Factors Associated with High Density Lipoprotein Cholesterol in a Population with High High Density Lipoprotein Cholesterol Levels

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A cross-sectional study of a random sample of 976 coloureds (mixed race) of the Cape Peninsula, ages 15 to 64 years old, revealed a population with unexpectedly high levels of high density lipoprotein (HDL) cholesterol. The mean level for men was 55.4±16.1 mg/dl (SD) and for women, 50.8±16.0 mg/dl. The ratio of HDL cholesterol to total cholesterol expressed as a percentage was 26.3%±9.5% for men and 28.1%±9.3% for women. The HDL cholesterol levels were apparently lower than those of black and Negro populations, yet higher than those of Caucasian populations. Men with levels of HDL cholesterol above the median reported a personal history and a family history of coronary heart disease less frequently than did men with lower levels, while women with high levels of HDL cholesterol were less likely to have a history of hypertension or diabetes. Stepwise multiple regression analysis of variables significantly associated with HDL cholesterol levels showed that they explained 29.7% and 24.7%, respectively, of the variation in HDL cholesterol in men and women. Those variables independently associated with HDL cholesterol in both men and women were: serum triglyceride (−), cigarette consumption (−), alcohol, body mass index (−), age, and serum low density lipoprotein cholesterol levels (−).

The reasons for the relatively high HDL cholesterol levels in this population are unknown. However, it would seem possible that these levels offer some protection against the high risk factors of smoking, hypertension, and hypercholesterolemia. (Arteriosclerosis 9:390–397, May/June 1989)

The role of the plasma concentration of high density lipoprotein (HDL) cholesterol as a protecting factor against coronary heart disease (CHD) has been strongly suggested in case–control studies and in some prospective and cohort studies. Although recently published results of the prospective British Regional Heart Study found a univariate association of HDL cholesterol with CHD, it differed from other studies in that the association did not remain statistically significant when controlled for other risk factors. However, the methodology and conclusions of this study have been challenged. The inverse relationship between the direct angio graphic measurement of atherosclerosis and HDL cholesterol has repeatedly been reported. The severity of clinical features of CHD in hypercholesterolemic patients is inversely related to HDL cholesterol levels irrespective of age, blood pressure, other lipoprotein levels, or coronary angiographic findings. Kennell suggested that the risk for CHD associated with the HDL cholesterol level in individuals is determined by the total cholesterol (TC) level associated with a particular HDL cholesterol level, and the ratio of HDL cholesterol to TC (%HDL/TC) has proved to be an efficient measure of CHD risk within populations with high TC levels.

The inverse relationship of HDL cholesterol with CHD found within populations does not hold for comparisons between populations. Marked differences are seen when comparing the HDL cholesterol levels of different populations of all ages. The mean HDL cholesterol concentrations show a distribution similar to that of mean TC levels: relatively low levels and low CHD incidence in the developing countries and relatively high levels and high CHD incidence in the more developed, Westernized countries.

Little was previously known about the HDL cholesterol levels and the %HDL/TC in South African population groups. Physically active South African black people living on a traditional diet seem to have higher HDL cholesterol levels and %HDL/TC (P.L. Jooste, unpublished data) than white people. No information existed about the HDL cholesterol levels of the coloured population, which originated from white, black, and Asian populations in South Africa.

Their increasing CHD mortality, the need to formulate a remedial strategy, and the lack of data on HDL cholesterol and other CHD risk factors in this population prompted the study of coronary risk factors in the coloured population of

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the Cape Peninsula (CRISIC study) of the Republic of South Africa (RSA).16-21

This article reports on the HDL cholesterol levels, the %HDL/TC, and the proportions of persons with protective HDL cholesterol levels in the study population. The disease profile of persons with and without protective %HDL/TC levels were compared. An attempt is made to identify the variables that contribute to the variation of HDL cholesterol in this population group.

Methods

Study Population

The subjects for the study were an age- and sex-stratified sample of 976 participants randomly selected by a multistaged probability sampling technique. The subjects were drawn from 48512 coloreds ages 15 to 64 years old who lived in the Cape Peninsula of the RSA (determined by the 1980 census). Only one member per household was selected. Exclusion criteria were pregnancy, being bedridden, mental retardation, carcinoma, leg amputation, antimicrobial drug therapy, hospitalization for more than 1 week during the previous 3 months, and inability or unwillingness to participate. Of those who qualified and were approached, 92.3% participated.

