Serum Lipids and Apparent Health of Italian-American Factory Workers in a Boston Area

A Four Year Follow-Up

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IN 1958 an initial report was published[1] in which the diet and blood lipids of a group of Italian men were compared with their apparent health status. The study was designed to afford an opportunity for a prospective investigation of the development of atherosclerosis in a highly discreet group of Italian men of similar genetic background, living and working in the Boston area whose parents had been born in the environs of Naples, Italy. The information obtained could reasonably be expected to bear upon the relative importance of environmental and constitutional factors in the development of overt manifestations of atherosclerosis. Such a comparative study was chosen despite the obvious bias introduced by the selection of one group of strong motivation, manifested by the drive necessary to accomplish successful emigration.

In the four years that have elapsed since the preparation of the first report, further experience has accumulated in the course of two subsequent biennial examinations. Although it is obvious that four years are a short lapse of time in comparison to the prolonged course of events inherent in the development of atherosclerosis, re-evaluation and comparison of the data appeared warranted.

MATERIALS AND METHODS

The methodology previously described was retained with minimal variations: lipoprotein determinations and computations of the fatty acids from dietary histories were not repeated. Of the 189 subjects originally included, repeat studies were obtained in 146. Subjects were primarily lost to follow-up through termination of employment with the B. F. Goodrich Company, secondarily through unwillingness to cooperate further. Efforts to contact those no longer employed yielded a few persons who graciously contributed their own time for repeat examinations. As far as could be ascertained from company records, none of the original subjects was lost because of either death or disability. Subjective analysis of the previous data obtained from those lost to follow-up failed to reveal any significant variation from the entire group.

RESULTS

The 146 subjects ranged in age from twenty-seven to fifty-four years. For the sake of convenience, age groupings were changed from those previously utilized: fifty-three subjects were between the ages of twenty-seven and thirty-nine, seventy-four between forty and forty-nine, and the remaining nineteen subjects were fifty years or older.

The serum cholesterol level is tabulated by these age groups in Table I. With progressive

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TABLE I
Mean Total Cholesterol (mg./100 ml.) Compared with Age

Age (yr.)	No.	Mean	S.D.*
27–39	53	232	46.6
40–49	74	232	44.7
50–54	19	240	49.5
All ages	146	233	46.1

* Standard deviation.

aging, no significant increase in cholesterol levels is apparent. In the previous data, a slight increase in cholesterol with aging was noted; it is no longer apparent because of a slight rise in the cholesterol level in the younger group and a slight decrease in the older group.

The serum cholesterol level of all age groups is well with the usual limits for other men in the Boston area. However, in view of the prognostic significance of elevated cholesterol levels,[2] further analysis was made of the thirty-two subjects with cholesterol levels above 260 mg. per cent. Eleven were between twenty-seven and thirty-nine years old, fourteen between forty and forty-nine, and seven were fifty years or older. In twenty-two of these, there had been a rise in cholesterol readings between 1956 and 1960. In twelve of these thirty-two, elevated blood pressure readings were obtained in 1960. Alterations in the electrocardiograms were diagnosed in nine of the thirty-two; these included suggestive evidence of an old myocardial infraction in one and S-T segment and T wave alterations of coronary insufficiency in three. The incidence of blood pressure and electrocardiographic alterations in this small group was somewhat higher than in the entire group. However, only three of these thirty-two subjects were obese, a proportion similar to that of the entire group.

Weight status was evaluated by determining relative weights from standard tables and by measurements of skinfold thicknesses. Standard tables,[3] despite their shortcomings, were used to broadly classify the degree of fatness for the group because of their wide availability. A prediction of total body fat was made for 145 men from a nomogram[4] using weight, height, age and the mean of two skinfold thicknesses. The degree of fatness estimated by this method correlated only slightly ($r = 0.71$) with relative weight, indicating a sizable variation unaccounted for in the prediction of weight status by standard tables. In Table II the total serum cholesterol is tabulated by age groups and relative weights. No tendency for cholesterol to increase with weight can be seen. It is perhaps of interest to note that in both the earlier and the present data the lowest serum cholesterol levels were found in the older, less obese subjects.

