Lipoproteins Sub-fractions (Ion mobility)

A New Horizon in CHD Risk Assessment

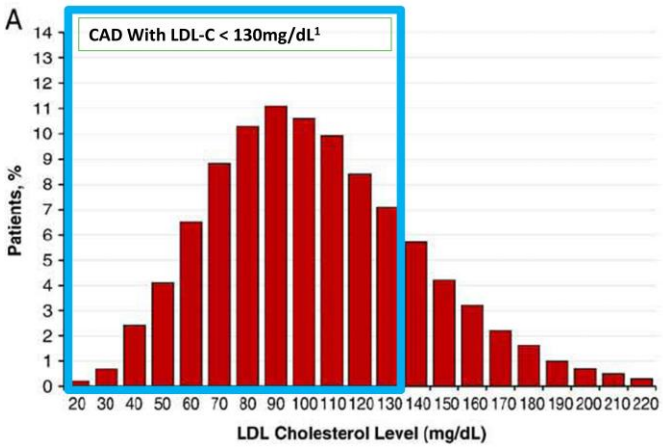
Small LDL

Over the past decades, evidence has revealed that standard lipoprotein measurements of triglycerides, total cholesterol, LDL-C, and HDL-C fail to identify many lipoprotein abnormalities that contribute to CHD and peripheral vascular disease risk.

Small, dense LDL has several characteristics that are linked to atherogenesis: long residence time in plasma, enhanced susceptibility to oxidation, arterial proteoglycan binding, and permeability through the endothelial barrier.

Together, these findings have led to the hypothesis that small, dense LDL is a potent atherogenic lipoprotein and a true determination of its value can be used to improve CHD risk prediction and evaluate response to lipid therapy.

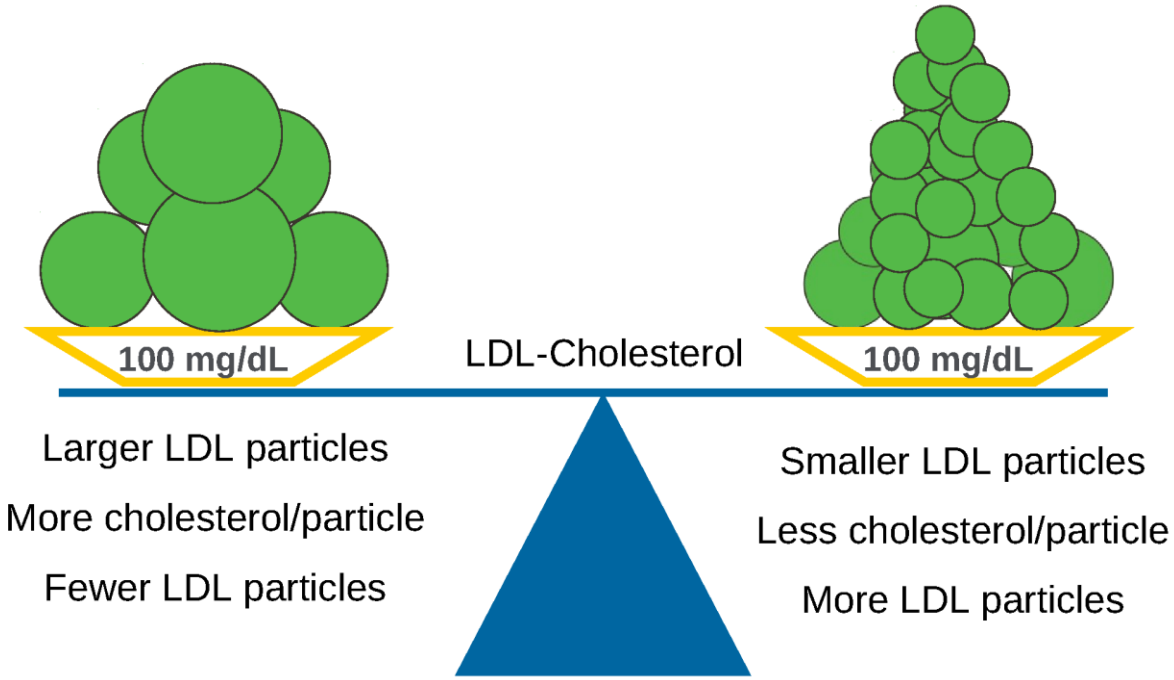
A predominance of small, dense LDL has been accepted as an emerging cardiovascular risk factor by the National Cholesterol Education Program Adult Treatment Panel III. LDL size seems to be an important predictor of cardiovascular events and progression of CHD. Evidence suggests that both quality (particularly small, dense LDL) and quantity (particle number) may increase cardiovascular risk. In multivariate analysis of large clinical trials, it has been shown that LDL peak particle diameter is statistically independent of traditional risk factors such as fasting TGs, LDL-C, HDLC, and body mass index.