Methods

Trained field workers visited participants in their homes. A risk factor questionnaire and a London School of Hygiene questionnaire20 for chest pain were completed. The questionnaire covered socioeconomic items including the level of education, number of occupants per habitable room, and classification of employment according to the Centre for Applied Social Sciences' (CASS) occupational category for coding of occupations in South Africa.23 A short medical history, a family history of ischemic heart disease, smoking habits, and physical activity patterns were recorded. Physical activities at work or leisure were grouped into one of three categories (sedentary, moderate, or vigorous activity) according to the duration and intensity of energy expenditure. The total energy expenditures at work and leisure were calculated by measuring the average time that each individual spent each week in a particular activity by the average rate of energy expenditure for that activity corrected for body weight.24,25,26

Blood samples were collected from each participant. The serum was separated within 6 hours of clotting at room temperature and was then frozen at -20°C. The TC and HDL cholesterol levels were measured on a Gilford auto-analyzer (Gilford Instrument Laboratories, Inc., Oberlin, OH) by using the Boehringer CHOD-PAP enzymatic method. HDL cholesterol was measured after precipitation of the apolipoprotein (apo) B containing lipoproteins with MgCl2-dextran sulfate.27 The triglyceride levels were determined by the Boehringer Perdichrom enzymatic method. In each case, the Gilford auto-analyzer was calibrated against Fracilip or Fracilip EL control sera, which were corrected by Boehringer Mannheim for the specific test kit in question. Two control samples were included in each batch analyzed. At least 7 days after the first sample, 100 random blood samples were re-collected to determine combined biological and technique variation. For TC values, the correlation coefficient for both samples was 0.88; for HDL cholesterol, 0.87, and for triglycerides, 0.80.

Blood pressures (BP) were recorded by trained field workers after participants had been seated for at least 5 minutes. A mercury manometer connected to a standard 12.5 x 23 cm cuff was used. The American Heart Association guidelines for measuring BP28 were applied. During the field work, the field workers' standard for BP readings was checked against the reference weekly. End-digit preference was not found on subsequent analysis. At least 7 days after the first reading, 100 random BP readings were repeated to determine any variation. This gave an acceptable reproducibility, as reflected in correlation coefficients of 0.77 for systolic and 0.75 for diastolic readings, which are similar to the findings of other studies.29

Anthropometric measurements were taken by using a metal measuring tape against a wall and a flat headboard at right angles to the wall to ensure correct readings for heights to the nearest 0.5 cm. Mass was determined on a good quality bathroom scale with the subject in light clothing and without shoes. The bathroom scales were standardized weekly against a beam balance to determine the zero setting. Thereafter, the field worker's own weight was used as a daily check before weighing each participant. Body mass index (BMI) was calculated as weight (kg)/height (m²).

To determine the nutrient intake of the participants, the field workers were trained by experienced dieticians in completing a dietary questionnaire, which included a 24-hour dietary recall. Interviewers were trained with the aid of food models and household measures to accurately record the amounts of food eaten and methods of food preparation. The amounts of food recorded in the 24-hour dietary recall were converted by the dietitians to weights of food eaten and then coded by using the National Research Institute for Nutritional Diseases (NRIND) Food Composition Tables.30 This enabled an analysis of food intake in terms of nutrient intake.

Univariate analyses were used to identify variables that were significantly associated with HDL cholesterol. These were then entered into a stepwise multiple regression analysis in an effort to explain the variation in HDL cholesterol. The odds ratio was calculated for participants with %HDL/TC levels above and below the median to compare a CHD-related medical history in the two groups. The same two groups were compared with respect to socioeconomic parameters.

Results

The mean HDL cholesterol levels did not increase with age, and the men had somewhat lower levels than the women (Table 1). Because of an increasing TC level with age, the %HDL/TC decreased with age. For both sexes, the %HDL/TC decreased up to the age of 54 years and remained fairly constant thereafter. Women between the ages of 15 and 44 years had a higher %HDL/TC than their male counterparts. Above this age, the ratio was similar for both sexes.
Table 1. HDL Cholesterol Levels and Ratio of HDL Cholesterol to Total Cholesterol in Study Population

| Age group (years) | Mean HDL cholesterol* | %HDL/TC | Mean HDL cholesterol* | %HDL/TC |
|-------------------|-----------------------|---------|-----------------------|---------|
|                   | No.                   | ± SD    | No.                   | ± SD    |
| 15-24             | 94                    | 55.0±12.4 | 30.9±8.8  | 103       | 61.9±14.7 | 33.8±2.8.6 |
| 25-34             | 96                    | 54.8±13.5 | 26.2±8.1  | 94        | 58.8±15.9 | 29.6±2.8.4 |
| 35-44             | 103                   | 55.7±22.8 | 25.1±10.4 | 112       | 61.5±17.4 | 28.4±2.9.2 |
| 45-54             | 95                    | 55.0±17.0 | 24.7±9.6  | 94        | 58.8±17.8 | 24.9±2.9.0 |
| 55-64             | 90                    | 55.3±18.8 | 24.2±10.8 | 95        | 60.8±18.2 | 24.2±2.8.3 |
| 15-64             | 478                   | 55.3±16.3 | 26.3±9.5  | 498       | 60.8±15.9 | 28.3±2.9.3 |

HDL = high density lipoprotein cholesterol; TC = total cholesterol.
%HDL/TC = ratio of HDL cholesterol to total cholesterol. SD = standard deviation.
*Values are mg/dl.

