LDL Particle Concentration
NMR, Plasma

Useful For
Assessment and management of a patient's risk for cardiovascular disease and events

Clinical Information
The key role of apolipoprotein-B (apo B) particles in the pathogenesis of cardiovascular disease is well recognized. A majority (90-95%) of these apoB particles are low-density lipoprotein particles. While low-density lipoprotein cholesterol (LDL-C) remains the primary focus for cardiovascular risk assessment and evaluation of pharmacologic effectiveness based on treatment target goals, evidence indicates that a narrow focus on LDL-C assessment and treatment alone is not the optimal strategy for patient care. What remains controversial is whether we are using the best measure of LDL to identify all individuals at risk and further stratify those who would benefit from additional or more aggressive therapeutic interventions.

There are several known limitations that make LDL-C a less accurate marker of cardiovascular risk than either non-high-density lipoprotein cholesterol (non-HDL-C), low-density lipoprotein particle number (LDL-P), or apolipoprotein-B. Furthermore, there is sufficient evidence that other triglyceride-rich lipoproteins (TRL) are atherogenic including very low-density lipoprotein (VLDL) remnants and intermediate-density lipoproteins (IDL). There continue to be numerous patients who succeed in meeting their target “LDL-C goal” but still develop complications from atherosclerotic vascular disease and suffer from cardiovascular events. These patients bear the burden of having residual risk not identified with traditional metabolic and cardiovascular markers.

Several studies have shown that quantitative measures of LDL particle concentrations, assessed by either nuclear magnetic resonance (NMR) or apolipoprotein B, are associated with cardiovascular disease to a much greater extent than either LDL size or LDL-C. This is due to the 1:1 relationship of apoB to non-HDL particles, meaning there is one apoB per LDL, IDL, Lp(a), VLDL and chylomicron particles. The numbers of atherogenic LDL particles are frequently elevated even though LDL cholesterol is not, particularly in patients with pre-diabetes, diabetes and/or insulin sensitivity. In the Veterans Affairs High Density Lipoprotein Intervention Trial (VA-HIT), which included a relatively large proportion of subjects with diabetes (30.4%) and insulin resistance (30%), both traditional risk factors and NMR analyses were assessed in patients treated with the lipid-modifying agent gemfibrozil or placebo. LDL cholesterol was not influenced by treatment with gemfibrozil, but HDL cholesterol increased by 6% and was associated with a 22% reduction in events. While LDL cholesterol remained unchanged, the total LDL
particle concentration decreased by 5%, small LDL particle concentration decreased by 20%, total HDL particle concentration increased by 10%, and large HDL particles increased by 21%. Interestingly, neither baseline nor on-trial concentrations of HDL cholesterol, LDL cholesterol, or triglycerides were significant predictors of CHD events. Among NMR lipoproteins measured, both baseline and on-trial concentrations of total LDL and HDL particle concentrations were independent predictors of new CHD events with on-trial p-values of 0.0003 and <0.0001, respectively. Neither LDL nor HDL particle size was related to CHD events.

**Interpretation**

Elevated total LDL particle concentration is associated with increased atherogenic particles and subsequent cardiovascular risk.

**Reference Values**

<table>
<thead>
<tr>
<th>TOTAL LDL PARTICLE CONCENTRATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; or =15 years: not established</td>
</tr>
<tr>
<td>Adults (&gt; or =16 years):</td>
</tr>
<tr>
<td>&lt;1,000 nmol/L (optimal)</td>
</tr>
<tr>
<td>1,000-1,299 nmol/L (near or above optimal)</td>
</tr>
<tr>
<td>1,300-1,599 nmol/L (borderline high)</td>
</tr>
<tr>
<td>1,600-2,000 nmol/L (high)</td>
</tr>
<tr>
<td>&gt;2,000 nmol/L (very high)</td>
</tr>
</tbody>
</table>

Interpretation of LDL lipoprotein concentration should be conducted within the context of standard lipid profile results (total cholesterol, triglycerides, HDL cholesterol, calculated LDL cholesterol and non-HDL cholesterol).

**Analytic Time**

Same day

**Days and Times Performed**

Monday through Friday; Continuous

---

**Clinical References**


2. Rosenson RS, Otvos JD, Freedman DS: Relations of lipoprotein subclass levels and low-density lipoprotein size to progression of coronary artery disease in the Pravastatin Limitation of Atherosclerosis in the Coronary Arteries (PLAC-I) trial. Am J Cardiol 2002;90(2):89-94


5. Otvos JD, Collins D, Freedman DS, et al: Low-density lipoprotein and high-density lipoprotein particle subclasses predict coronary events and are favorably changed by gemfibrozil therapy in the Veterans Affairs High-Density Lipoprotein Intervention Trial. Circulation 2006;113(12):1556-1563