LIPOMAP: LIPID TESTING BY NMR

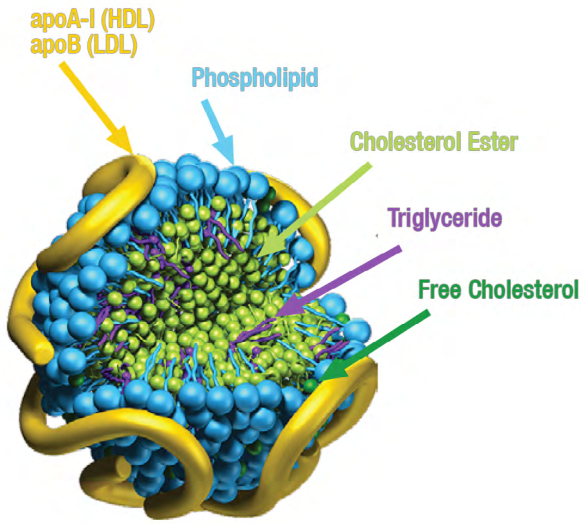
Overview, Clinical Significance & Treatment Summary

TEST NAME LipoMap

TEST CODE 98050

ASSAY DESCRIPTION NMR

SPECIMEN REQUIREMENT 1.0 mL Fasting (8 hr minimum) serum collected in Greiner Bio-one Vacuette Z-serum clot activator, red/yellow top tube; or approved alternatives: NMR LipoTube (manufactured by Greiner, Inc.), or S-Monovette® Serum (Sarstedt).



ASSAY METHODOLOGY

Nuclear magnetic resonance (NMR) is widely used to determine the levels and structure of molecules by examining their frequency characteristics in response to electromagnetic signals. NMR is an ideal method for assessing the lipid and protein content in lipoprotein particles of varying sizes and densities.[1] NMR using 400 MHz machines has been used to assess plasma or serum low-density lipoprotein particle number (LDL-P) and high-density lipoprotein particle number (HDL-P).

Boston Heart Diagnostics offers state of the art lipid and lipoprotein particle assessment using 600 MHz machines with about 50% greater resolution of lipoprotein particles than NMR using 400 MHz machines.[1] This methodology allows for the precise measurement of total cholesterol, cholesteryl ester, free cholesterol, triglyceride, apolipoprotein (apo) A-I, apoA-II, and apoB within serum lipoproteins of varying densities and sizes.[1] Phospholipids are shown on the surface of lipoprotein particles. See image to the left.

ATHEROSCLEROSIS AND CARDIOVASCULAR DISEASE

- Cardiovascular disease (CVD) is the leading cause of death in men and women. CVD often presents as sudden cardiac death because it wasn't diagnosed and managed early enough.
- 50% of people who suffer a heart attack or stroke have normal LDL cholesterol.[2,3] More thorough lipid testing can identify the hidden risk and improve clinical outcomes.
- Patients with CVD often have elevated LDL-P levels and decreased HDL-P levels as compared to control subjects.[4-8]
- It has been documented that LDL-P and HDL-P are superior to LDL-cholesterol (LDL-C), HDL-cholesterol (HDL-C), and cholesterol efflux capacity measurement in CVD risk assessment. [2-11]

METABOLIC SYNDROME

- Insulin resistance and obesity are extremely commonplace in clinical practice. These patients are at increased risk of type 2 diabetes, CVD and related conditions including dyslipidemia, kidney disease and hypertension.
- Dyslipidemia, characterized by hypertriglyceridemia, increased LDL-P and small dense LDL-P, and decreased HDL-P, is a hallmark of metabolic syndrome, and is often associated with fatty liver and increased inflammatory markers, as well as markedly increased CVD risk.
- The LipoMap helps clinicians identify these abnormalities so they can provide appropriate therapy and improve CVD risk.