Table 2. Prevalence of Persons in Study Population with Protective and Adverse HDL Cholesterol Levels

| Age group (years) | % with protective HDL cholesterol levels >45 mg/dl | % with adverse HDL cholesterol levels <35 mg/dl | % with protective HDL cholesterol levels >55 mg/dl | % with adverse HDL cholesterol levels <35 mg/dl |
|-------------------|-----------------------------------------------|-----------------------------------------------|-----------------------------------------------|-----------------------------------------------|
|                   |                                              |                                              |                                              |                                              |
| 15-24             | 81.9                                          | 3.2                                          | 65.0                                          | 0                                             |
| 25-34             | 74.0                                          | 4.2                                          | 59.6                                          | 5.3                                           |
| 35-44             | 64.0                                          | 9.7                                          | 58.0                                          | 3.6                                           |
| 45-54             | 73.7                                          | 7.4                                          | 56.4                                          | 5.3                                           |
| 55-64             | 87.8                                          | 6.7                                          | 56.8                                          | 1.1                                           |
| 15-64 crude rate  | 72.3                                          | 6.1                                          | 59.1                                          | 3.0                                           |
| SA coloured rate* | 75.0                                          | 8.3                                          | 60.9                                          | 3.7                                           |

HDL = high density lipoprotein cholesterol; RSA = Republic of South Africa.
*Age-adjusted rates against the coloured population of the RSA, 1980 census.

Table 3. Proportion of Population with CHD-associated Medical History Stratified by Median of HDL to Total Cholesterol Ratio (%HDL/TC)

| Medical History | Subjects | % of group > median | %HDL/TC | % of group < median | %HDL/TC | Odds ratio | 95% confidence interval |
|-----------------|----------|---------------------|---------|---------------------|---------|------------|------------------------|
| % with family history of CHD | All       | 26.5                | 30.0    | 1.2                 | 0.9-1.6 |            |                        |
|                  | Men       | 23.0                | 31.0    | 1.5                 | 1.0-2.3 |            |                        |
|                  | Women     | 30.0                | 29.1    | 1.0                 | 0.7-1.4 |            |                        |
| % with history of CHD by questionnaire | All       | 13.0                | 19.6    | 1.6                 | 1.2-2.3 |            |                        |
|                  | Men       | 11.3                | 19.7    | 1.9                 | 1.2-3.2 |            |                        |
|                  | Women     | 14.6                | 19.5    | 1.4                 | 0.9-2.3 |            |                        |
| % with self-reported history of CHD | All       | 3.5                 | 7.1     | 2.1                 | 1.2-3.8 |            |                        |
|                  | Men       | 2.9                 | 9.6     | 3.5                 | 1.5-8.4 |            |                        |
|                  | Women     | 4.1                 | 4.8     | 1.2                 | 0.5-2.8 |            |                        |
| % with hypertension history | All       | 17.1                | 23.3    | 1.5                 | 1.1-2.0 |            |                        |
|                  | Men       | 10.9                | 15.1    | 1.5                 | 0.8-2.5 |            |                        |
|                  | Women     | 23.1                | 31.1    | 1.5                 | 1.0-2.2 |            |                        |
| % with diabetes history | All       | 2.9                 | 6.1     | 2.2                 | 1.2-4.2 |            |                        |
|                  | Men       | 2.9                 | 5.4     | 1.9                 | 0.7-4.9 |            |                        |
|                  | Women     | 2.8                 | 6.8     | 2.5                 | 1.0-6.1 |            |                        |

HDL = high density lipoprotein cholesterol. CHD = coronary heart disease.
*N = 239 men and 249 women. YN = 239 men and 251 women. 1London School of Hygiene questionnaire.

Table 2 shows that fewer women (60.9%) than men (75.0%) were found to have "protective" HDL cholesterol levels above 45 mg/dl in men and 55 mg/dl in women. The youngest age group (15 to 24 years old) had a higher prevalence of protective HDL cholesterol levels than did any of the other age groups.

Using the cut-off points selected by the Expert Panel of the National Cholesterol Education Program, for HDL cholesterol levels, indicating increased CHD risk when HDL cholesterol are below 35 mg/dl, only 6.3% of men and 3.7% of women in the study population had adversely low levels.
Table 4. Variables That Contributed Significantly to Regression of HDL Cholesterol in Men

| Variable                      | Coefficient | Standard error of the mean | Standardized coefficient* | Partial correlation | Probability | Adjusted \( R^2 \)† |
|-------------------------------|-------------|----------------------------|----------------------------|---------------------|-------------|-------------------|
| Triglyceride                  | -0.0533     | 0.00944                    | -0.2747                    | -0.2936             | <0.0001     | 0.1043            |
| Dietary carbohydrate/day (g)  | -0.0521     | 0.01081                    | -0.3879                    | -0.2272             | <0.0001     | 0.1287            |
| Alcohol used/week (g)         | 0.01445     | 0.00302                    | 0.2122                     | 0.2555              | <0.0001     | 0.1910            |
| Total energy intake/day       | 0.00594     | 0.00139                    | 0.3399                     | 0.2019              | <0.0001     | 0.2141            |
| BMI                           | -0.8207     | 0.2034                     | -0.2032                    | -0.1918             | <0.0001     | 0.2290            |
| Diastolic blood pressure      | 0.2115      | 0.0547                     | 0.1756                     | 0.1838              | <0.0001     | 0.2632            |
| Number of cigarettes smoked   | -0.2392     | 0.0675                     | -0.1524                    | -0.1690             | 0.0004      | 0.2819            |
| Age                           | 0.1418      | 0.0522                     | 0.1317                     | 0.1302              | 0.0006      | 0.2887            |
| LDL cholesterol               | -0.0434     | 0.0175                     | -0.1113                    | -0.1186             | 0.0140      | 0.2970            |

HDL=high density lipoprotein, BMI=body mass index, LDL=low density lipoprotein.
*Coefficient of standardized variables. †Proportion of variation in dependent variable accounted for by the predictor variables adjusted for degrees of freedom.

