 2—Prevalence of Ischemic Heart Disease by Age (Cardiovascular Health Center—Examination I)

Age	Total	No Ischemic Heart Disease	Ischemic Heart Disease					
			Total Number	Rate per 1,000	MI Hist.	MI No Hist.	AP	AX
Total	1,913	1,843	70	36	29	8	18	15
Under 40	84	83	1	12	1	–	–	–
40–44	665	658	7	11	3	–	2	2
45–49	675	647	28	41	10	4	8	6
50–54	481	447	34	71	15	4	8	7
55 and over	8	8	–	–	–	–	–	–

Table 3—Response to Self-Administered Questionnaire Item "Do You Feel Pain, Heaviness or Discomfort in the Chest?" (Cardiovascular Health Center—Examination I)

	Total	Response		Per cent
		Yes	No	Yes
Total	1,913	644	1,269	34
Normal	1,843	596	1,247	32
Ischemic heart disease	70	48	22	69

cardial infarction; 18 had angina pectoris; and 15 showed only an abnormal electrocardiographic response to exercise. The diagnosis of previous myocardial infarction could be established in almost all cases by the history alone (Table 2). The very high rate of false affirmative responses on the questionnaire to the question on chest pain indicated the necessity of skilled medical evaluation of this symptom (Table 3). Individuals considered to be clinically free of ischemic heart disease showed no consistent pattern in their responses to the question on chest pain in three consecutive questionnaires. About 24 per cent of the survivors of a myocardial infarction showed a normal resting electrocardiogram. Eighty-three per cent of those suffering from angina pectoris, without a previous, recognized myocardial infarction, likewise had a normal resting electrocardiogram. Twenty-three individuals with histories of ischemic heart disease were exercised and 19, or (again) 83 per cent, yielded normal electrocardiographic responses (Table 4). The problem of false-positive electrocardiographic responses to exercise is difficult to evaluate in the otherwise asymptomatic group of 15, but

Table 4—Electrocardiograms at Rest and Postexercise in Ischemic Heart Disease (Cardiovascular Health Center—Examination I)

	Electrocardiogram at Rest			
	MI		AP	
	Normal	Abnormal	Normal	Abnormal
Total	9 (24%)	28	15 (83%)	3
Normal postexercise	3	5	10	1
Abnormal postexercise	–	4	–	–
Not done	6	19	5	2

Table 5—Ballistocardiogram at Rest in Normal Individuals by Age and Relative Weight (Cardiovascular Health Center—Examination I)

Age	Less Than 20 Per cent Over Ideal Weight				20 Per cent or More Over Ideal Weight			
	Total	GR. II-III-IV	BCG Not Done	Per cent II-III-IV *	Total	GR. II-III-IV	BCG Not Done	Per cent II-III-IV *
Total	1,244	252	289	26.4	315	115	72	47.3
Under 40	56	–	50	–	13	–	9	–
40–44	465	69	102	19.2	117	32	24	34.4
45–49	434	101	86	29.3	112	47	24	52.8
50–54	284	81	51	35.2	71	34	15	60.7
55 and over	5	1	–	–	2	2	–	–

* By criteria of Brown and DeLalla [10] based on the total number of BCG's done.

it may be significant that one of these individuals has since sustained a myocardial infarction and two others have succumbed to the disease.

The ballistocardiogram proved to be of no diagnostic value. Approximately one-third of the subjects regarded as clinically free of ischemic heart disease showed abnormal ballistic patterns which correlated with increasing age and with overweight (Table 5). The postexercise ballistic patterns were of even less diagnostic value because of obscuring artefacts caused by tachycardia and tachypnea.