By standard tables, twenty-six patients were classified as obese with relative weights of 120 per cent or greater. Analysis of this group revealed a high incidence of hypertension and electrocardiographic abnormalities. In fourteen the blood pressure reading was elevated in 1960. Moreover, only seven of these twenty-six patients had failed to show at

TABLE II
Mean Total Serum Cholesterol Compared with Age and Relative Weight

Age (yr.)	Relative Weight					
	Under 100		100–119		120 and over	
	No.	Cholesterol	No.	Cholesterol	No.	Cholesterol
27–39	13	224	26	237	14	228
40-49	15	237	47	231	12	227
50–54	8	219	11	255	...	...
All ages	36	228	84	236	26	227

TABLE III
Mean Total Serum Cholesterol Compared with Age and Skinfold Thickness
(Triceps plus Subscapular in millimeters)

Age (yr.)	Skinfold Thickness			
	9 to 23 mm.		23 to 60 mm.	
	No.	Cholesterol	No.	Cholesterol
27–39	19	236	34	229
40–49	23	231	50	232
50–54	11	229	8	256
All ages*	53	232	92	233

* No data obtained on one subject.

least one systolic pressure reading of 140 mm. Hg or greater or a diastolic pressure of 90 mm. Hg or higher over the three examination periods. Thirteen of these twenty-six subjects had borderline abnormalities in the electrocardiograms; one patient showed S-T and T wave alterations of coronary insufficiency. Only four of these obese patients had serum cholesterol levels greater than 260 mg. per cent.

In Table III the mean serum cholesterol levels are compared with age and skinfold thickness (triceps plus subscapular in millimeters). A relation between serum cholesterol and increased subcutaneous fat is evident in only a small number of subjects in the older age group. Similar findings had been noted previously.

In Table IV the serum cholesterol level is compared with physical activity and age. The level of physical activity was taken from the company's job classification. A good relationship was obtained from the individual's own estimation of his job: in the majority, agreement was close and the same number tended to overestimate as to underestimate the strenuousness of their work. No attempt was made in compiling the data to compensate for outside work, since only a small number would admit to carrying a second job or stated that they worked "hard" at home. No relationship between physical activity and serum cholesterol can be seen. In 1956 the data indicated some tendency for serum cholesterol levels to be higher in the low activity group. To some extent this variation may be due to changes in the level of activity of some of the subjects.

In Table V physical activity is compared with relative weight and age. There is a distinct tendency for relative weight to increase with physical activity, as well as for relative weights to decrease with progressive age. Neither correlation was previously apparent.

Table VI relates cigarette smoking to cholesterol levels and age. When the subjects are divided among non-smokers, light smokers (one pack or less per day), and heavy smokers (more than one pack, but less than three packs per day), there is a tendency for the serum cholesterol levels to be higher in the heavy smokers. The findings are in essential agreement with those previously reported. A positive correlation ($p < 0.01$) between higher serum cholesterol levels and cigarette smoking

TABLE IV
Mean Total Cholesterol Compared with Physical Activity and Age

Age (yr.)	Physical Activity					
	Low		Moderate		High	
	No.	Cholesterol	No.	Cholesterol	No.	Cholesterol
27–39	16	230	30	233	7	227
40–49	19	220	42	238	13	243
50–54	8	239	8	242	3	237
All ages	43	227	80	234	23	238

has been obtained by Damon[5] when the group was divided into smokers and non-smokers.

The relationship between the electrocardiographic findings and the serum cholesterol level is tabulated in Table VII. The cardiograms were read independently by two physicians without reference to history, physical findings or cholesterol levels. Differences in interpretation were reconciled at simultaneous review. For the purpose of classification, a tracing was considered abnormal in the presence of pathologic Q waves or with depressed S-T segments and inverted T waves, as seen in coronary insufficiency or heart strain pattern.

TABLE V
Relative Weight Compared with Physical Activity and Age

Age (yr.)	Physical Activity					
	Low		Moderate		High	
	No.	Relative Weight	No.	Relative Weight	No.	Relative Weight
27–39	16	106	30	110	7	113
40–49	19	107	42	108	13	111
50–54	8	96	8	96	3	108
All ages	43	104	80	108	23	111

TABLE VI
Mean Total Serum Cholesterol Compared with Cigarette Smoking and Age

Age (yr.)	Packs of Cigarettes per Day					
	None		One or Less		Over 1 but less than 3	
	No.	Cholesterol	No.	Cholesterol	No.	Cholesterol
27–39	24	236	18	212	11	252
40–49	29	230	24	226	21	237
50–54	3	265	12	241	3	238
All ages*	56	235	54	225	35	241

* No data obtained on one subject.