Table 5. Variables That Contributed Significantly to Regression of HDL Cholesterol in Women

| Variable                      | Coefficient | Standard error of the mean | Standardized coefficient* | Partial correlation | Probability | Adjusted \( R^2 \)† |
|-------------------------------|-------------|----------------------------|----------------------------|---------------------|-------------|-------------------|
| Triglyceride                  | -0.0664     | 0.00871                    | -0.3625                    | -0.3341             | <0.0001     | 0.1591            |
| Number of cigarettes smoked   | -0.3723     | 0.0696                     | -0.2202                    | -0.2407             | <0.0001     | 0.1948            |
| Age                           | 0.2318      | 0.0497                     | 0.2305                     | 0.2117              | <0.0001     | 0.2064            |
| BMI                           | -0.3985     | 0.0967                     | -0.1618                    | -0.1605             | 0.0005      | 0.2256            |
| % energy from saturated fat   | 0.4429      | 0.1552                     | 0.1998                     | 0.1250              | 0.0070      | 0.2333            |
| Alcohol used/week (g)         | 0.01793     | 0.00748                    | 0.0978                     | 0.1111              | 0.0186      | 0.2416            |
| LDL cholesterol               | -0.03271    | 0.01588                    | -0.0950                    | -0.0953             | 0.0400      | 0.2468            |

Abbreviations are the same as in Table 4.
*Coefficient of standardized variables.
†Proportion of variation in dependent variable accounted for by the predictor variables adjusted for degrees of freedom.

The odds ratios (OR) of CHD-associated medical history of persons above and below the age- and sex-specific median %HDL/TC are shown in Table 3. The male participants with low %HDL/TC had 1.9 times the risk (confidence intervals [CI] 1.2 to 3.2) of reporting CHD (a positive response to the London School of Hygiene questionnaire for chest pain) of those with high %HDL/TC, and 3.5 times the risk (CI 1.5 to 8.4) of reporting CHD on direct questioning of those with high %HDL/TC. Women failed to show this association. The group with %HDL/TC below the median as a whole had 1.5 times the risk (CI 1.1 to 2.0) of reporting hypertension and 2.2 times the risk (CI 1.2 to 4.2) of reporting diabetes, compared to the group with %HDL/TC above the median.

The variables that were found to be significantly associated with HDL cholesterol in either men or women in the univariate analysis were: daily cigarette consumption (inverse), systolic and diastolic BP, uric acid, triglyceride levels (inverse), low density lipoprotein (LDL) cholesterol (inverse), BMI (inverse), physical activity at work, grams of alcohol used, and the following three variables identified from the 24-hour dietary recall: total energy intake per day, percentage energy intake from carbohydrates (inverse), and percentage energy intake from saturated fat. In a stepwise multiple regression analysis, the significantly associated variables "explained" 29.7% and 24.7%, respectively, of the variation in HDL cholesterol in men (Table 4) and women (Table 5). In men, serum triglyceride, daily dietary carbohydrate intake, grams of alcohol used weekly, total energy intake per day, BMI, diastolic BP, number of cigarettes smoked daily, age, and LDL cholesterol levels contributed independently (in this order of selection) to the variation of HDL cholesterol. In women, there were twelve outlying observations characterized by high HDL cholesterol levels. These were deleted from the subsequent analysis. In women, the variables, in order of their independent contribution to HDL cholesterol were: triglyceride levels, number of cigarettes smoked daily, age, BMI, percentage energy from saturated fat, grams of alcohol used weekly, and LDL cholesterol levels.

The group of participants with age- and sex-specific %HDL/TC above the median for low CHD risk had socioeconomic parameters indicating lower standing than those below the median. The mean number of occupants per habitable room of those with %HDL/TC above the median was 1.94, while those below the median had a mean occupancy rate of 1.86 (p<0.0001 Mann-Whitney U-test). The mean CASS Occupational Category as defined by Schenmer et al. for those participants who were employed and had %HDL/TC above the median was 3.32 compared to that of 3.06 (p=0.025 Mann-Whitney U-test) for those below the median. (The CASS Occupational Categories range from 1 to 5 and are comparable to Social Class 1 to 5 categories used elsewhere.) The level of education of the two groups of men was not significantly different, while the women with %HDL/TC above the median had significantly higher levels of education than those below.
Discussion

