

# Low High-Density Lipoprotein Cholesterol And Other Coronary Heart Disease Risk Factors In Patients With Total Cholesterol Levels Greater Than 5.17 mmol/L (200 mg/dL) In Family Practice

*A Report from CEN*

**Abstract:** *Background:* A multisite, open-label, prospective study in 327 family practices across the United States analyzed the demography of a large population of dyslipidemic patients and examined the effects of diet and exercise, as well as of gemfibrozil therapy, on serum levels of total cholesterol, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, and triglycerides.

*Methods:* The 3328 patients enrolled comprised a heterogeneous population who had wide age range (20 to 88 years), were of both sexes and various ethnic backgrounds, and had multiple cardiac risk factors. All had a history of serum cholesterol levels of 5.17 mmol/L (200 mg/dL) or more, and some may have been previously identified as having an HDL of 1.03 mmol/L (40 mg/dL). After determining their cardiac risk factor and lipid profiles, eligible patients were assigned to a protocol of diet and exercise, followed by concomitant gemfibrozil therapy, if warranted. Treatment efficacy data will be reported in a subsequent paper.

*Results:* The study population was 60 percent men. Ninety-four percent of the patients were white, 4.1 percent were black, and 1.9 percent were of other races. Women patients tended to be more overweight, and elderly women had more hypertension; they were less likely to have angina pectoris or to have had previous myocardial infarctions, angioplasty, or bypass surgery. The prevalence of low HDL cholesterol ( $< 1.03$  mmol/L [40 mg/dL]) was substantially higher in men. Statistically significant differences between men and women were observed for mean values of total cholesterol, 6.47 versus 6.84 mmol/L (250.3 versus 264.4 mg/dL); HDL cholesterol, 0.94 versus 1.18 mmol/L (36.3 versus 45.5 mg/dL); LDL cholesterol, 4.62 versus 4.76 mmol/L (178.7 versus 184.2 mg/dL); non-HDL cholesterol, 5.54 versus 5.66 mmol/L (214.1 versus 218.9 mg/dL); and the total cholesterol-HDL ratio, 6.84 versus 5.64.

*Conclusions:* Current National Cholesterol Education Program (NCEP) guidelines suggest lipoprotein analysis at cholesterol levels between 5.17 and 6.21 mmol/L (200 and 240 mg/dL) only if two or more risk factors are also present. Persons whose total cholesterol values are less than 6.21 mmol/L (240 mg/dL) can still be at risk because of the presence of other cardiovascular risk factors or a low level of HDL cholesterol. In this study, 74.3 percent of men and 41.3 percent of women with total cholesterol  $\geq 5.17$  mmol/L (200 mg/dL) were also found to have a low HDL level,  $< 1.03$  mmol/L (40 mg/dL). The prevalence of other risk factors in this patient population was also high: 40.5 percent had hypertension, 9.6 percent had diabetes, and 20.3 percent smoked. These data suggest that routine lipoprotein analysis in the family practice setting could reveal low HDL cholesterol as an additional risk factor in a patient population where other risk factors have already been identified. (J Am Board Fam Pract 1991; 4:285-97.)

For many years attention focused on the relation between elevated levels of total cholesterol in the blood and increased risk of coronary heart disease (CHD).<sup>1</sup> More recently, however, the protective

effect of high levels of the high-density lipoprotein (HDL) fraction has been appreciated.<sup>2</sup> In a review of the Framingham Study, corroborated by data from other sources, it was suggested that HDL cholesterol appears to be the most powerful single lipoprotein indicator of risk.<sup>3</sup>

The 5-year Helsinki Heart Study of dyslipidemic men aged 40 to 55 years provided more evidence that elevating HDL cholesterol and lowering LDL cholesterol with gemfibrozil therapy were both effective in the primary prevention of CHD.<sup>4</sup> The Helsinki Heart Study showed that a 10 percent increase in HDL cholesterol accompa-

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nied by an 8 percent reduction in total cholesterol resulted in a 34 percent reduction in CHD.<sup>4</sup>

