

sdLDL at a Glance

- Small dense LDL is strongly correlated with increased CHD risk, especially the proportion and absolute concentrations. (B. Lamarche, Quebec, Canada)
- Small dense LDL has prolonged plasma residence time compared to large LDL as shown by stable isotope kinetics (B. Lamarche, Quebec, Canada)
- Small dense LDL is associated with CHD independent of LDL, HDL and ApoB
- Benefits of the "Seiken" sdLDL method:
 - Quantitative measurement of sdLDL
 - Technically less challenging
 - Lower cost
 - Commercially available reagents
 - Better precision
 - Candidate for standardization

Related Information

sdLDL is frequently requested in conjunction with:

- Apolipoprotein A-1, B100
- CETP Activity
- Lipid Panel (total cholesterol, HDL, LDL, triglycerides)
- Lipoprotein Subfractions (GGE)
- LpPLA2, oxidized LDL
- PAI-1, Paraoxonase
- RLP-C
- sdLDL-Apo B

sdLDL is a useful efficacy biomarker for drug classes:

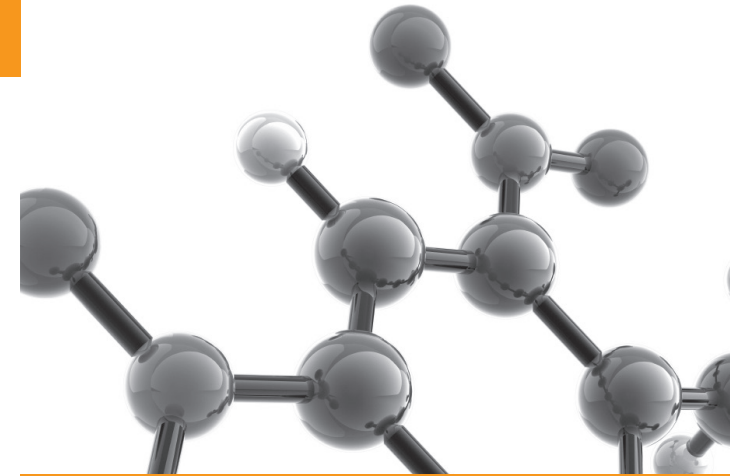
- Apo A-1 Mimetics
- Bile Acid Sequestrants, Fibrates
- Bile Acid Inhibitors
- Cholesterol Acyltransferase Inhibitors
- CETP Inhibitors, IBAT Inhibitors
- LpPLA2 Inhibitors
- MTPi (Microsomal Transfer Protein Inhibitors)
- Niacin, Squalene Synthase Inhibitors
- PPAR (Peroxisome Proliferator – Activated Receptor)
- Statins, Cholesterol Absorption Inhibitors

Frequently Requested Testing

Cardiovascular Risk – Diabetes, Dyslipidemia, Metabolic Syndrome & Obesity

- Adiponectin
- Apolipoproteins (i.e. AI, B48, CIII, etc.)
- CETP (Cholesterol Ester Transfer Protein: Activity and Mass)
- Cholesterol (Total, Esterified, and Free)
- E – Selectin
- Fibrinogen
- Fructosamine
- Glycerol, Free
- Glycomark™
- HDL Cholesterol Subclasses by Ppt. or GGE
- HDL Cholesterol
 - CDC Designated Comparison Method
 - CDC Reference Method
 - Chemical Precipitation (Hep Mg or DS)
 - Direct Homogeneous Method
- HDL Particle Assay, LpAI:All
- Homocysteine
- ICAM and VCAM
- Leptin
- LDL Cholesterol
 - β – Quantification
 - Direct Homogeneous Method
 - Friedewald Estimation
 - sdLDL
- LDL Cholesterol Subclasses by GGE
- Lp (a) [Lipoprotein (a)]
- LpPLA2
- Myeloperoxidase
- Non-Esterified Fatty Acids (NEFA or FFA)
- Oxidized LDL (antigen and autoantibody)
- PAI – 1 (plasminogen activator inhibitor)
- Paraoxonase
- RLP-C & RLP-Tg
- Triglycerides
- VLDL

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FEATURED ASSAY:

sdLDL

A simple precipitation method for the quantification of sdLDL.

SAMPLE REQUIREMENTS

Optimum volume: 600 μ L

Sample Type: Serum or EDTA Plasma

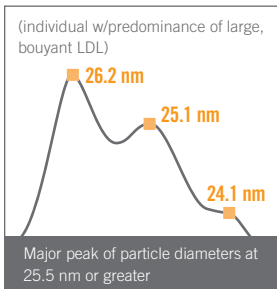
Method: Colorimetric

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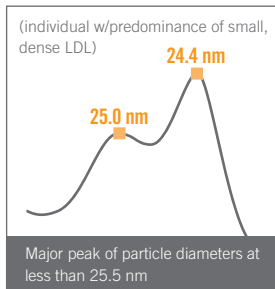
Background Information

LDL particles are considered the most atherogenic component of serum cholesterol. However, LDL particles are heterogeneous with respect to their size, density, and lipid composition. Two subclass patterns (A and B) have been described. Individuals with a predominance of small dense LDL (i.e. pattern B) have a 3-fold increased risk of myocardial infarction (1).