In 136,905 patients hospitalized with CAD

- 70% after acute coronary syndrome
- 30% with chest pain and prior CAD

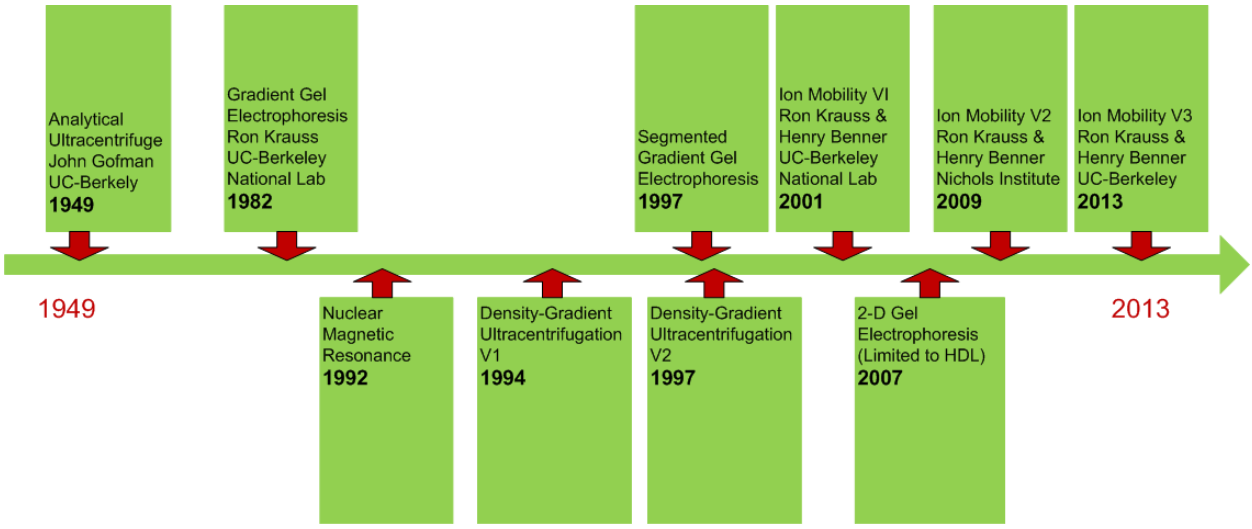
- **83% had LDL-C <130 mg/dL**
- **<u>50% had LDL-C <100 mg/dL</u>**
- **17.6% had LDL-C <70 mg/dL**



Advanced Lipoprotein Testing

Advanced lipoprotein tests (ALTs) lend insight into subtle yet important aspects of lipoproteins and atherosclerosis that help to explain the relative failure of the LDL-C–lowering strategy to stem the epidemic of atherosclerosis. ALTs can be utilized in 4 basic ways: (1) to enhance the accuracy of atherosclerosis risk prediction, (2) to enhance the accuracy of outcome prediction, (3) to assist in treatment selection and dose adjustment, and (4) to counsel first-degree relatives of patients with atherosclerosis.

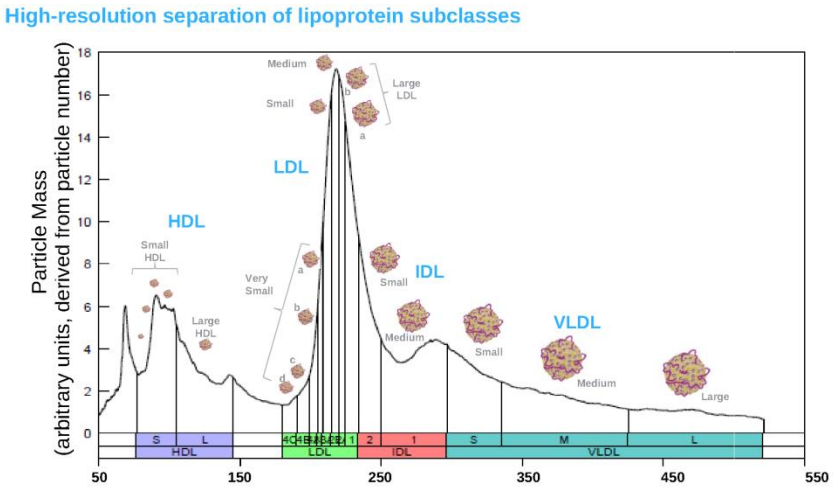
Historically, ALTs have been relegated to research laboratories and clinical trials and thus unavailable to clinicians. Subfractionation of lipoproteins was accomplished in university research laboratories by methods such as analytic ultracentrifugation, density gradient ultracentrifugation, gradient gel electrophoresis, immune-affinity chromatography, and 2-dimensional gel electrophoresis.