DISLIPIDEMIA AND LIPID DISORDERS

- A wide variety of lipid disorders exist and the best way to unmask lipid disorders is to have a thorough tool to measure and optimize the full spectrum of lipids lipoproteins and apolipoproteins.[12-18]
- Dysbetalipoproteinemia: Combined elevations of triglycerides, cholesterol, VLDL-C, VLDL particle number, IDL-C and IDL particle number are associated with dysbetalipoproteinemia, the apoE2/2 genotype or other apoE variants, and an increased risk of cardiovascular disease (CVD). These patients should be treated with lifestyle modification, fenofibrate and statins.
- Combined Hyperlipidemia: Combined elevations of triglycerides, VLDL particles, LDL-C, and LDL particles are often due to familial combined hyperlipidemia (the most common cause of high serum cholesterol) associated with cholesterol overproduction and an increased CVD risk. These patients should be treated with lifestyle modification and statin therapy.
- Certain genetic HDL-C deficiencies or liver diseases cause abnormal cholesterol esterification which can be detected using the ratios of free cholesterol to esterified cholesterol (cholesterol with a fatty acid attached).

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Category	Tests and Description	Clinical Considerations
Lipid, Lipoprotein, and Apolipoproteins	• Includes basic lipids, direct LDL-C, sdLDL-C, apoA-I, apoA-II, and apoB, as well as the atherogenic ratios of LDL-C/HDL-C and apoB/apoA-I. • Greater than 97% concordance and correlation with standard chemistry tests.	• Patients with high abnormal levels can be treated with lifestyle modification, statins, ezetimibe, and if necessary PCSK9 inhibitors. • Lipid lowering medications reduce the concentration of all LDL particles, while lifestyle changes improve the size distribution. • Severe Hypercholesterolemia (LDL-C >190 mg/dL) in the absence of secondary causes is often due to familial hypercholesterolemia with mutations at the LDLR, APOB, and/or PCSK9 gene loci. Occasionally Severe Hypercholesterolemia is due to sitosterolemia caused by ABCG5/8 mutations. These patients are at very high CVD risk. • Severe Hypertriglyceridemia (TG >500 mg/dL) along with increased VLDL particles is associated with an increased risk of pancreatitis and should be treated with lifestyle modification (animal and dairy fat and sugar restriction), fenofibrate, omega-3 fatty acids, and if necessary, statins to optimize LDL-C. • Rule out secondary causes such as obesity, diabetes, hypothyroidism, liver disease, and kidney disease if possible, and/or the use of oral estrogens, testosterone, or steroids.
Atherogenic Lipoprotein Particles	• Includes LDL, IDL, and VLDL particle numbers as well as apoB, cholesterol, and triglyceride levels in these particles. • Provides particle number for six LDL sub-particles, with the smaller particles being the most atherogenic.	
ApoB-100 and Triglyceride in Atherogenic Lipoproteins	• Includes measurements of the amount of apoB-100 and triglycerides contained in the LDL, IDL, and VLDL particles. • High values may be associated with an increased risk of CVD.	
HDL Particles	• This value indicates the number of HDL particles. • HDL particles protect against CVD and participate in reverse cholesterol transport to remove cholesterol from the body. • Low values of HDL-P are associated with an increased risk of CVD.	• Lifestyle modifications improve the concentration and effectiveness of HDL particles. • Very low HDL is often due to secondary causes such as hypertriglyceridemia, diabetes, inflammation, and or testosterone replacement, but may also be due to various genetic disorders including defects in the APOAI, ABCA1, and/or LCAT genes. • Patients with apoA-I deficiency have very low serum apoA-I levels and usually normal LDL-C levels, and increased CVD risk. Patients with ABCA1 defects often have mild hypertriglyceridemia, normal LDL-C and increased CVD risk. • The treatment of HDL-related disorders requires identification and treatment of secondary causes and/or the optimization of all other risk factors for CVD including hypertension, diabetes, smoking, and lipid disorders.
Lipoprotein Cholesterol Esterification	• LDL-FC/LDL-C and HDL-FC/HDL-C are the ratios of free cholesterol to esterified cholesterol (cholesterol with a fatty acid attached) within LDL and HDL. • A high ratio indicates markedly decreased cholesterol esterification as seen in patients with liver disease or certain genetic HDL deficiency disorders.	• An LDL-FC/LDL-C esterification index $\geq$ 0.50 indicates decreased LDL cholesterol esterification which can be due to liver disease and/or lecithin:cholesterol acyl transferase (LCAT) deficiency. • An HDL-FC/HDL-C index $\geq$0.50 indicates decreased HDL cholesterol esterification which can be due to liver disease or selective lecithin:cholesterol acyl transferase (LCAT) deficiency affecting on HDL (known as fish-eye disease). Patients with LCAT deficiency are at increased risk of developing kidney failure.