Incidence

In the 31 months from the initiation of the program to the completion of the second round of reexaminations, 18 deaths occurred, or an annual death rate of 3.6 per 1,000. These deaths are analyzed in Table 6. Forty new cases of ischemic heart disease were diagnosed in this period, an incidence rate of 9 per 1,000 per year. The 1,843 individuals considered clinically free of ischemic heart disease at the initial examination are considered to be the population at risk in calculating incidence rates of ischemic heart disease. The 231 nonrespondents are included in this denominator: 39 of them are lost from Civil Service records, while of the remaining 192 only one has died—of hepatic cirrhosis. The true incidence of ischemic heart disease is probably underestimated since nothing further is known of the health status of this nonrespondent group. On the other hand, the incidence rate for the whole 31 months could be increased from 22 per 1,000 to 23 per 1,000 by adding two deaths certified as arteriosclerotic heart disease and a third certified as coronary sclerosis (Table 6). Twenty-two of the new cases of ischemic heart disease had survived a first acute myocardial infarction while 10 others had developed angina pectoris. Eight, diagnosed as having ischemic heart disease because of the solitary manifestation of an abnormal electrocardiographic response to exercise, represent a category unique to this program (Table 7). The difference between the annual incidence rate of 9 per 1,000 observed in Albany, and the rate of 7 per 1,000 reported from the Los Angeles and the Framingham studies, can be accounted for by the inclusion of this unique group.[11, 12]

Table 6—Deaths During 31 Months' Observation (Cardiovascular Health Center)

Case	Age at Death	CVHC Dx	Date of Last Examination	Date of Death	Cert. Cause of Death
1	53	IHD–MI	3–53	4–53	ASHD
2	48	IHD–AX	9–53	1–54	ASHD
3	51	Diabetes mellitus IHD–MI	10–53	2–54	Diabetes mellitus
4	47	RHD	1–53	4–54	RHD
5	51	No disease	4–53	6–54	Coronary sclerosis
6	52	IHD–MI	5–53	8–54	ASHD
7	50	No disease	5–54	12–54	Carcinoma lung
8	48	No disease	10–53	3–55	Carcinoma bronchus
9	45	EH	7–54	3–55	Carcinoma kidney
10	56	Intermittent claudication	11–54	5–55	Rupture abdominal aorta
11	52	EH	1–55	8–55	ASHD
12	54	EH	11–54	12–55	Carcinoma pancreas
13	52	No disease	6–55	4–56	ASHD
14	56	IHD–AX	6–55	4–56	ASHD
15	54	HHD–Tbc.	3–55	6–56	Carcinoma lung
16	54	HHD	1–55	8–56	Failure of heart and blood circulation
17	54	IHD–MI	9–55	9–56	ASHD
18	51	IHD–MI	3–55	10–56	Rupture abdominal aorta

Etiologic Trends

The small number of cases of newly observed ischemic heart disease justifies only conjectures on characteristics which may predispose to or afford relative protection from ischemic heart disease. Neither job classification nor self-assessed ratings of "tension" could be related to the age-adjusted incidence rate of ischemic heart disease. Information concerning diet and habitual physical activity was insufficient to permit any deductions. Ischemic heart disease occurred more frequently as the

Table 7—Incidence of Ischemic Heart Disease During 31 Months' Observation (Cardiovascular Health Center)

Age	Population at Risk	New Cases		Manifestation		
		Number	Rate per 1,000	MI	AP	AX
Total	1,843	40	22	22	10	8
Under 40	84	—	—	—	—	—
40–44	665	10	15	6	2	2
45–49	675	14	21	7	3	4
50–54	481	16	33	9	5	2
55 and over	8	—	—	—	—	—

Table 8—Incidence of Ischemic Heart Disease During 31 Months' Observation by Serum Total Cholesterol Level mg/100 ml

(Cardiovascular Health Center)

Serum Total Cholesterol (mg/100 ml)	Population at Risk	New Cases	Rate per 1,000
Total	1,843	40	22
Less than 200	457	5	11
200–274	995	14	14
275 and over	209	13	62
Not done	182	8	44

No adjustment for age was made since cholesterol levels showed no tendency to increase with age over the span 39–55.