TABLE VII
Mean Total Serum Cholesterol Compared with Age and Electrocardiographic Abnormalities

Age (yr.)	Electrocardiogram					
	Normal		Borderline		Abnormal	
	No.	Cholesterol	No.	Cholesterol	No.	Cholesterol
27–39	37	241	13	217	3	221
40–49	51	235	16	221	7	232
50–54	17	234	1	272	1	310
All ages	105	237	30	221	11	236

TABLE VIII
Mean Serum Cholesterol Compared with Blood Pressure and Age

Age (yr.)	Blood Pressure					
	Normal		Borderline		Abnormal	
	No.	Cholesterol	No.	Cholesterol	No.	Cholesterol
27–39	35	227	10	252	8	239
40–49	51	233	11	221	12	238
50–54	12	227	5	259	2	254
All ages	98	230	26	240	22	240

All other S-T and T wave abnormalities, and the one instance of nodal arrhythmia encountered, were considered "borderline." Incomplete right bundle branch block, in the absence of other stigmata of disease in the cardiogram, was not considered to be a significant electrocardiographic finding. No conclusions can be drawn from these data (Table VII) because of the relatively few patients with abnormalities in the cardiograms.

A review of the findings in the eleven patients with abnormal electrocardiograms failed to reveal striking alterations. Past history was contributory in only one of three patients with abnormal Q waves, who admitted to a history suggestive of angina pectoris; in addition, information obtained on this patient subsequent to the 1960 examination confirmed the diagnosis of coronary artery disease with myocardial infarction, based on elevations of the SGOT determinations and serial electrocardiographic alterations. All three subjects with pathologic Q waves had frequent, if not consistent, elevations of blood pressure. Only one had an elevated serum cholesterol. In all three, relative weights were less than 120 per cent. In the eight patients with S-T and T wave alterations, only two had abnormal serum cholesterol levels, and five had moderate and often inconsistent elevations in blood pressure.

Blood pressure readings are compared with age and serum cholesterol levels in Table VIII. There is some tendency for elevations in blood pressure to correlate with an increase in serum cholesterol. The tendency is less striking than that previously recorded, but, as before, appears to be limited to the youngest and oldest age groups.

The forty-eight patients with borderline elevations (systolic pressure between 140 and 159 mm. Hg or diastolic pressure between 90 and 94 mm. Hg) and abnormal pressures (systolic greater than 160 mm. Hg or diastolic above 95 mm. Hg) can be divided into two groups. In fifteen of the forty-eight, all previous blood pressure recordings had been within the normal range; in only four were electrocardiographic abnormalities encountered, consisting of minor T wave alterations. Of the remaining thirty-three patients, electrocardiographic abnormalities were encountered in nineteen, including three with pathologic Q waves suggestive of old myocardial infarction and three with changes of coronary insufficiency. No such pronounced effect on serum cholesterol levels is observable.

In Table IX mean total serum cholesterol is compared with pertinent family history and age. Serum cholesterol levels were higher in the group with two or more diseases (hypertension, diabetes, cerebrovascular accidents and coronary artery disease) in members of the immediate family. These data are more consistent, than that previously reported especially in the younger age group. This is presumably explainable on the basis that the lapse of four years has allowed time for more illnesses to appear in the family history.

In the seven subjects with the strongest family history (three or more diseases), the incidence of abnormalities was high. Choles-

TABLE IX
Mean Total Cholesterol Compared with Pertinent Family History and Age

Age (yr.)	Number of Familial Diseases					
	None		One		Two or More	
	No.	Cholesterol	No.	Cholesterol	No.	Cholesterol
27–39	22	225	17	237	14	243
40–49	22	234	28	225	24	246
50–54	8	228	5	220	6	256
All ages	52	229	50	228	44	249

terol levels averaged 252, ranging from 233 to 281 mg. per cent. Elevations in blood pressure were recorded in six of the seven. Electrocardiographic abnormalities, consisting of nonspecific T wave abnormalities, were present in five.

COMMENTS

Certain phenomena have been implicated as contributing to the process of atherogenesis. One of these, the role of emotions and stressful situations, cannot be evaluated in this study. In addition, the role of other diseases which are considered to predispose to the development of atherosclerosis, notably diabetes, hypothyroidism and the nephroses, have been excluded by the selection of patients. This study has been designed to help evaluate some of the remaining factors—diet, obesity, physical activity, genetic background and hypertension.