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TESTS AND REFERENCE RANGES

Test Name	Optimal	Borderline	Increased Risk
Lipid, Lipoprotein, and Apolipoprotein Parameters and Ratios			
Total Cholesterol (TC)	<200	200 - 240	>240 mg/dL
Direct LDL-cholesterol (LDL-C)	With CVD: <70 Without CVD:<100	70 - 100 100 - 160	>100 mg/dL >160 mg/dL
HDL-cholesterol (HDL-C)	Male: >50 Female: >60	40 - 50 50 - 60	<40 mg/dL <50 mg/dL
Non HDL-cholesterol (Non-HDL-C)			
Triglycerides (TG)	<150	150 - 200	>200 mg/dL
Small Dense LDL-cholesterol (sdLDL-C)	<20	20 - 40	>40 mg/dL
% Small Dense LDL- cholesterol (%sdLDL-C)	<20	20 - 30	>30 %
IDL-cholesterol (IDL-C)	<7	7 - 12	>12 mg/dL
VLDL-cholesterol (VLDL-C)	<30	30 - 40	>40 mg/dL
Apolipoprotein-AI (ApoA-I)	Male: >160 Female: >180	120 - 160 140 - 180	<120 mg/dL <180mg/dL
Apolipoprotein-AII (ApoA-II)	Male: >32 Female: >35	30 - 32 32 - 35	<30 mg/dL <32 mg/dL
Apolipoprotein-B (ApoB)	<80	80 - 120	>120 mg/dL
Total Cholesterol/HDL-cholesterol ratio (TC/HDL-C)	With CVD: <3 Without CVD: <4	3 - 5 4 - 6	>5 >6
Apolipoprotein-B/Apolipoprotein-A ratio (ApoB/ApoA-I)	With CVD: <0.5 Without CVD: <0.6	0.5 - 0.7 0.6 - 0.9	>0.7 >0.9
Atherogenic Lipoprotein Particles			
Total ApoB carrying Particle Number (Total ApoB-P)	<1400	1400 - 2000	>2000 nmol/L
LDL Particle Number (LDL-P)	<1200	1200 - 1800	>1800 nmoles/L
IDL Particle Number (IDL-P)	<70	70 - 100	>100 nmoles/L
VLDL Particle Number (VLDL-P)	<120	120 - 180	>180 nmoles/L

Test Name	Optimal	Borderline	Increased Risk
LDL Particles			
LDL-1 Particle Number (LDL1-P)	<140	140 - 190	>190 nmol/L
LDL-2 Particle Number (LDL2-P)	<150	150 - 200	>200 nmol/L
LDL-3 Particle Number (LDL3-P)	<190	190 - 260	>260 nmol/L
LDL-4 Particle Number (LDL4-P)	<230	230 - 330	>330 nmol/L
LDL-5 Particle Number (LDL5-P)	<290	290 - 400	>400 nmol/L
LDL-6 Particle Number (LDL6-P)	<300	300 - 450	>450 nmol/L
ApoB-100 and TG in Atherogenic Lipoproteins			
LDL-ApoB (LDL-apoB)	<70	70 - 100	>100 mg/dL
IDL-ApoB (IDL-apoB)	<4	4 - 6	>6 mg/dL
VLDL-ApoB (VLDL-apoB)	<6	6 - 10	>10 mg/dL
LDL-Triglycerides (LDL-TG)	<24	24 - 28	>28 mg/dL
IDL-Triglycerides (IDL-TG)	<6	6- 10	>10 mg/dL
VLDL-Triglycerides (VLDL-TG)	<60	60 - 90	>90 mg/dL
HDL Particles			
HDL Particle Level (HDL-P)	Male: >38.0 Female: >42.0	33.0 - 38.0 37.0 - 42.0	<33.0 µmol/L <37.0 µmol/L
Lipoprotein Cholesterol Esterification Tests			
LDL-Free Cholesterol/LDL-cholesterol (LDL-FC/LDL-C)	<0.5		≥0.5
HDL-Free Cholesterol/HDL-cholesterol (HDL-FC/HDL-C)	<0.5		≥0.5