serum total cholesterol level rose. Thus, above a level of 275 mg/100 ml the risk of ischemic heart disease was six times greater than at a level of 200 mg/100 ml or less (Table 8). A detailed study of the lipoprotein patterns of this population showed that the discriminatory value of the individual cholesterol level was of a low order because of the large overlap in values of the clinically normal and abnormal groups.[13] A body weight up to 39 per cent over the Metropolitan Life Insurance Company standard weight carried little increased risk of ischemic heart disease,[14] while gross overweight, defined as a level 40 per cent or more over ideal weight, quadrupled the risk (Table 9). On the other hand, increase of body weight of more than 20 per cent above any weight level existing at the age of 25 doubled the risk of developing ischemic heart disease (Table 10). A soft, apical systolic murmur (Table 11), proteinuria or red

Table 9—Incidence of Ischemic Heart Disease During 31 Months' Observation by Relative Weight

(Cardiovascular Health Center)

Relative Weight	Population at Risk	New Cases	Rate per 1,000
Total	1,843	40	22
Less than 20% over ideal	1,419	27	19
20%–39% over ideal	335	8	24
40% or more over ideal	77	5	65
Not stated	2	—	—

Table 10—Incidence of Ischemic Heart Disease During 31 Months' Observation by Weight Gain from Age 25

(Cardiovascular Health Center)

Weight Gain from Age 25	Population at Risk	New Cases	Rate per 1,000
Total	1,843	40	22
Less than 20% gain	1,334	24	18
20% or more gain	415	14	34
Not stated	95	2	21

Table 11—Incidence of Ischemic Heart Disease During 31 Months' Observation by Presence or Absence of a Murmur

(Cardiovascular Health Center)

Murmur	Population at Risk	New Cases	Rate per 1,000
Total	1,843	40	22
Absent	1,707	35	21
Present-non-significant	108	5	46
Present-significant	24	—	—
Not stated	4	—	—

Table 12—Incidence of Ischemic Heart Disease During 31 Months' Observation by Urinalysis

(Cardiovascular Health Center)

Urinalysis	Population at Risk	New Cases	Rate per 1,000
Total	1,843	40	22
Albumin present	51	2	39
Albumin absent	1,777	38	21
Not stated	15	—	—
White blood cells in sediment	128	5	39
Red blood cells in sediment	55	2	36
Casts in sediment	26	2	—
Sediment absent	1,653	32	19
Not stated	15	—	—

or white blood cells in the urinary sediment (Table 12) were associated with double the risk of ischemic heart disease. Nonspecific abnormalities of the T wave in the resting electrocardiogram were associated with a three times higher incidence of ischemic heart disease (Table 13), an observation also recently made by others.[15] A family history of vascular disease, the somatotype, the density and distribution of hair on the head and body, the consumption of tobacco and of alcohol, and the level of the arterial diastolic blood pressure all failed to show significant associations with ischemic heart disease.

Table 13—Incidence of Ischemic Heart Disease During 31 Months' Observation by Resting Electrocardiogram

(Cardiovascular Health Center)

Resting Electrocardiogram	Population at Risk	New Cases	Rate per 1,000
Total	1,819*	40	22
Normal	1,689	32	19
Abnormal*	125	7	56
Not done	5	—	—

* Exclusive of 24 cases of rheumatic heart disease 18 of which were characterized by abnormal resting electrocardiograms.

Summary and Conclusions

A group of 1,913 male office workers aged 39–55 years has been carefully studied over a three and a half year period. Seventy cases of ischemic heart disease were found on the initial survey, a prevalence rate of 36 per 1,000 population. Forty new cases of ischemic heart disease were found during the next two examinations, an annual incidence rate of 9 per 1,000 population. A carefully evaluated medical history is still the single best method of diagnosis. The electrocardiogram provides valuable confirmatory evidence of ischemic heart disease; nonspecific abnormalities of the T wave appear to be of prognostic importance; a significant number of diagnostic electrocardiographic abnormalities can be induced by exercise. Individuals with high levels of serum total cholesterol tend more often than normocholesterolemic individuals to develop ischemic heart disease.