In 1988, the National Cholesterol Education Program (NCEP) Expert Panel on the Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults<sup>5</sup> recommended the use of specific ranges to classify persons as having desirable < 5.17 mmol/L (200 mg/dL), borderline-high 5.17–6.18 mmol/L (200–239 mg/dL), and high  $\geq$  6.20 mmol/L (240 mg/dL) concentrations of serum cholesterol. They recognized a number of separate risk factors for CHD, including obesity, hypertension, diabetes, smoking, male sex, a history of cerebrovascular or occlusive peripheral vascular disease, a family history of CHD, and HDL cholesterol levels < 0.90 mmol/L (35 mg/dL). The NCEP Expert Panel developed guidelines for detecting hypercholesterolemia and caring for patients who are at risk of CHD by virtue of above-normal concentrations of LDL cholesterol ( $\geq$  4.14 mmol/L, 160 mg/dL). They acknowledged that concentrations of HDL cholesterol of 0.90 mmol/L (35 mg/dL) and greater offer some protection against the development of CHD but did not outline specific recommendations regarding measurement of HDL levels.

The publication of the NCEP guidelines has led to a greater awareness of the need for total cholesterol screening. Various community screening programs and studies on the management of hypercholesterolemia in family practice settings have been described.<sup>6–8</sup> These studies recognize the lack of adequate management by some physicians. They also criticize the NCEP guidelines for the lack of data about HDL cholesterol levels. Community screening programs have detected hypercholesterolemia in many persons whose subsequent lipid profiles proved essential in the diagnosis of low HDL levels.<sup>6,9</sup>

The NCEP guidelines advocate a low-cholesterol diet and exercise as first-line therapy for dyslipidemia; the guidelines recommend that lipid-altering drugs be reserved for patients who have high levels of LDL cholesterol or low levels of HDL cholesterol, plus risk factors for CHD, and who fail to respond to diet and exercise. Several categories of drugs to treat dyslipidemia are available.

This study (based on the NCEP guidelines) of dyslipidemic persons in a heterogeneous population seen in family practice was undertaken to

ascertain the effects of diet and exercise and, when appropriate, drug intervention on serum levels of total cholesterol, triglycerides, LDL cholesterol, and especially HDL cholesterol and to learn about the characteristics of such a population.

This report describes the identification and prevalence of dyslipidemia and focuses on HDL cholesterol levels in this population. A future report will discuss the results of intervention with diet, exercise, and gemfibrozil. This study was conducted by 327 family physicians who are part of the Clinical Experience Network (CEN<sup>™</sup>), a nationwide affiliation of board-certified family physicians. The physicians are distributed among family practices in 49 states and the District of Columbia. The majority of the participating physicians are in private practices, which average 3 physicians per site. A small percentage practice in industrial settings (13 percent), health maintenance organizations (9 percent), neighborhood clinics (8 percent), and in medical school or teaching hospital environments (22 percent).

More than 40 percent of the CEN physicians have participated in previous phase IV studies\* that examined a wide cross-section of patients presenting to family physicians.<sup>10,11</sup> Whereas most clinical research is conducted in large medical centers or academic institutions, and often on atypical populations, CEN provides a framework in which family physicians can conduct coordinated clinical investigations in standard medical practices and obtain results that are representative of the general population.

Importantly, the study sought to investigate a heterogeneous population of patients who were more representative than the asymptomatic Finnish men, aged 40 to 55 years, who were enrolled in the Helsinki Heart Study.<sup>12</sup> To this end, women, as well as blacks and members of other races of various ages, were enrolled.

## Methods

### Study Design

This prospective, open-label, multisite study had a target population of 4000 patients whose

\*Studies conducted by CEN are approved by the Investigational Review Board of the Baptist Medical Center, Kansas City, MO. Practices such as the completion of patient consent forms are observed.

serum cholesterol levels were 5.17 mmol/L (200 mg/dL) and greater and whose HDL cholesterol levels were low. In a trial arm of the study, 10 percent of the patients were targeted to be randomized to either diet and exercise only or to diet and exercise plus drug intervention. The rest of the patients were nonrandomized. At each of 327 study sites, investigators were to enroll approximately 10 patients, both men and women, the majority of whom did not have CHD.