PATTERN A



PATTERN B



Subclass pattern B, small dense LDL (sdLDL) particles, are thought to be more atherogenic as a result of their penetration of the arterial wall, lower binding affinity for the LDL receptor, longer plasma half-life, and weaker resistance to oxidative stress (2,3).

SdLDL is generated from large triglyceride rich VLDL (4). Hepatic production of VLDL is stimulated by insulin resistance, thus sdLDL has been highlighted as a useful new marker for the cardiovascular risk or type 2 diabetes (5,6).

Measurement of small dense LDL particles may be considered medically necessary when the patient meets at least one of the following criteria:

- Carotid, coronary, or peripheral arterial disease
- Hyperlipidemia or dyslipidemia
- Hypertension
- Diabetes mellitus

DEFINITIONS FOR SMALL, DENSE LDL

Lipoproteins	VLDL	LLDL	sd LDL*	HDL
Diameter (nm)	30 - 80	25.5 - 28.0	22.0 - 25.5	7 - 10
Density (g/mL)	<1.006	1.019 - 1.044	1.044 - 1.053	1.053 - 1.210

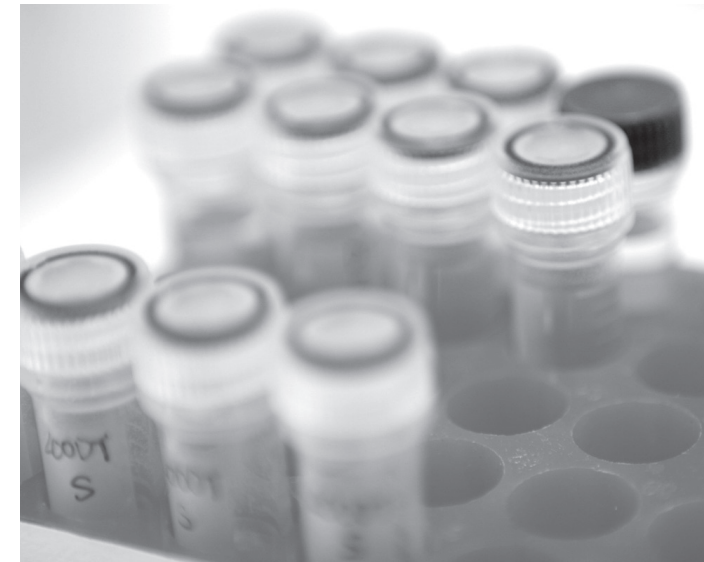
*Definition used by Denka Seiken. The density range of 1.044-1.063 g/mL corresponds to a diameter range of 22.0-25.5 nm, that is Pattern B.

LIPOPROTEIN SUBCLASS MEASUREMENTS

Currently there is no standard for measuring sdLDL. The following GGE, NMR, and UC methods are technique demanding, require special equipment and may not be suitable for routine use.

METHOD	PRINCIPLE	REPORTING	AVAILABILITY
GGE	<ul style="list-style-type: none"> • Non-denaturing gradient gel • Separate by size in electrical field 	Size, % fraction of cholesterol subclasses	Home brew / proprietary commercial lab
NMR	<ul style="list-style-type: none"> • Proton NMR • Separate by methyl group signal 	Size and particle number, quantification by convoluted algorithm	Proprietary commercial lab
UC	<ul style="list-style-type: none"> • Sequential or density gradient UC • Separate by density • Direct component measurement 	Size, lipid components; subclass quantification by convoluted algorithm in sequential UC	Home brew / proprietary commercial lab
Polyanion-cation Precipitation	<ul style="list-style-type: none"> • Heparin-Mg precipitation • Apo content selective detergent and enzymes • Direct component measurement 	Small dense LDL cholesterol and other components	Commercially available from Denka Seiken

The sdLDL "Seiken" (polyanion-cation precipitation) is a simple method for quantitative determination of sdLDL consisting of two steps:
 1. filter out large, buoyant LDL and other apoB-containing lipoproteins by forming aggregates with polyanion and divalent cation-based reagent
 2. measure small, dense LDL-cholesterol on automated chemistry analyzers. This procedure is simple, requires no special equipment, and is completed within 60 minutes. This method is being considered as a candidate for a standardized automated routine method.



References: (1) Austin MA, et al JAMA 1988 (2) Chapman MJ, Guerin M, Bruckert E: Eur Heart J 1998 (3) Bjornheded T, Babyi A, Bodjers G, Wiklund O: Atherosclerosis 1996 (4) Packard CJ, Shepherd J: Artheroscler Thromb Vssc Biol. 1997 (5) Berneis KK, Krauss RM: J Lipid Res 2002 (6) Austin MA, Mykkanen L, Kuusisto J, Edwards KL, Nelson C, Haffner SM, Pyorala K, Laakso M: Circulation 1995