In this study, women older than 44 years had HDL cholesterol levels similar to those of men, thus differing from other studies\(^3\) in which women had higher HDL cholesterol levels than men at all ages. In the coloured population, this could be explained by the high prevalence (72%) of overweight or obese women (BMI > 24).\(^8\)

The mean HDL cholesterol level and standard deviation of the coloured men in this study (55.3 ± 16.3 mg/dl) was found to be significantly higher (\(t\) test \(p < 0.0005\)) than that of white men (47.6 ± 12.0 mg/dl) studied in the southwestern Cape. This study was a total population study in which 82% of the target population ages 15 to 64 years participated.\(^3\) The HDL cholesterol was determined at the RIND laboratory by the same method and standardization procedures. Higher levels of physical activity and a lower mean BMI in coloureds may have contributed. No significant difference was found when comparing the HDL cholesterol levels of coloured and white women (60.8 ± 15.9 mg/dl vs. 59.3 ± 14.5 mg/dl). Coloured women smoked many more cigarettes than white women and obesity was also more common in coloured women than in white women.\(^8\) The benefit of higher HDL cholesterol levels seems to have been obliterated by these HDL cholesterol-reducing factors.

When the HDL cholesterol levels of the coloured population are compared with those reported for the South African black population, the levels of urban coloureds tend to be lower than those of rural blacks. Walker et al.\(^3\) studied the HDL cholesterol levels of Tswana consuming a traditional diet. The sample size was 50 men and 50 women ages 16 to 18 years, and 98 men and 184 women ages 60 to 69 years. Enzymatic kits similar to the RIND laboratory kits were used, although the precipitation of apo B containing lipoprotein was done with heparin and MgCl.\(_2\). Sampling procedures were not described. Mean HDL cholesterol levels and SD for young and older men and young and older women were 56.1 ± 11.2 mg/dl and 70.0 ± 13.9 mg/dl, and 65.8 ± 12.0 mg/dl and 80.1 ± 13.2 mg/dl, respectively. Their %HDL/TC levels, in the same order, were 42% and 45%, and 48% and 49%, indicating a low TC, reflective of their traditional diet, which is a strict cholesterol-lowering diet. Vorst et al.\(^8\) found that a group of 50 black farmworkers had a mean and SD of 60 ± 15.2 mg/dl for HDL cholesterol and 35.2 ± 12.1% for %HDL/TC. Laboratory determinations were similar to the results of the present study. Sampling procedures were not reported, but a detailed dietary analysis showed that these rural blacks also consumed a cholesterol-lowering, prudent diet.

Although limited, these two studies are of interest because they illustrate that rural blacks on a traditional low-fat, high-carbohydrate diet have higher HDL cholesterol levels than the urban coloured population who consume a typical Western diet. On the other hand, a group of 218 black manual laborers in a single large industry in Cape Town (ages 16 to 64 years) seemed to have HDL cholesterol levels comparable to those of the coloured population (P.L. Jooste, unpublished data). HDL cholesterol determinations were done at RIND laboratories with identical procedures. This urbanized group represented approximately half of the inhabitants of the company hostel, and their diet was intermediate between that of the traditional blacks and the coloureds. Their mean HDL cholesterol, %HDL/TC, and standard deviations were 55.0 ± 17 mg/dl and 34.0 ± 10.1%, respectively.

The HDL cholesterol levels reported in white and Japanese men from Framingham, Albany, Honolulu, San Francisco, Evans County, and Puerto Rico\(^7\) are similar to those of South African white men studied in the Cons study\(^4\) and, thus, lower than those of the coloured men participating in this study. The South African coloured men, in turn, had lower HDL cholesterol levels than the black men who participated in the Evans County study. The HDL cholesterol levels of the coloured women in this study were similar to those reported for the white participants, but lower than those for the black participants in the Evans County study.\(^7\) However, the methodology used by Castelli et al.\(^7\) for HDL cholesterol determinations were not identical in all their centers and not the same as in the South African studies. These international comparisons should, therefore, be interpreted with some caution.

It would seem that the lack of protection against CHD due to low levels of %HDL/TC is experienced more by men than by women (Table 3). This could be partly explained by lower median cut-off points for men. However, in Table 1 the difference in %HDL/TC between men and women was found only in the younger age groups, while the reporting of CHD was found mainly in the older age groups where the difference in %HDL/TC between men and women had disappeared.

The search for factors that determine the level of HDL cholesterol in individuals and populations has not been completed, as only a small proportion of the variation found in HDL cholesterol levels in populations have been explained by factors studied to date.\(^6\)\(^8\)\(^1\) In an effort to identify any factors in the present data set that may contribute to the level of HDL cholesterol, particularly if such a contributing factor was amenable to change, univariate analyses followed by stepwise multiple regression analysis was done.

The variables that contributed to the variation of HDL cholesterol in the coloured population were those previously described in the literature.\(^1\)\(^4\)\(^5\)\(^6\)\(^7\)\(^8\)\(^9\)\(^10\)\(^11\) with the following exceptions: the very low positive association of HDL cholesterol and diastolic BP in men and the inverse relationship with LDL cholesterol in men and women. The underlying mechanisms involved in most of these associations have not been fully elucidated, but metabolic and clinical studies have suggested some possible explanations.