### **Patient Selection**

Patients enrolled in the study were patients in a family practice setting who had histories of total cholesterol levels  $\geq 5.17$  mmol/L (200 mg/dL). The study protocol did not require patients entered into the study to have a low HDL, although some previously encountered patients may have been identified as having an HDL of less than 1.03 mmol/L (40 mg/dL). Patients had to meet the following inclusion criteria: age at least 20 years, either sex, and any race or ethnic group. Excluded from enrollment were pregnant women, nursing mothers, patients with known contraindications to gemfibrozil, those who were soon to undergo surgery or had done so within the previous 6 months, and patients who had taken any lipid-lowering agent within the previous 6 weeks (6 months in the case of probucol). Also excluded were patients receiving concomitant therapy with any steroid hormone or anticoagulant, those who had been given an experimental drug within the previous 3 months, those with a history of drug abuse, and patients with a serious psychiatric disorder or an anticipated inability to follow instructions.

During the selection-enrollment process, all patients with cholesterol  $\geq 5.17$  mmol/L (200 mg/dL) had a lipoprotein analysis performed. If this profile fit the study criteria as described below and if all other entry criteria had been met, a low-cholesterol diet and an exercise program were prescribed. The lipid profile criteria were as follows: total cholesterol level  $\geq 5.17$  mmol/L (200 mg/dL), HDL cholesterol level  $< 1.03$  mmol/L (40 mg/dL), LDL cholesterol level 3.36–4.11 mmol/L (130–159 mg/dL) with CHD, or 4.14–4.89 mmol/L (160–189 mg/dL) with two or more CHD risk factors, or 4.91 mmol/L (190 mg/dL).

Age, sex, and race were recorded during the selection-enrollment process, as well as medical history, family history, and CHD risk factors. At this time, any prior interventions, such as cholesterol-lowering medication, previous low-cholesterol diet, or exercise program, were recorded. Complaints and concurrent use of medications were also noted. Included in the physical examination were height, weight, blood pressure, and pulse rate measurements.

Following the diet and exercise phase of the study, a second lipid profile was performed to determine whether patients qualified for drug intervention. This report describes the demographic features of the patients who were enrolled in the study, some of whom did not require further intervention or continuation in the study protocol.

### **Laboratory Procedures**

Blood samples drawn after a 12-hour fast at entry, after 6 weeks of diet and exercise, and after 6 weeks and 12 weeks of gemfibrozil therapy were analyzed for total cholesterol, triglycerides, HDL cholesterol, and LDL cholesterol. The sample drawn after diet and exercise was also analyzed for thyroxine, aspartate aminotransferase (AST), alanine aminotransferase (ALT), and serum creatinine to detect abnormalities that would contraindicate gemfibrozil therapy.

To prevent posture or stasis from affecting the determination of cholesterol, the patient was made to sit quietly for at least 5 minutes before venipuncture, and the tourniquet was used for the shortest possible time. One full 10-mL serum-separator tube of blood was collected, inverted five times, and allowed to clot for 30 minutes. That tube was centrifuged within 45 minutes of venipuncture and sent to a Centers for Disease Control-certified lipid reference laboratory for analysis (MetPath Labs, Inc, Teterboro, NJ). A central laboratory was chosen for all analyses to rule out interlaboratory and methods variations.

In the laboratory, the concentration of triglycerides was determined after their conversion to free fatty acids and glycerol using a standard enzymatic technique to measure quinoneimine dye formation on a Hitachi 736 analyzer. The concentration of total cholesterol was similarly determined. For HDL cholesterol, precipitation and removal of very-low-density lipoprotein (VLDL)

**Table 1. Demographic Profile of Nonrandomized Hypercholesterolemic Patients (n = 3328).**

Characteristics	All Patients	Men	Women
Age (yrs)			
Mean	52.8	50.9	55.6
Standard error	0.23	0.29	0.34
Number*	3325	1928	1397
Weight (kg)			
Mean	83.91	90.02	75.12
Standard error	0.34	0.39	0.51
Number*	2567	1515	1009
Height (cm)			
Mean	171.7	177.5	163.0
Standard error	0.20	0.18	0.23
Number*	2472	1473	956
Body mass index (kg/m <sup>2</sup> )			
Mean	28.5	28.6	28.4
Standard error	0.01	0.01	0.02
Number	2454	1461	950
Race (%)			
White (n = 3127)	94.0	93.5	94.3
Black (n = 137)	4.1	5.0	3.5
Other (n = 64)	1.9	1.5	2.2