"Advanced" lipoprotein testing and the knowledge that it brings to cardiovascular disease management can now be incorporated into routine clinical care.

Lipoproteins Sub-fractions (Ion mobility)

Ion mobility lipoprotein fractionation is a technology that uses gas-phase (laminar flow) electrophoresis to separate unmodified lipoproteins on the basis of size. Following the separation, each lipoprotein particle is directly detected and counted as it exits the separation chamber.



Ion mobility fractionation is the latest technology in the evolution of advanced lipid subclass measurement. It has evolved from the analytical ultracentrifugation (AnUC)

and segmented gradient gel electrophoresis (SGGE) technologies developed at the University of California, Berkeley.

	Size (Angstroms)	Optimal	Moderate	High
LDL Particle Number		<1260	1260-1538	>1538
LDL Peak Size	218.2-222.5	>222.5	218.2-222.5	<218.2
Pattern		A	NA	B

Ion mobility incorporates and improves on the best features of advanced lipoprotein measurement methods. It combines high resolution separation of the full spectrum of lipoprotein particles along with direct quantitation of particles in each lipoprotein subclass. The high resolution of ion mobility's lipoprotein subfractionation is comparable to that seen with AnUC and SGGE methods. Thus, the extensive literature supporting the clinical use of lipoprotein subclasses derived from these 2 methods can be applied to ion mobility-derived subclasses as well.

Clinical Utility

1-Determination of Residual Risk in Asymptomatic subjects with normal lipid panel

2-Monitoring following therapy

3-Metabolic Syndrome and diabetics follow-up

4-CHD treated patients

5-CHD on treatment with recurrent events

6-Imaging positive patients with normal lipid profile

Effective Therapies for Lowering LDL-C , LDL-P, Small, Medium LDL and for Raising HDL

Drug/ Modification	LDL-C	LDL-P	Small LDL	HDL-C, HDL-P
Statins	↓ [1]	↓ [2]	↓ [2]	↑ [2]
Fibrates	↓ (moderate) [1,3]	↓ [1]	↓ [1]	↑ [1]
Niacin	— [4] ↓ (moderate) [3,5,6]	↓ [7]	↓ [5]	↑ [5,7]
Omega-3 fatty acids (fish oil)	— [8] ↓ (moderate) [9,10,11]	↓ [9,10,11]	↓ [9,10,11]	↑ (moderate) [9] ↓ [10] — [12]
Diet	↓ (moderate) [12, 13]	↓ [14]	↓ [14]	— [13]

1. Tenenbaum A, Fisman EZ. *Cardiovasc Diabetol.* 2012;11:125. **2.** Homma Y, Michishita I, Hayashi H, et al. *J Atheroscler Thromb.* 2010;17:1049-5. **3.** Wi J, Kim JY, Park S, et al. *Atherosclerosis.* 2010;213:235-40. **4.** Kane MP, Hamilton RA, Addesse E, et al. *Pharmacotherapy.* 2001;21:1473-8. **5.** AIM-HIGH Investigators, Boden WE, Probstfield JL, et al. *N Engl J Med.* 2011;365:2255-67. **6.** Bays HE, Shah A, Lin J, et al. *Am J Cardiovasc Drugs.* 2012;12:197-206. **7.** Kuvin J, et al. *Am J Cardiol.* 2006;98:743–5. **8.** Jeppesen C, Schiller K, Schulze MB. *Curr Diab Rep.* 2013;13:279-88. **9.** Maki KC, Bays HE, Dicklin MR, et al. *J Clin Lipidol.* 2011;5:483-92. **10.** Bays HE, Braeckman RA, Ballantyne CM, et al. *J Clin Lipidol.* 2012 ;6:565-72. **11.** Superko RH, MD, McGovern M , Raul E et al. *Am J Card* 2004;94:588-94 **12.** Garaiova I, Muchová J, Nagyová Z, et al. *Nutr J.* 2013;12:7. **13.** Kulick D, Langer RD, Ashley JM, et al. *BMC Fam Pract.* 2013;14:59. **14.** Krauss RM, Blanche PJ, Rawlings RS, et al. *Am J Clin Nutr.* 2006;83:1025-31.

Ordering Information

Test Name: Lipoprotein Sub-fractions (Ion mobility)
Sample Requirement: 1.0 ml serum frozen
Test Code: 1743