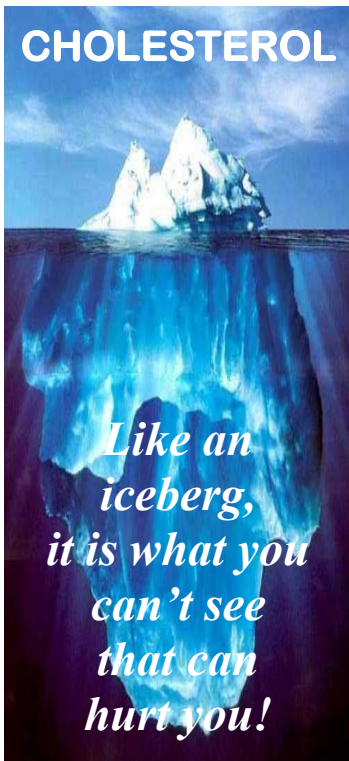




LDL

CHOLESTEROL



LDL Sub-fractions

Coronary Artery Disease (CAD) is a leading cause of morbidity and mortality in the western world. Increased levels of low-density lipoprotein Cholesterol (LDL-C) are associated with the high incidence of CAD, thus the national Cholesterol Education Program Adult Treatment Panel III recommended using LDL-C levels as the main determinant for therapy.

Plasma lipoproteins are spherical particles responsible for the transport of cholesterol, triglycerides and phospholipids. There are 5

major lipoprotein classes: chylomicrons, very low density lipoproteins (VLDL), intermediate density lipoprotein (IDL), low density lipoprotein (LDL), and high density lipoprotein (HDL). Low HDL cholesterol is a strong independent predictor of coronary heart disease (CHD) [1]. Increased LDL cholesterol (LDL-C) has been identified as a major risk factor for CHD [2].

It is known that the lipoprotein classes are heterogeneous, consisting of multiple sub-fractions that vary with respect to particle size, density and

chemical composition.

Research studies have focused their attention on the association of subclasses of LDL and CAD. Heterogeneity within LDL has led to the identification of at least 2 patterns based on particle size. Low density lipoprotein cholesterol circulate as LARGE, buoyant LDL particles known as LDLI (phenotype A), the intermediate LDLII and the SMALL, dense particles known as LDLIII (phenotype B). ❖

Small, Dense LDL

SMALL DENSE LDL (Phenotype B)

The small dense particle (phenotype B) is more commonly associated with increased levels of triglyceride (TG) and fibrinogen and reduced levels of HDL. These smaller particles have less antioxidant capability and are therefore considered to be an atherogenic moiety. While LDL cholesterol is a strong risk factor for CAD, more than 50% of the subjects with CAD have normal LDL

cholesterol levels.

The increased prevalence of CAD among subjects with normal LDL can be explained by LDL particle size. Studies have shown small dense LDL to be more prone to oxidation and conformational changes. This results in the reduction of LDL clearance by its receptors, with increased production of scavengers, which triggers immunological changes resulting in atherosclerosis.

As a patient's LDL sub-fractions become smaller and denser, they are more prone to building arterial plaque blocking coronary blood vessels.

An atherogenic lipoprotein pattern characterized by a predominance of small dense LDL, moderately elevated plasma triglycerides and low HDL levels, is the most powerful risk factor for CAD. ❖

It's NOT just ABOUT having NORMAL Total CHOLESTEROL.. Know your LDL Sub-fractions!



Direct LDL vs. Calculated LDL

The calculated low density lipoprotein cholesterol is determined from measurements of total cholesterol, high-density lipoprotein cholesterol, and triglyceride using the Friedewald equation ($LDL-C = TC - HDL-C - TG/5$), whereas the direct homogeneous LDL-C procedures use various physicochemical combinations of surfactants, polymers, and specific binding molecules to determine LDL-C in situ.

Discrepancies between the results of calculated LDL-C and the results of the direct homogeneous LDL-C assays are primarily caused by elevated TG serum values and, to a lesser extent, by associated insulin resistance, kidney and liver diseases, and genetic dyslipoproteinemic states.