\*Complete data on certain patients not available.

cholesterol and LDL cholesterol were followed by enzymatic reactions and photometric determination of the concentration of the remaining HDL cholesterol. The concentration of LDL cholesterol was calculated by computer from the values for total cholesterol, HDL cholesterol, and triglycerides, according to the following formula:

$$\text{LDL} = \text{Total cholesterol} - (\text{HDL cholesterol} + [\text{Triglycerides} \times 0.16])^*$$

### Statistical Analysis

Standard statistical procedures were employed using the SAS statistical analysis package. Both parametric and nonparametric statistical methods were used for the continuous variables, including paired and nonpaired t-tests, analysis of variance with and without logarithmic transformations, Wilcoxon matched pairs, and rank sum and Kruskal-Wallis analysis of variance. Categorical data were analyzed using chi-square contingency table methods and the Fisher exact test.

### Results

There were 3328 patients with serum total cholesterol levels  $\geq 5.17$  mmol/L (200 mg/dL) enrolled in the study (Table 1).

\*If the concentration of triglycerides exceeds 4.52 mmol/L (400 mg/dL), this method of calculating the concentration of LDL cholesterol is no longer valid.

### Sex, Age, and Race

Women made up 42 percent of the patient population. Patients ranged in age from 18 to 88 years; mean age was 52.8 years (50.9 years for men, 55.6 years for women). Ethnically, the patient population was 94 percent white, 4.1 percent black, and 1.9 percent other races. The racial distribution was similar for men and women.

### Weight, Height, and Body Mass Index

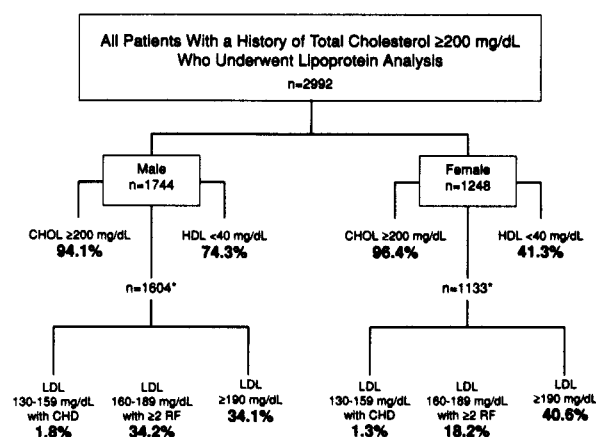
The mean weight was 90.02 kg for men and 75.12 kg for women. Corresponding mean heights were 177.5 cm and 163 cm, respectively. The body mass indices (BMIs) were 28.6 kg/m<sup>2</sup> and 28.4 kg/m<sup>2</sup> for men and women, respectively.

### Risk Factors for Coronary Heart Disease

For the entire population for whom relevant data were available (n = 2980), the mean number of risk factors for CHD was 2.44 for whites, 2.56 for blacks, and 2.36 for other races (Table 2). In every age group, men had more risk factors for CHD because male sex is in itself a risk factor (Table 3). A low level of HDL cholesterol (1.03 mmol/L or 40 mg/dL) occurred in 60.1 percent of whites, 51.7 percent of blacks, and 51.8 percent of other races; as was expected, in every age group the percentage of men with low HDL cholesterol exceeded that of women.

Hypertension was present in 39.4 percent of whites, 68.6 percent of blacks, and 42.9 per-





**Figure 1. Distribution of patients according to lipoprotein profile.** CHOL = total cholesterol, HDL = high-density lipoprotein, LDL = low-density lipoprotein, RF = risk factors.

cent of other races. In the United States, the prevalence of hypertension is 28.8 percent in whites and 38.2 percent in blacks.<sup>13</sup> In patients older than 70 years, the percentage of women with hypertension exceeded that of men, a trend seen in the general population.<sup>13</sup>

A family history of CHD existed in 23.7 percent of whites, 16.1 percent of blacks, and 23.2 percent of other races. Smokers comprised 20.6 percent of whites, 14.4 percent of blacks,

and 14.3 percent of other races. Obesity existed in 16.4 percent of whites, 22.9 percent of blacks, and 17.9 percent of others; in every age group, the percentage of women who were obese exceeded that of men. Diabetes occurred in 9.0 percent of whites, 22.9 percent of blacks, and 16.1 percent of other races. The frequency of occurrence of risk factors for CHD, arranged by age and sex of the patients, is shown in Table 3.