This study shows the potentialities as well as the limitations of an intensive application of the best available clinical methods of diagnosing ischemic heart disease in a susceptible population. Until atherosclerosis can be recognized prior to the advent of its ischemic complications, the effectiveness of control measures cannot be evaluated. Meanwhile, prospective studies should amplify our present knowledge of the natural history of ischemic heart disease. Semicaptive populations, such as those of the Cardiovascular Health Center, provide a unique source of normative data as

well as an opportunity to pursue short-term research studies.

REFERENCES

1. Hilleboe, H. E.; James, G.; and Doyle, J. T. Cardiovascular Health Center. I. Project Design for Public Health Research. A.J.P.H. 44:851, 1954.
2. James, G.; Hilleboe, H. E.; Filippone, J. F.; and Doyle, J. T. Cardiovascular Health Center. II. First Year's Operation. A. General Observations and Hypertension. New York State J. Med. 55:774, 1955.
3. Abell, L. L.; Levy, B. B.; Brodie, B. B.; and Kendall, F. E. A Simplified Method for the Estimation of Total Cholesterol in Serum and Demonstration of Its Specificity. J. Biol. Chem. 195:357, 1952.
4. Keys, A., and Brozek, J. Body Fat in Adult Man. Physiol. Rev. 33:245, 1953.
5. Starr, I. On the Later Development of Heart Disease in Apparently Healthy Persons with Abnormal Ballistocardiograms. Am. J. M. Sc. 214:233, 1947.
6. Master, A. M. The Two-Step Exercise Electrocardiogram: A Test for Coronary Insufficiency. Ann. Int. Med. 32:842, 1950.
7. Erickson, L.; Simonson, E.; Taylor, H. L.; Alexander, H.; and Keys, A. Energy Cost of Horizontal and Grade Walking on the Motor-Driven Treadmill. Am. J. Physiol. 145:391, 1946.
8. Mattingly, T. W.; Fancher, P. S.; Bauer, F. L.; and Robb, G. P. The Value of the Double Standard Two-Step Exercise Tolerance Test in Detecting Coronary Disease: A Follow-Up Study of 1,000 Military Personnel. Army Med. Service Grad. Sch., Walter Reed Army Med. Center, Washington, September, 1954.
9. Nomenclature and Criteria for Diagnosis of Diseases of the Heart and Blood Vessels (5th ed.). New York: New York Heart Association, 1953.
10. Brown, H. R., Jr.; DeLalla, V., Jr.; Epstein, M. A.; and Hoffman, M. J. Clinical Ballistocardiography. New York: Macmillan, 1952.
11. Chapman, J. M.; Goerke, L. S.; Dixon, W.; Loveland, D. B.; and Phillips E. Measuring the Risk of Coronary Heart Disease in Adult Population Groups: The Clinical Status of a Population Group in Los Angeles Under Observation for Two to Three Years. A.J.P.H. Part 2, 47:4 (Apr.), 1957.
12. Dawber, T. R.; Moore, F. E.; and Mann, G. V. Coronary Heart Disease in the Framingham Study. Ibid., 1957.
13. Doyle, J. T.; DeLalla, L. S.; Baker, W. H.; Heslin, A. S.; and Brown, R. K. Serum Lipoproteins in Preclinical and in Manifest Ischemic Heart Disease. J. Chronic Dis. (In press.)
14. Metropolitan Life Insurance Company. Ideal Weights for Men. Statist. Bull. Metrop. Life Insur. Co. 23:6, 1942.
15. Keissling, C. E.; Schaaf, R. S.; and Lyle, A. M. Mortality Studies of Isolated Electrocardiograhic T-Wave Changes. 64th Ann. Meet. Assoc. Life Insurance Medical Directors, October, 1955.