Piitinen et al.\(^4\) Katan,\(^4\) and others have reported that high-fat diets resulted in high HDL cholesterol levels, irrespective of the fatty acid composition of the diets. In addition, high carbohydrate intake resulted in reduced HDL cholesterol and raised serum triglyceride levels.\(^4\)

This inverse relationship of HDL cholesterol and serum triglyceride levels could possibly be mediated via a raised activity of lipoprotein lipase and/or hepatic lipase.\(^6\)\(^7\) It
has also been suggested that weight loss could lead to an increased adipose tissue lipoprotein lipase activity, which could in turn explain the raised HDL cholesterol and reduced triglyceride levels found in persons who lose weight. Induction of liver microsomal enzymes by agents such as ethanol, phenytoin, and phenobarbital have all been shown to increase HDL cholesterol levels and could be the biological basis of the correlation found between alcohol intake and HDL cholesterol levels in this study. The inverse relationship found between HDL and LDL cholesterol levels could possibly be due to an indirect up-regulation of LDL receptors in a response to a more effective reverse cholesterol transport in participants with higher HDL cholesterol levels. The explanation of the apparently contradictory finding of a direct correlation of HDL cholesterol with increasing calories, but a negative association with BMI, may lie in the increased physical activity of those with high HDL cholesterol levels. In this study, we could not demonstrate an independent contribution of physical activity to HDL variation. Although in men energy expenditure at work was significantly associated in the univariate analysis, the method of measuring physical activity was relatively crude. It is possible that energy intake is a more accurate reflection of physical activity. An inverse relationship between energy and BMI has been described by others and a high "energy throughput" state has been suggested as protective against CHD.

In a review by Knuiman et al. on the dietary factors related to HDL cholesterol, inter- and intrapopulation studies again highlighted the association with BMI, carbohydrate intake, and the proportion of energy from total fat. It has been found quite consistently that replacement of fat by carbohydrate lowers HDL cholesterol. The diet of the coloured population of the Cape Peninsula, determined by the 24-hour dietary recall method, reflected a typical Western type diet with high animal protein and high fat intake. Fat contributed 37% to total energy intake. The polyunsaturated to saturated fatty acid ratio of the diet was relatively high at 0.8.

The value of the 24-hour dietary recall lies mainly in the assessment of the average intake of a group of people, consisting of at least 50 persons. Due to its speed and relative simplicity, this method is frequently used for dietary intake determinations in large population-based studies. Due to large intraindividual variation, the use of results from the 24-hour recall method for studies of intraindividual correlations with other variables is limited and may fail to identify dietary factors related to, for example, HDL cholesterol levels unless a strong association is present. Therefore, weak dietary associations with HDL cholesterol levels may have been missed in this study, but those factors that have been identified in the multiple linear regression of HDL cholesterol could be considered not only statistically but also biologically significant. In this study, significant independent associations with total energy intake in men and percentage energy from saturated fat in women were found even when physical activity was included in the analysis.

The measures of socioeconomic status did not show a uniform association with %HDL/TC, but overall it would appear that lower socioeconomic status is associated with a more favorable %HDL/TC.

Recently a number of studies have appeared that suggest that a large part of the individual variation of HDL cholesterol could be ascribed to genetic factors. Whether genetics could determine population HDL cholesterol levels is not clear, but it is of interest that the coloured levels are midway between those of American and South African blacks and whites.

The reasons for the relatively high HDL cholesterol in this population are unknown. Genetic or environmental factors not examined in this report will have to be looked for to explain the high HDL cholesterol levels in this population.

Nationally, the CHD mortality of coloured people is lower than that of whites in South Africa, while in Cape Town it approaches that of the whites (D. Bourne, unpublished observations). This is despite the higher level of risk the Cape Town coloured population carries due to the high prevalence of smoking, hypertension, and hypercholesterolemia compared to the rural South African whites of the Coris study. One possible explanation is that it could be due to the protection that coloureds receive from their relatively high HDL cholesterol levels.

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References

1. Heise G, Johnson NJ, Retalland S, Davis CE, Tyrler HA. The epidemiology of plasma high-density lipoprotein cholesterol levels. The Lipid Research Clinic's Program Prevalence Study Summary. Circulation 1960; 62(suppl V):116–136
2. Miller NE, Thistle DF, Forda OH, Mjos OD. The Tromso Heart Study, high density lipoprotein and coronary heart disease. A prospective case-control study. Lancet 1977; 1:965–968
3. Gordon T, Castelli WP, Hjortland MC, Kannel WB, Dawber TR. High density lipoprotein as a protective factor against coronary heart disease. Am J Med 1977; 62:707–714
4. Goldbourt U, Medalie JH. High density lipoprotein cholesterol and incidence of coronary heart disease. The Israeli Ischaemic Heart Disease Study. Am J Epidemiol 1979; 109:296–303
5. Poockin SJ, Shaper AG, Phillips AN, Walker M, Whitehead TP. High density lipoprotein cholesterol is not a major risk factor for ischaemic heart disease in British men. Br Med J 1988; 292:515–519
6. Editorial. HDL and ischaemic heart disease in Britain. Lancet 1986; 1:481–482
7. Miller NE, Hammel F, Setlész S, et al. Relation of angiographically defined coronary artery disease to plasma lipoprotein fractions and apolipoproteins. Br Med J 1981; 282:1741–1744
8. Kanamori K, Nishijima H, Kojima S, et al. Relationship between lipids and angiographically defined coronary artery...
disease in Japanese patients. Am Heart J 1984;108: 1209-1212