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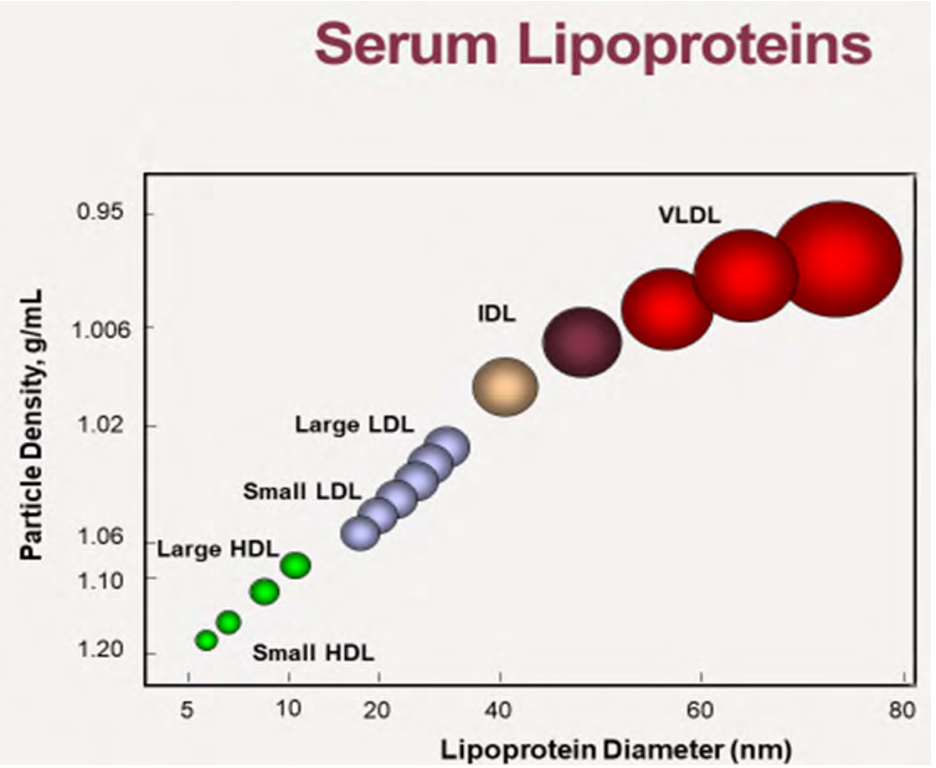
TREATMENT PRINCIPLES

- The majority of lipid abnormalities can be normalized by lifestyle changes and/or medications, which are complementary treatment modalities.
- Lifestyle can improve many parameters, including the size distribution of the LDL, and effectiveness of HDL particles.
- Prior to the use of lipid lowering agents, it is important to identify and treat secondary causes including obesity, diabetes, hypothyroidism, liver disease, and kidney disease if possible, and/or the use of oral estrogens, testosterone, or steroids.
- For high risk patients and those with established CVD, it is very important to optimize LDL particle number, LDL-C, sdLDL-C, and LDL6-P, which may require medications including statins, ezetimibe, and if necessary proprotein convertase subtilisin kexin 9 (PCSK9) inhibitors.
- In addition to the LipoMap, consider measuring Lp(a), Cholesterol Balance®, Fatty Acid Balance™ and inflammatory, metabolic and genetic markers as indicated to optimize diagnosis and treatment.



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