From a clinical perspective, a high LDL-C value (>190 mg/dL) with differing

results is meaningless because the goal is to lower the LDL-C to an optimal level. Likewise, low (<100 mg/dL) but differing LDL-C results are meaningless because the value is in the optimal range, and further intervention is unnecessary.

However, when the LDL-C value is borderline, requiring a decision to treat or not to treat, such a difference would

such be of concern.

The direct homogeneous method is preferred over the current practice of using calculated LDL-C for samples with TG serum levels greater than 400 mg/dL (4.52 mmol/L).

Analysis of problems with the calculated LDL-C values suggests that the direct homogeneous LDL-C method is preferred. ■

THE NATIONAL CHOLESTEROL EDUCATION PROGRAM (NCEP) RECOMMENDS THE DIRECT MEASURED TESTING OF LDL CHOLESTEROL AS THE PRIMARY TARGET FOR CORONARY HEART DISEASE RISK ASSESSMENT AND MONITORING.

Don't
base
Important
treatment
decisions
on
calculation!

Flash!

The National Institute of Health (NIH) identifies LDL cholesterol as the primary target of cholesterol lowering therapy. However, the common method of determining LDL by calculation = based on total cholesterol, HDL cholesterol and triglycerides is reported to be accurate only 70% of the time. Nearly one in three derived LDL values may be wrong.

The major problem with the calculation is triglycerides.

If the triglyceride value is abnormally high = due to a patient not following fasting requirement, for example = the derived LDL number will be artificially low. And when a patient's triglyceride value is above 400 mg/dl, the calculation can't be used at all. Whenever the calculation is used in the presence of elevated triglycerides, your patient could be misclassified and consequently may not receive the appropriate lipid lowering therapy.

NCEP Criteria for Standardization of Cholesterol Assays:

In order to promote the

standardization of cholesterol measurements, the NCEP has issued performance guidelines for the measurement of HDL and LDL cholesterol.

It is important that the laboratory conducting the determinations utilizes a type of assay or kit that meets the NCEP guidelines for precision and accuracy.

The national Cholesterol Education program (NCEP) recommends the direct, measured testing of LDL cholesterol as the primary target for coronary heart-disease risk assessment and monitoring. ■

LDL Cholesterol and Coronary Artery Disease (CAD)

Lipoproteins have long been implicated as important components in the genesis of atherosclerosis. Lipoproteins are heterogenous, consisting of multiple subclasses that vary with respects to particle size, density and chemical composition.

The National Cholesterol Education Program (NCEP) has been addressing the crucial role of lipoproteins in its Adult Treatment Panel (ATP) guidelines. In 2001 the latest iteration of these guidelines (ATPIII) was released. Special emphasis was given to the level of Low Density Lipoprotein (LDL) cholesterol as a decision point for intervention, with or without drug treatment.

It is well known that under certain circumstances, e.g. in Metabolic Syndrome, triglycerides are elevated, HDL is decreased and the LDL particle population is

shifted towards the smaller, denser particles.

This prompted the American Association of Clinical Endocrinologists (AACE) recently to draw attention to the fact that small, dense LDL particles seem to be especially atherogenic and commonly precede Coronary Artery Disease (CAD). Patients may carry these particles despite normal LDL-C levels.

A comprehensive set of guidelines to address the current patterns of under evaluation and under treatment of dyslipidemia, a major risk factor of CAD, was subsequently issued by the AACE.

Recently, intermediate density lipoprotein (IDL) which can be identified with the new LDL Sub-fraction System was also found to be significantly involved in the atherosclerotic process.

Normal levels have been established in the latest NCEP (ATPIII) guidelines:

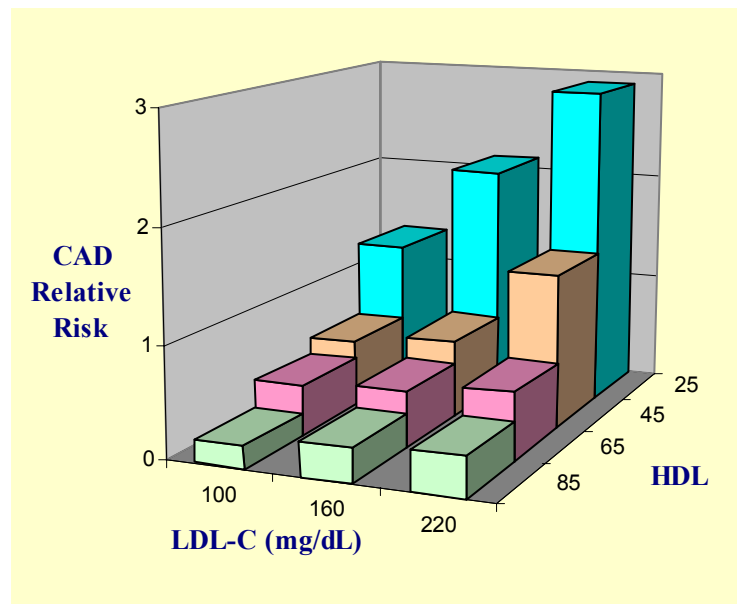
Cholesterol : <200 mg/dl
Triglycerides : <150 mg/dl
LDL-C : <130 mg/dl
HDL-C : >40 mg/dl

Facts:

- The medical cost estimate

for treating cardiovascular disease in the U.S. is over \$150 billion yearly.

- 50% of people that suffer from cardiovascular disease have ATPIII normal cholesterol levels.
- Individuals with SMALL, DENSE LDL are at threefold risk for CAD independent of other risk factors. ■



LDL Sub-fraction System

Lipoprint[®], the FDA cleared method for the determination of cholesterol in the sub-fractions of LDL, is an integrated system consisting of hardware, software and ready-to-use reagents.

The system components have been optimized to provide clinical laboratories with the only do it yourself LDL sub-fraction solution currently available in the market place.

The clinical utility of the system to screening and monitoring of patients is demonstrated in exemplary case studies. Unlike other methods, the new system measures the cholesterol levels in each lipoprotein sub-fraction down to 1 mg/dl which allows for the unequivocal identification of the highly atherogenic small dense LDL and IDL subspecies. This makes the LDL Sub-fractionation sys-

tem a valuable adjunct in the determination of a wide spectrum of conditions, e.g. small dense LDL dyslipidemia associated with metabolic syndrome as well as type-3 dyslipidemia frequently present with large LDL particles and consequently classified as normal when using particle size or classification into pattern A and B only.

ABC Laboratories is now

offering the new LDL lipoprotein sub-fraction testing method which has been validated in a growing number of laboratories, including The Lipids and Lipoprotein Laboratory at the Mayo Medical Laboratories. These laboratory validations have shown this new testing method to correlate well with the traditional methods, while allowing for a faster sample turnaround time at a lower cost. ■

LDL Sub-fraction System... (continued)

The new LDL Sub-fraction System offers an accurate testing platform that is less prone to testing variability, has high throughput and is easy to perform.

ADVANTAGES:

1). LDL Sub-fraction System resolves up to 12 lipoprotein fractions and sub-fractions: VLDL, Mid-bands C, B, A; IDL, Remnant Lipoproteins and Lipoprotein (a) (Lp(a)) LDL sub-fractions

(subclasses): Large (LDL-1, 2) and small dense (LDL-3 to LDL-7) HDL.

2). LDL Sub-fraction System accurately quantifies lipoprotein cholesterol.

3). LDL Sub-fraction System also provides profile classification for comparability with the legacy methods.