9. Skeaff CA, Buckley BH, Achuff SC, Kwiterovich PO, Gordon L. The association of low levels of HDL cholesterol and arteriographically defined coronary artery disease. Am J Epidemiol 1979;109:285-295

10. Brook JG, Avram IM, Vlietinck A, Slihansky E, Markiwicz W. High-density lipoprotein subfractions in nonapoliprotein patients with coronary atherosclerosis. Circulation 1982; 66:925-928

11. Nye ER, Robertson NC, Sutherland WHF. Clinical features of ischemic heart disease correlated with high density lipoprotein cholesterol levels in men with hyperbeta lipoproteinemia. N Z Med J 1984;97:437-438

12. Kannel WB, Castelli WP, Gordon T. Cholesterol in the prediction of atherosclerotic disease: New perspectives based on the Framingham Study. Ann Intern Med 1979; 90:85-91

13. Gordon T, Kannel WB. Multiple risk function for predicting coronary heart disease. The concept, accuracy and application. Am Heart J 1982;103:1031-1039

14. Castelli WP, Abbott RD, McMurry SP. Summary estimates of cholesterol used to predict coronary heart disease. Circulation 1983;67:730-734

15. Knutman JT, Hermus RJJ, Hautvast JGAJ. Serum total and high density lipoprotein cholesterol concentrations in rural and urban boys from 16 countries. Atherosclerosis 1980;36:53-539

16. Chiba K, Kobzumi A, Kumel M, Watanabe T, Ikeda M. Nationwide survey of high-density lipoprotein cholesterol among farmers in Japan. Prev Med 1983;13:508-522

17. Gruenek C, Gartelke P, Lietzenzwek P, Khoury P, Tynker H. High-density lipoprotein cholesterol in blacks and whites: Potential ramifications for coronary heart disease. Am Heart J 1984;108:815-826

18. Steyn K, Jooost P, Langenhoven ML, et al. Coronary risk factors in the coloured population of the Cape Peninsula. S Afr Med J 1984;69:165-169

19. Steyn K, Jooost P, Fourie JM, Pary CDH, Rossouw JE. Hypertension in the coloured population of the Cape Peninsula. S Afr Med J 1984;69:165-169

20. Steyn K, Jooost P, Langenhoven ML, et al. Smoking patterns in the coloured population of the Cape Peninsula. CRISIS Study. S Afr Med J 1987;71:145-148

21. Steyn K, Benadé AJS, Langenhoven ML, Joubert G, Rossouw JE. Hypercholesterolaemia in the coloured population of the Cape Peninsula. CRISIS Study. S Afr Med J 1987;71:483-486

22. Rose GA. The diagnosis of ischemic heart pain and intermittent claudication in field surveys. Bull WHO 1967; 27:645-656

23. Schihammer L, Storpfort A. A guide to the coding of occupations in South Africa. Centre for Applied Social Sciences, University of Natal. Fact paper 4, 1979

24. Passmore R, Durbin JGVA. Human energy expenditure. Physiol Rev 1953;33:801-840

25. Fox SM, Naughton JP, Gorman PA. Physical activity and cardiovascular health. III. The exercise prescription, frequency and type of activity. Mod Concepts Cardiovasc Dis 1972;41:8-16

26. Durbin JGVA. Energy consumption and its measurements in physical activity. Am Clin Rex 1982;14 (suppl 34):6-11

27. Finley PR, Schmitz RB, Williams RJ, Lucht DA. Cholesterol in high-density lipoprotein: Use of Mg2+/dextran sulfate in its enzymic measurement. Clin Chem 1976;24:931-933

28. American Heart Association. Recommendations for human blood pressure determination by sphygmomanometers. Dallas: American Heart Association, 1967

29. Armitage P, Rose GA. The variability of measurements of casual blood pressure. Clin Sci 1966;30:325-335

30. Gouws E, Langenhoven ML, NHIRD food composition tables 1981. Cape Town: South African Medical Research Council, 1982

31. Castelli WP. Cardiovascular disease and multifactorial risk: challenge of the 1980s. Am Heart J 1983;106:1191-1200

32. The Expert Panel. Report of the National Cholesterol Education Program Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol In Adults. Arch Intern Med 1988;148:36-89

33. Gomo ZAR. The effect of age, sex, alcohol consumption and cigarette smoking on serum concentrations of lipids and apolipoproteins in Zimbabwean blacks. Atherosclerosis 1986; 81:149-154

34. Rossouw JE, Du Plessis JP, Benadé AJS, et al. Coronary risk factor screening in three rural communities: the CORIS baseline study. S Afr Med J 1983;64:430-436

