ORIGINAL CONTRIBUTION

New Guidelines from the National Cholesterol Education Program: What is the Impact on Risk Assessment?

J. Alexander Lowden, MD, PhD

The National Cholesterol Education Program has developed a set of guidelines for optimal levels of serum lipids that are recommended to reduce the risk of coronary artery disease. This article compares those values to lipid levels found in insurance applicants.

Address: LabOne Canada, 25 Valleywood Dr., Unit 7, Markham, ON L3R 5L9, Canada.

Correspondent: J. Alexander Lowden.

Key words: Cholesterol, high density lipoprotein, low density lipoprotein, triglycerides.

The National Cholesterol Education Program (NCEP) regularly convenes a panel of experts from cardiology, internal medicine and clinical chemistry to review guidelines for the optimal maintenance of serum lipid levels. Recently, they released their third report. The recommendations in the report outline ideal lipid levels and provide methods to achieve these levels in individuals who fall outside the limits.

The report can be viewed in full on the Internet (*http://wwwnhlbi.nih.gov/index.htm*) or in a summary was published in the *Journal of the American Medical Association* (*JAMA*).[1] It follows the pattern of the earlier report,[2] but this report takes new directions. Known as the Adult Treatment Panel III (ATP III), it examines cardiovascular risks associated with variations in serum lipid levels. It also considers elevations of cholesterol and decreases of high density lipoprotein cholesterol (HDL), and it changes definitions of risk levels for these analytes and adds risk factors associated with hypertriglyceridemia. The new report describes risk associated with the metabolic syndrome and notes that type 2 diabetics should be considered in the same risk category as individuals with known coronary heart disease.

The report, which is 200 pages in length, has been summarized in a 2001 issue of *JAMA*.[1] The summary is recommended reading for all insurance medical directors. It provides a conservative approach to risk assessment based on lipid measurements, build, blood pressure and history that is perhaps too conservative for the average insurance applicant. It does outline an excellent set of criteria for preferred risk underwriting, and more importantly, it offers preventive strategies that should improve outcomes, recommending, for example, that the use of statins should be increased three-fold in the United States to adequately manage mild dyslipidemia. The report develops a paradigm not unlike that for hypertension—treat the abnor-

mal finding before the symptoms and avert the risk.

I have reviewed the recommendations and, when possible, compared them to specific analyte measurements made on serum samples from over 175,000 consecutive insurance applicants recently analyzed at LabOne. It is clear that although the average American applicant does not meet the NCEP guidelines, we know that some individuals can still be insured at a profit. Nevertheless, the guidelines do emphasize some changes that may well alter underwriting practices when considering lipid analyses.

LDL SHOULD BE < 100MG/DL

Insurers tend to look first at cholesterol levels when considering lipids and cardiac risk. The basis of the NCEP guidelines in earlier iterations[2] has been the assessment of low density lipoprotein cholesterol (LDL). This practice persists in the current version. Unfortunately, in most laboratories LDL is not assayed directly but is a calculated value based on the formula:[3]

LDL = Total cholesterol

− (HDL + triglycerides/5)

The calculation is quite accurate when triglycerides are less than 200 mg/dL but gradually loses validity as the triglycerides approach 400 mg/dL and is rarely calculated above that value. LDL can be assayed directly in the presence of elevated triglycerides, but in practice, the added cost is difficult to justify in most cases when the triglycerides are normal or only mildly elevated.

Calculated LDLs at LabOne average 122 (± 35) mg/dL with slightly higher values in males (127 mg/dL) than in females (115 mg/dL). Of the applicants we have analyzed, 30% do not meet the NCEP guideline for LDL.

TOTAL CHOLESTEROL

Total cholesterol should be maintained at less than 200 mg/dL according to the report. This figure is frequently used in preferred
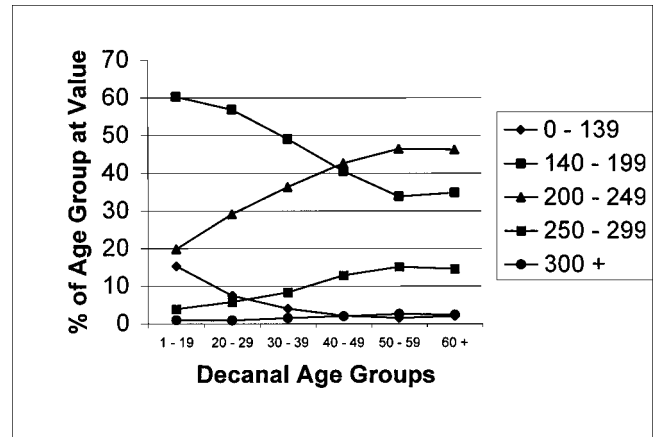