### Lipid Analysis—Sex Differences

Among the 2992 preselected patients (history of total cholesterol levels  $\geq 5.17$  mmol/L or 200 mg/dL) for whom a lipoprotein analysis was performed, 94.1 percent of men and 96.4 percent of women had serum total cholesterol levels  $\geq 5.17$  mmol/L (200 mg/dL) (Figure 1). Low levels of HDL cholesterol ( $< 1.03$  mmol/L or 40 mg/dL) were found in 74.3 percent of men and 41.3 percent of women. Most patients had LDL-cholesterol values that were either  $\geq 4.91$  mmol/L (190 mg/dL) (34.1 percent of men and 40.6 percent of women) or between 4.14 and 4.89 mmol/L (160–189 mg/dL), with two or more risk factors for CHD present (34.2 percent of men and 18.2 percent of women). Only 1.8

**Table 2. Cardiac Risk Factor Profile Differences Among Ethnic Groups.**

Cardiac Risk Factor	Percentage with Risk Factor			P Value*
	White (n = 2807)	Black (n = 117)	Other (n = 56)	
Family history of coronary heart disease	23.7	16.1	23.2	0.16
Smoker	20.6	14.4	14.3	0.14
Hypertension	39.4	68.6	42.9	<0.001
Diabetes mellitus	9.0	22.9	16.1	<0.001
Cerebrovascular or peripheral vascular disease	7.6	6.8	3.6	0.50
Obesity	16.4	22.9	17.9	0.18
High-density lipoprotein cholesterol $< 1.03$ mmol/L (40 mg/dL)	60.1	51.7	51.8	0.09
Total cholesterol $\leq 5.17$ mmol/L (200 mg/dL)	95.0	94.7	98.2	0.51
Low-density lipoprotein cholesterol (3.36–4.14 mmol/L (130–159 mg/dL))§	1.7	0.0	0.0	0.25
Low-density lipoprotein cholesterol 4.14–4.89 mmol/L (159–189 mg/dL)¶	27.7	23.6	34.0	0.39
Low-density lipoprotein cholesterol $\geq 4.91$ mmol/L (190 mg/dL)	36.0	50.0	42.0	0.009
Mean number of risk factors (SE)†	2.44 (0.02)	2.56 (0.10)	2.36 (0.16)	0.52‡

SE = Standard error.

\*Values  $< 0.05$  are statistically significant.

†Includes male sex, family history, smoker, hypertension, diabetes mellitus, cerebrovascular or peripheral vascular disease, obesity, and high-density lipoprotein cholesterol  $< 1.03$  mmol/L (40 mg/dL).

‡Kruskal-Wallis test; all other values from chi-square contingency tables.

§With coronary heart disease.

¶With two or more risk factors.