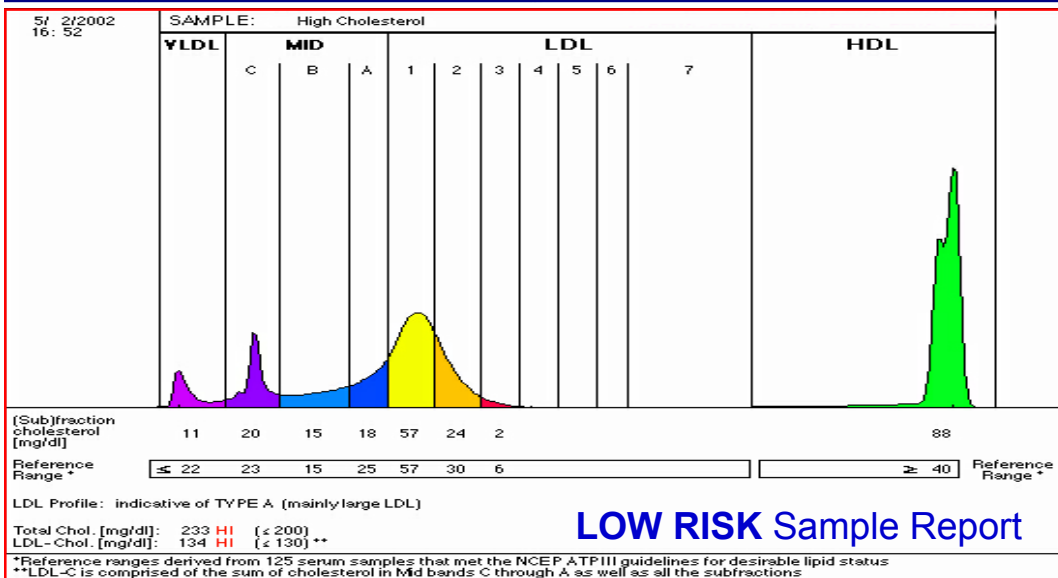
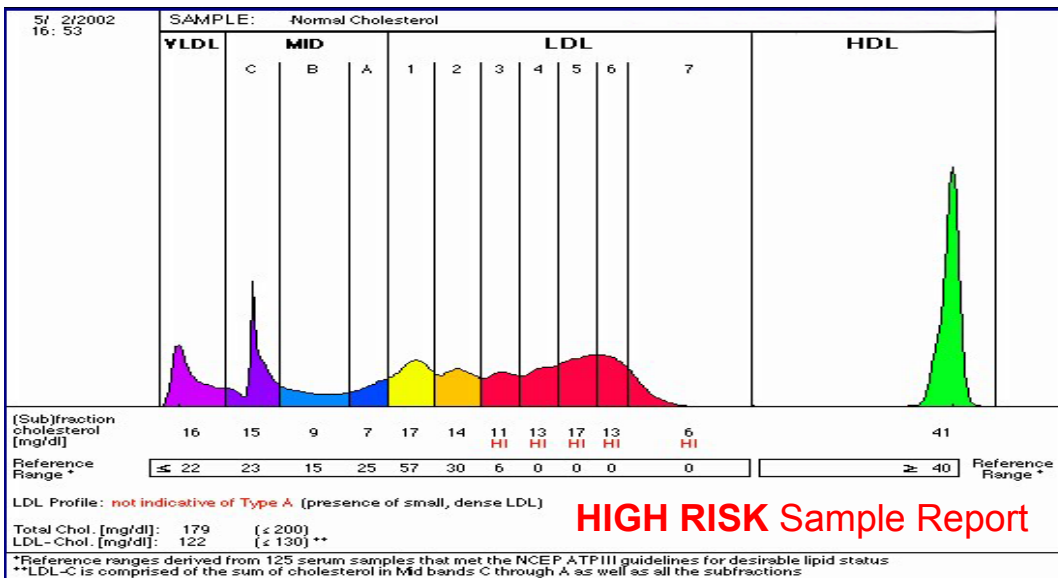
4). LDL Sub-fraction System provides normal reference

ranges for the cholesterol contained in each fraction and sub-fraction. These ranges were established from a normal population conforming to the latest NCEP lipid guidelines (ATPIII).

The System provides an easy to interpret color print-out showing the good HDL fraction in green for "desirable", the large, less atherogenic LDL-1 and 2 in

yellow for "caution" and the highly atherogenic LDL 3 through 7 in red for "high risk" (Figures: Sample Reports).

Doctors, Private practitioners and drug companies planning to offer the tests to their clients to validate new cardiac risk factor therapeutics needing to utilize this more cost-effective sub-fraction testing system, may contact: **ABC LABORATORIES: (323) 222-6688.**



Use Direct LDL or LDL Sub-fractionation to identify those at RISK!

Learn more about the advantages of LDL Sub-fraction testing!

For more information, contact:

Customer Service Department
 American Bio-Clinical Laboratories
 (323) 222-6688