Figure 1. *Effect of age on serum cholesterol. The graph shows the percentage of all applicants in each age group with serum cholesterols in the defined ranges obtained from a sample of 175,000 consecutive specimens. Approximately 80% of all cholesterol values fall below 250 mg/dL but with age, a descreasing proportion of the applicants had cholesterol levels that satisfied the NCEP guidelines.*

underwriting guides and has been adopted by LabOne in our revised reference ranges. Serum cholesterol in many applicants is much higher than 200 mg/dL (Figure 1). Serum cholesterol tends to rise with age in insurance applicants (and most others) and, in most instances, is directly related to lack of exercise and inappropriate caloric intake. Cholesterol values are clearly related to coronary artery risk,[4] but more than half of all myocardial infarctions occur in people with normal cholesterol levels.[5]

HDL LOWER LIMIT RAISED

Under the new guidelines, the lower limit of HDL has been raised from 35 mg/dL to 40 mg/dL in males and 50 mg/dL in females. At LabOne the mean value for HDL is 53.9 mg/dL (± 13.5). The average male value is just above the new NCEP level at 49.5 mg/dL and the female value is 60.7 mg/dL. Clearly, there are many applicants with HDL levels below the recommended levels. Using the old (35 mg/dL) lower limit for HDL, we compared males and females falling below this level at different age groups and note that in the 30- to 39-year-old group, 7% of males have less than optimal HDL levels (Figure 2).
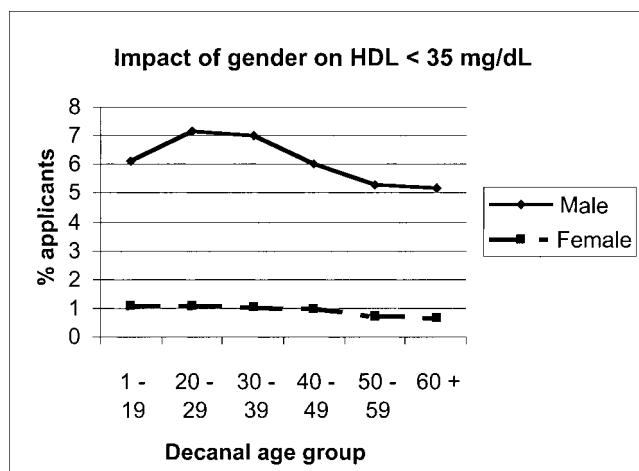
Figure 2. *Effect of age and gender on serum high density lipoproteins. The chart shows the percentage of all applicants at various age groups, in a cohort of 175,000 consecutive samples, who had HDL levels less than 35 mg/dL. Note that the new NCEP guidelines suggest that the lower limit for males should be 40 mg/dL and for females 50 mg/dL.*

TRIGLYCERIDE UPPER LIMIT LEVEL LOWERED TO 150 MG/DL

Triglycerides are often largely ignored in underwriting unless the value is extremely high (> 400 mg/dL). This rather casual approach results from the nature of blood testing of insurance applicants. The NCEP panel recommends testing only fasting individuals, but this situation is rare in an insurance setting. In spite of instructions to agents and parameds, 75% of all samples received at LabOne come from non-fasted subjects. Depending on the nature of the foods eaten, triglycerides usually rise by only about 50–150 mg/dL following a meal. A few people have an exaggerated chylomicronemia after a fatty meal. That situation likely indicates a specific genetic dyslipidemia and should be viewed with caution. Triglycerides over 400 mg/dL are clearly abnormal in any circumstance. There is strong evidence that elevations in triglycerides are associated with increased cardiac risk, independently of abnormalities of cholesterol and HDL.[6]

In spite of the non-fasting state of most of our specimens, over 58% of the samples have triglyceride levels less than 150 mg/dL (Figure 3). In our examination of the changes with age, the serum triglycerides rose slowly
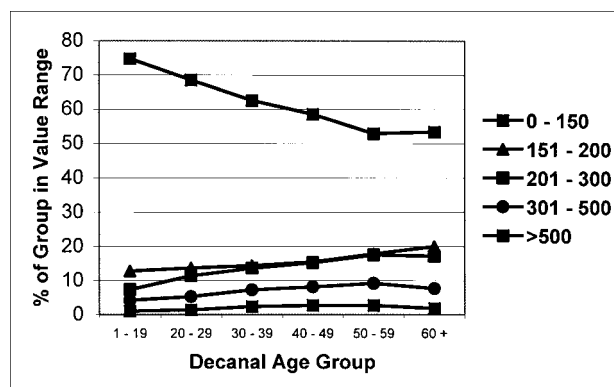
Figure 3. *Effect of age on serum triglycerides. Note that most applicants had triglycerides less than 200 mg/dL, and although there is a gradual fall in the percentage of applicants with triglycerides under the NCEP guideline of 150 mg/dL even in the older ages, more than 50% of applicants achieved that benchmark.*

in the older ages but even in samples from applicants over 50 years of age, more than half had triglyceride levels that were within the NCEP guidelines.