**Table 3. Cardiac Risk Factor Profile of Patients by Age and Sex.**

Age Group (yr)	No.	Mean No. of Risk Factors (SE)	Percentage of Patients						
			Family History of CHD	Smoker	Hyper-tension	Low HDL	Diabetes Mellitus	Vascular Disease	Obesity
20-39									
Men	346	2.67 (0.05)	28.6	22.0	23.4	72.6	2.3	0.9	15.1
Women	155	1.48 (0.09)	28.7	22.6	18.9	37.8	4.3	1.8	25.0
P value		< 0.0001†	NS	NS	NS	, 0.001	NS	NS	0.007
40-49									
Men	529	2.74 (0.05)	22.7	25.7	32.7	71.0	4.5	3.0	12.1
Women	241	1.81 (0.08)	27.2	28.7	29.9	43.3	7.7	2.7	27.6
P value		< 0.0001	NS	NS	NS	< 0.001	0.06	NS	0.001
50-59									
Men	414	3.03 (0.06)	25.2	24.0	46.1	71.3	11.9	9.0	13.3
Women	301	1.91 (0.07)	25.5	23.6	46.0	40.7	12.4	4.9	25.2
P value		< 0.0001	NS	NS	NS	< 0.001	NS	< 0.04	0.001
60-69									
Men	334	3.00 (0.06)	19.8	13.3	51.2	75.4	12.7	16.3	9.8
Women	311	1.86 (0.07)	19.9	15.4	50.3	40.7	16.9	9.3	20.8
P value		< 0.0001	NS	NS	NS	< 0.001	NS	< 0.007	0.001
> 70									
Men	152	2.85 (0.09)	14.6	7.0	46.2	69.0	10.8	22.5	8.2
Women	194	1.95 (0.08)	18.0	7.8	63.1	49.0	16.0	13.6	16.0
P value		< 0.0001	NS	NS	0.001	0.001	NS	< 0.03	< 0.03
All patients	2977	2.44 (0.02)	23.4	20.3	40.5	59.6	9.6	7.5	16.7

SE = standard error, CHD = Coronary heart disease, HDL = high-density lipoprotein cholesterol < 1.03 mmol/L (40 mg/dL), NS = not statistically significant.

\*P values < 0.05 are traditionally considered statistically significant.

†Kruskal-Wallis test—all other values from chi-square contingency tables.

percent of men and 1.3 percent of women had LDL-cholesterol values between 3.36 and 4.11 mmol/L (130 and 159 mg/dL) and evidence of CHD.

The lipid analyses performed at time of entry into the study (n = 2992) showed mean total cholesterol was 6.47 mmol/L (250.3 mg/dL) for men and 6.84 mmol/L (264.4 mg/dL) for women (Table 4). Women had significantly higher values than men for HDL, LDL, and non-HDL cholesterol and significantly lower values than men for the ratios of total cholesterol to HDL, triglycerides to HDL, and LDL to HDL. There was no statistical difference between triglyceride levels.

#### Cardiovascular Status at Entry

Evaluation of the cardiovascular status of patients entering the study showed that both men and women had an increased prevalence of angina pectoris with increased age (Table 5). In men, the rate of previous myocardial infarction increased with increased age (1.7 percent at 20 to 39 years to 17.5 percent at > 70 years). The rate of bypass surgery, angioplasty, or

previous myocardial infarction was very low in women.

#### Prior Intervention

In this study, 44.5 percent of men and women alike (n = 2548) had already attempted some form of low-cholesterol diet at the time of their enrollment as a consequence of prior intervention. Among 2623 patients at time of entry, 25.5 percent lived sedentary lives, whereas 28.0 percent exercised regularly, and 46.4 percent exercised irregularly. In all three categories, men reported more activity than women.

#### Discussion

This study provides a new and useful breakdown of demographic data for a large group of patients with a history of total serum cholesterol  $\geq$  5.17 mmol/L (200 mg/dL). Although this population was not randomly selected but was composed of patients who met certain criteria, it is a good sample of patients with abnormal cholesterol levels who come to a family physician's office. Such a sample provides useful information about the

prevalence of risk factors for CHD, lipid profiles, prior intervention, and age groups and the relations among them.

### Obesity

Men and women in this patient population were more obese than persons comprising the national norms, with BMIs of 28.6 kg/m<sup>2</sup> for men and 28.4 kg/m<sup>2</sup> for women. In all five age groups studied, the percentage of obese women was significantly greater than that of men (Table 3). Based on 1983 Metropolitan Life Insurance Company weight-for-height tables, the national means for BMIs were 22.4 kg/m<sup>2</sup> for men and 22.5 kg/m<sup>2</sup> for women.<sup>14</sup>

Two studies have highlighted the significance of obesity in hypercholesterolemic persons, especially women. An 8-year study of 116,000 women, aged 30 to 55 years, confirmed that women who were even mildly to moderately overweight (BMI of 25.0 to 28.9 kg/m<sup>2</sup>) had a risk of coronary

disease 80 percent higher than their lean counterparts.<sup>15</sup> A study of the possible relations of endogenous sex steroid hormones to serum lipids and lipoproteins in white, postmenopausal women showed that the degree of obesity, as estimated by BMI, was the primary predictor of HDL-cholesterol and triglyceride levels.<sup>16</sup>