Several dietary factors have been implicated in the pathogenesis of atherosclerosis; currently it is widely held that the ratio of "polyunsaturated" to saturated fatty acids are of major importance.[6] In the previous report no apparent relationship between dietary nutrients and the circulating lipids was apparent. A further reassessment of the diet at this time again failed to reveal any clear-cut statistical association with the serum cholesterol levels. These dietary findings will be reported in detail elsewhere.[7]

Obesity has achieved wide notoriety as a lethal factor in the causation of atheromas. This has been largely based on insurance statistics,[8] but some support has been obtained from autopsy studies.[9] Recent studies, prospectively oriented, tend to cast doubt on the validity of the relation of obesity to coronary heart disease.[10] Our data also fail to support any relationship between either weight or skinfold thickness and evaluation of cholesterol levels.

The role of physical activity in atherogenesis has been difficult to evaluate. It appears certain on widespread clinical evidence that in some instances extreme and sudden activity can be regarded as a precipitating factor, especially in the development of an acute myocardial infarction. However, in many other cases the onset of the acute manifestations coincides with a period of inactivity or occurs during sleep. Some authorities[11] have concluded that it is the socioeconomic factors which are determinant, those factors leading to sedentary occupations favoring the development of atherosclerosis. Whether the predisposition is mediated through dietary differences, greater emotional stresses in various socioeconomic strata, or still other forces is not clear. In this relatively homogeneous social group functioning in an industrial background, the data fail to relate the level of physical activity with serum cholesterol levels; previously serum cholesterol levels tended to be higher in the lower activity group.

Genetic factors have been accepted as predisposing to the development of overt manifestations of atherosclerosis.[11] However, genetic factors are also important to other

diseases, notably hypertension and diabetes, which in turn are related to the frequency of atheromas; it is, therefore, difficult to evaluate the relative importance of any of several genetic factors. It is noteworthy, nonetheless, that our subjects with strong family histories of these illnesses manifested a disturbing number of abnormalities, including electrocardiographic alterations and high, if not abnormal, serum cholesterol levels. This tendency had been previously noted and the passage of four years has only served to accentuate the phenomenon.

Significant hypertension has been related clearly to atherosclerosis.[12] Moreover, hypertension can be statistically related to other factors, notably obesity, family background and emotional stresses. These factors, in turn, have been related to the causes of atheromatous disease. It is likely that hypertension is the common channel through which these factors act upon the process of atherogenesis. In our group, abnormalities were more frequent in those with hypertension than in the group as a whole, even though serum cholesterol levels were not significantly altered.

In view of the multiplicity of factors involved, comparison of discreet groups must be made with caution. However, some data are available on a population group comparable to ours. Keys[13] has presented data on the serum cholesterol levels of a group of Italian residents in the city of Naples. Perhaps the most striking difference obvious at this time between these two groups is the tendency for the serum cholesterol levels in the subjects in Naples to rise from a low in the working class to a high among the "upper class" bankers. In the absence of any evidence for such social stratification in our cholesterol data, environmental rather than constitutional factors would appear to be implicated. A similar conclusion has been based on experiences with the Japanese in whom coronary artery disease is exceedingly rare in the home islands[14] despite not infrequent cerebral atherosclerotic manifestations,[15] more common among the partially occidentalized Japanese in Hawaii; while on the mainland U.S.A., it closely approaches the incidence of the entire population.

No conclusions are warranted, either from the data presented or from a comparison with the preceding report. In part this is due to the short lapse of time (four years) in a disease which develops over a course of time that must be measured in decades rather than years. In addition, the group has so far remained in continuing good health—only one patient has had a diagnosable myocardial infarction (subsequent to the 1960 examination), and in two others electrocardiographic evidence suggestive of myocardial infarctions have developed without corroborative history, an incidence of asymptomatic coronary occlusion similar to that reported elsewhere.[16,17] In the remainder of the patients, in the absence of any clear manifestations of overt complications of atherosclerosis, neither the presence nor the absence of atheromas can be surmised.

SUMMARY

One hundred and forty-six Italian-Americans, whose parents had been born in Naples, living and working in the Boston area were seen in a third biennial examination. Few significant findings have developed, except for one overt coronary occlusion and the appearance of electrocardiographic evidence of a myocardial infarction without corroborative evidence by history in two subjects.

Serum cholesterol determinations of all age groups were within the usual limits, but blood pressure and electrocardiographic abnormalities were more frequent in the thirty-two subjects with elevated cholesterol levels, than in the group as a whole.

No correlation could be demonstrated between serum cholesterol levels and body weight, physical activity or electrocardiographic abnormalities. There was some tendency for cholesterol levels to increase with heavy smoking, blood pressure abnormalities and pertinent family history.

The possible significance of these factors in the pathogenesis of atherosclerosis is discussed.

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