DIABETES

For the first time, the NCEP identified a specific risk from diabetes. The panel developed a model risk assessment program raising diabetics to a risk equivalent to that for persons with diagnosed coronary heart disease. They describe a classification of risk previously unrecognized by the NCEP and now called metabolic syndrome (formerly syndrome X).[7] The panel recommends that those who qualify (Table 1) should undertake intensive therapeutic lifestyle changes.

RISK ASSESSMENT

To assess risk, the panel followed a model developed by the Framingham Heart Study using debit points to develop a 10-year risk evaluation.[1] The model calculates gender-specific scores based on age, cholesterol, HDL, smoking status and systolic BP. It then sums the points and provides a 10-year risk of a coronary event. This useful model was described in detail at an ACLI Medical Section meeting and should be considered by medical underwriters.

Table 1. Diagnostic Features of the Metabolic Syndrome

Abdominal obesity (>102 cm: 40″ in male)
  (>88 cm: 35″ in female)
Dyslipidemia
  elevated triglycerides (>150 mg/dL)
  elevated small LDL particles
  low HDL (<40 mg/dL male; <50 md/dL female)
Elevated blood pressure (>135/85 mm Hg)
Insulin resistance (fasting glucose > 110 mg/dL)
Prothrombotic state
Proinflammatory state (elevated CRP)

These features, which used to be referred to as syndrome X, carry a risk equivalent of coronary heart disease.

Table 2. Risk Factors That Modify LDL Goals

LDL levels
Coronary Heart Disease (CHD)
Smoking
Hypertension (BP >140/90)
Low HDL (<40 mg/dL)
Family history of premature CHD
  in a first degree male relative <55 yrs
  in a first degree female relative <65
Age
  men >45 years
  women >55 years
Diabetes (a CHD risk equivalent)

LDL goals for therapeutic intervention

	LDL: Goal (mg/dL)
CHD and CHD equivalent	<100
Multiple risk factors (2+)	<130
0–1 risk factors	<160

TREATMENT

The ATP III guidelines on lipid levels are tied closely to methods to mitigate the risks associated with failing to reach appropriate levels. They target changes in LDL cholesterol at different LDL levels according to the presence of risk factors (Table 2) and stress the importance of lifestyle changes (diet and exercise), as well as the initiation of lipid-lowering drug therapy.

Dietary recommendations include: less than 7% of total calories as saturated fat, total fat of 25–35% and cholesterol less than 200 mg per day. Total calories should be balanced to achieve ideal weight while maintaining regular exercise that will consume approximately 200 kcal/day. They note that a higher intake of unsaturated fat can help to reduce triglycerides and raise HDL in persons with the metabolic syndrome. Plant stanols and sterols, as well as viscous soluble fiber (20–30g/d), are recommended daily.

Finally, they recommend the use of lipid-lowering drugs, nicotinic acid, bile acid sequestrants and, particularly, statins when LDL levels are greater than 190 mg/dL in risk-free individuals and when greater than 130 mg/dL in those with coronary heart disease or its equivalent (eg, diabetes). They stress that lifestyle changes must be maintained even when statins are being used regularly in order to mitigate coronary risk.

The guidelines provide an interesting view of cardiac risk from the laboratory perspective. Values in a large portion of the samples we test fall outside the levels proposed by ATP III. At LabOne, total cholesterol levels in 50-year-olds applying for life insurance average 214 mg/dL, but the skewed distribution has an upper limit (+2 SD) of 294 mg/dL. While females rarely have low HDLs, in males up to 7% of the analyzed samples fall below the old guideline level of 35 mg/dL (Figure 2). We estimate that 15% of male applicants will be below the new cutoffs. Even triglycerides come under criticism. While 50% of the oldest applicants have triglycerides below the guideline level, there are significant numbers that do not meet that goal (Figure 3).

Importantly, the panel has stressed the need for lifestyle (diet and exercise) changes and the addition of lipid-lowering agents when lipid values are excessive. They point out that these changes will lower risk. For the insurance underwriter, cardiac risk accounts for more mortality than all other classes of disease. Perhaps adoption of the guidelines will lead to early recognition and appropriate

management that can improve outcomes for both the insured and the insurer.

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