The mean HDL-cholesterol levels found in this study—0.94 mmol/L (36.3 mg/dL) for men and 1.18 mmol/L (45.5 mg/dL) for women (Table 4)—are compatible with the view of the Framingham Study investigators in 1977 that a person who is obese, has glucose intolerance, or has a high triglyceride level is more likely to have a low HDL-cholesterol level than a high one.<sup>17</sup>

### Risk Factors for Coronary Heart Disease

The Framingham Offspring Study, which included 792 men and 853 women aged 30 to 69 years, has been especially valuable for its complete and accurate history of parental CHD.<sup>18</sup> The fa-

**Table 4. Mean Lipid Values of Patients at Initial Screening.**

Lipid	Men	Women	P Value
Total cholesterol mmol/L (mg/dL)			
Mean	6.47 (250.3)	6.48 (264.4)	< 0.001
Standard error	0.87	1.8	
Number	1744	1248	
Triglyceride mmol/L (mg/dL)			
Mean	2.59 (229.6)	2.53 (223.8)	0.084
Standard error	3.22	3.90	
Number	1742	1247	
HDL cholesterol mmol/L (mg/dL)			
Mean	0.94 (36.3)	1.18 (45.5)	< 0.001
Standard error	0.21	0.40	
Number	1745	1248	
LDL cholesterol mmol/L (mg/dL)			
Mean	4.62 (178.7)	4.76 (184.2)	0.002
Standard error	0.83	1.16	
Number	1604	1133	
Non-HDL cholesterol mmol/L (mg/dL)			
Mean	5.54 (214.1)	5.66 (218.9)	0.009
Standard error	0.87	1.23	
Number	1744	1248	
Total cholesterol HDL ratio			
Mean	7.26	6.32	< 0.001
Standard error	0.05	0.06	
Number	1744	1248	
Triglyceride/HDL ratio			
Mean	6.84	5.64	< 0.001
Standard error	0.11	0.12	
Number	1742	1247	
LDL/HDL ratio			
Mean	5.17	4.40	< 0.001
Standard error	0.04	0.05	
Number	1604	1133	

\*P values < 0.05 are traditionally considered statistically significant; Wilcoxon rank sum test.

HDL = high-density lipoprotein.

LDL = low-density lipoprotein.

Table 5. Cardiovascular Status of Patients By Age and Sex at Time of Entry into Study.

Age Group (yrs)	No.*	Percentage of Patients			
		Angina Pectoris	Previous Myocardial Infarction	Previous Angioplasty	Previous Bypass Surgery
20-39					
Men	306	1.3	1.7	0.7	0.3
Women	135	0.0	0.0	0.0	0.0
40-49					
Men	474	3.2	3.8	2.2	0.6
Women	211	2.4	3.3	0.0	1.4
50-59					
Men	371	11.2	11.0	5.6	7.3
Women	263	6.6	5.4	2.0	2.0
60-69					
Men	308	20.9	20.7	5.0	11.3
Women	268	9.9	3.1	1.9	1.5
> 70					
Men	137	23.1	17.5	4.4	17.0
Women	172	17.0	8.4	1.2	5.5

\*Complete data on certain patients not available.

mial incidence of CHD in that study was most prevalent in the youngest age group and decreased with age. For the 2977 persons in this study (Table 3), the pattern for prevalence of a family history of CHD paralleled that one exactly. In both populations, men and women showed an increase in percentage of patients with hypertension with each increase in age; the same was true for diabetes and for cerebrovascular or peripheral occlusive vascular disease. In neither population was there any systematic age-related change in percentage of patients with low levels of HDL cholesterol. For men and women in both studies, the highest percentage of smokers was in the 40- to 49-year age group. In each study, men had more than twice as many risk factors as did women in every age group, reflecting the inclusion of male sex as a risk factor.