35. Walker ARP, Walker BF. High-density lipoprotein cholesterol in African children and adults in a population free of coronary heart disease. Br Med J 1978;2:1336-1338

36. Vorster HH, Silvis N, Venter CS, et al. Serum cholesterol, lipoproteins, and plasma coagulation factors in South African blacks on a high-fat low intake. Am J Clin Nutr 1987; 46:52-57

37. Castelli WP, Cooper GR, Doyle JT, et al. Distribution of triglyceride and total LDL and HDL cholesterol in several populations: A cooperative lipoprotein phenotyping study. J Chronic Dis 1977;30:147-169

38. Hultey S, Ahamm P, Kuller L, Lassèr N, Sherwin R. HDL cholestrol levels in the multipr risk factor intervention trial (MRFIT) by the MRFIT Research Group. Lipids 1979; 14:119-125

39. Criqui MH, Wallace RB, Heise G, Miskiel MA, Schonfeld G, Jones G. Cigarette smoking and plasma high density lipoprotein cholesterol. The Lipid Research Clinics Program Prevalence Study. Circulation 1980;62(suppl IV);7-70-76

40. Haffner SM, Applebaum-Rowden D, Wahl PW, et al. Epidemiological correlates of high density lipoprotein subfractions, apolipoprotein A-I, A-11, and D, and lecithin cholesterol acyltransferase effect of smoking, alcohol and obesity. Atherosclerosis 1985;51-169-177

41. Rikkind BM. Nutrient-high density lipoprotein relationship: An overview. Prog Biochem Pharmacol 1983;19:89-109

42. Goldbourt U, Yaari S, Cohen-Mandelzweig L, Neufeld RN. High-density lipoprotein cholesterol: correlation with biochemical, anthropometric, behavioral, and clinical parameters in 6,650 Israeli men. Prev Med 1988;15:559-561

43. Pietinen P, Huttunen JK. Dietary determinants of plasma high-density lipoprotein cholesterol. Am Heart J 1987; 113:620-626

44. Katan MD. Diet and LDL. In: Miller GJ, Miller NE, eds. Metabolic aspects of cardiovascular disease. Vol 3. Clinical and metabolic aspects of high-density lipoproteins. Oxford: Elsevier; 1984;103-132

45. Menasnik RP, Katan MB. Effect of monounsaturated fatty acids versus complex carbohydrates on high-density lipoproteins in healthy man and women. Lancet 1987;1:122-125

46. Nikkila EA, Taikkinen M, Keldii M. Relation of plasma high-density lipoprotein cholesterol to lipoprotein-lipase activity in adipose tissue and skeletal muscle of man. Atherosclerosis 1983;48:497-501

47. Breier CH, Drezel H, Lisch H. Essential role of post-heparin lipoprotein lipase activity and of plasma testosterone in coronary artery disease. Lancet 1985;1:1242-1244

48. Schwartz RS, Brunzel JD. Increase of adipose tissue lipoprotein lipase activity with weight loss. J Clin Invest 1981; 67:1425-1430

49. Luoma PV, Sotaniemi EA, Petkonen RO. Inverse relationship of serum LDL cholesterol and the LDL/HDL cholesterol ratio to liver microsomal enzyme induction in man. Res Commun Chem Pathol Pharmacol 1983;42:173-176

50. Alexander JK. Obesity and coronary heart disease. In: Conner WE, Bristow JD, eds. Coronary heart disease. Philadelphia: JB Lippincott, 1985;111-121

51. Langenhoven ML, Steyn K, Steyn M, Van Eck M. Nutrient intake in the coloured population of the Cape Peninsula. The CRISIS Study. Ecology of Food Nut 1988;22:97
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52. Block O. A review of validations of dietary assessment methods. Am J Epidemiol 1982;115:492-505
53. Sistonen P, Ehnholm C. On the heritability of serum high density lipoprotein in twins. Am J Hum Genet 1980;32:1-7
54. Whittle JD, Martin NG. Plasma lipids in twins: Environmental and genetic influences. Atherosclerosis 1983;48:265-277
55. Hayakawa K, Shimitzu T, Ohbe Y, Tomioka S. Lifestyle factors affecting intrapair differences of serum apoproteins and cholesterol concentrations in adult twins. Atherosclerosis 1987;66:1-9
56. Bucher KD, Kaplan EB, Namboodiri KK, Glueck CJ, Laskarzewski P, Rifkind BM. Segregation analysis of low levels of high-density lipoprotein cholesterol in the collaborative Lipid Research Clinics Program Family Study. Am J Hum Genet 1987;40:489-502
57. Austin MA, King M-C, Bewol RD, Hulley SB, Friedman GD. Risk factors for coronary heart disease in adult female twins. Am J Epidemiol 1987;125:308-318
58. Wyndham CH. The loss from premature deaths of economically active manpower in the various populations of the RSA. S Afr Med J 1981;60:411-419

Index Terms: lipoprotein • HDL cholesterol • Cape Peninsula • South Africa • risk • coronary heart disease