The results of a 10-year study of 2541 white men, aged 40 to 69 years at baseline, have suggested that the potential impact of changes in lipid levels on the risk of death from CHD can be much greater for men with preexisting cardiovascular disease than for healthy men.<sup>2</sup>

### **Lipids and Lipoproteins**

In the Cooperative Lipoprotein Phenotyping Study, mean HDL cholesterol levels for women were about 0.26 mmol/L (10 mg/dL) higher than those for men.<sup>19</sup> Again, in the 1986 Framingham Study report, women had a higher mean HDL cholesterol level than did men at first measure-

ments (1.50 mmol/L or 58.0 mg/dL versus 1.19 mmol/L or 46.0 mg/dL) and at follow-up 8 years later (1.40 mmol/L or 54.2 mg/dL versus 1.15 mmol/L or 44.5 mg/dL).<sup>20</sup> The second National Health and Nutrition Examination Survey (NHANES) also reported higher mean HDL cholesterol levels in women compared with those in men.<sup>21</sup> That same sex differential was noted in this study (Table 4). Not surprisingly, women in every age group in this study had a significantly lower prevalence of low HDL cholesterol (< 1.03 mmol/L, 40 mg/dL) than did men (Table 3). Total cholesterol was also higher in women than in men, which supports earlier findings.<sup>20</sup> The mean values for total cholesterol were higher in this study, 6.47 mmol/L (250.3 mg/dL) in men and 6.83 mmol/L (264.4 mg/dL) in women, than in the Framingham Study, 5.70 and 6.25 mmol/L (220.0 and 241.6 mg/dL), respectively; which may reflect that the Framingham Study patients were older (men 61 years and women 62 years, compared with 50.9 and 55.6 years, respectively).

In a study of 3600 white men and 500 black men, aged 31 to 45 years, the mean level of HDL cholesterol was 0.21 mmol/L (8 mg/dL) higher among blacks.<sup>22</sup> This finding was consistent with the findings in this study, which showed that the prevalence of low HDL cholesterol was 60.1 percent in whites, 51.7 percent in blacks, and 51.8 percent in other races (Table 2). Representation of nonwhite races in this study was typical of the



average family practice for patient-racial distribution.<sup>23,24</sup> In addition, socioeconomic factors may have excluded enrollment of more blacks in this study.

## Conclusions

The private encounter between the patient and physician is rarely analyzed in detail when the results of large drug trials are discussed, yet it is in this setting that most clinical decisions are made.<sup>25</sup> This study shows that family practice patients with dyslipidemia (elevated LDL cholesterol or low HDL cholesterol, or both) often have other multiple risk factors (hypertension, smoking, obesity, diabetes, cerebrovascular disease, family history) that predispose them to CHD. For example, 40.5 percent of these hypercholesterolemic patients were also hypertensive, 20.3 percent were smokers, and 16.7 percent were obese. Sixty-four percent of the patients had LDL cholesterol levels > 4.14 mmol/L (160 mg/dL). Sixty percent had HDL cholesterol levels < 1.03 mmol/L (40 mg/dL)—74.3 percent of the men and 41.3 percent of the women. These findings point to the importance of lipoprotein analysis in the family practice patient who has total cholesterol levels  $\leq$  5.17 mmol/L (200 mg/dL) because LDL cholesterol and HDL cholesterol are independent risk factors for CHD. Conversely, because there appears to be a correlation among dyslipidemia and hypertension, obesity, and smoking, it may be prudent to perform lipoprotein analysis in patients who have these risk factors, even if total cholesterol is not elevated, to detect such abnormalities as low HDL cholesterol or high triglycerides.

Based on the NCEP guidelines, about one-third of all adults will require medical counseling and intervention for dyslipidemia.<sup>26</sup> The first line of treatment is diet and exercise, and for many that will be sufficient. If an adequate trial shows a patient's failure to respond to such a regimen, however, use of a lipid-regulating medication may be warranted.

In the search for an optimal therapy for treating dyslipidemia, the ideal lipid response would appear to be the one that raises HDL cholesterol and lowers LDL cholesterol.<sup>3</sup> Interventions that affect only one of these lipoprotein fractions in a

favorable way may be less promising than those that improve values for both HDL and LDL cholesterol.<sup>3</sup> A subsequent report based on this study will focus on the efficacy of gemfibrozil therapy in various subgroups of dyslipidemic patients.

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