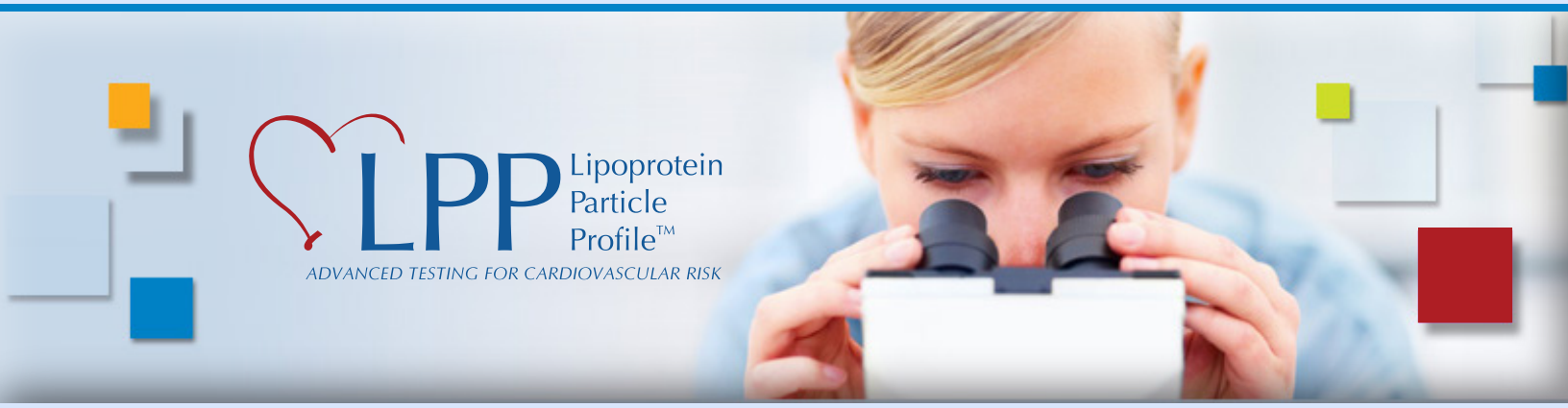
SpectraCell Laboratories
Science + Health + Solutions



Profile Components

HDL2b

What is HDL2b?

High Density Lipoprotein (HDL) has two important subgroups: the larger, more buoyant HDL2 and the smaller, denser HDL3. These subgroups are important indicators of the efficiency of reverse cholesterol transport by HDL, or how well HDL is clearing excess cholesterol from the body. HDL is formed in the liver as dense HDL3 and as it travels through the body and accumulates cholesterol, it becomes the larger and lipid-enriched HDL2b, the largest and most buoyant HDL. Since HDL2b is an indicator of how well excess lipids are removed from cells, it positively correlates with heart health.

Why measure HDL2b?

According to the National Cholesterol Education Program (NCEP), only about half of the variability in coronary heart disease risk can be attributed to conventional risk factors (i.e. LDL, HDL and triglyceride levels). Other, more specific risk factors, enhance predictive power of cardiovascular disease in individuals. HDL2b is one of these specific risk factors that may be independent of other lipid-related risk factors.

NCEP Specific Risk Factors:

- Lp(a)
- RLP
- **HDL2b**
- Small-dense LDL

The presence of coronary heart disease is more strongly associated with the HDL subgroups than with total HDL cholesterol levels. More specifically, the extent of atherosclerosis is associated with decreased HDL2 rather than HDL3 values.

How is low HDL2b treated?

Exercise increases HDL2b and may also promote a slight decrease in HDL3. Treatment with niacin may also raise HDL cholesterol.

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Additional references at http://www.spectracell.com/online-library-lpp-hdl-abstract

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Lp(a)

What is Lp(a)?

Lipoprotein(a) is an LDL particle with an apolipoprotein(a) attached to it. It is involved in the formation of plaque and is a very strong independent risk factor for cardiovascular disease. Lp(a) accumulates in atherosclerotic plaque and its plasma concentration is predictive of heart disease in many patients. Because the density of Lp(a) overlaps that of dense LDL and buoyant HDL, separation of Lp(a) by density alone is inherently difficult. For this reason, it is important to measure Lp(a) directly with a specific Lp(a) assay in order to get truly accurate results.

Why measure Lp(a)?

According to the National Cholesterol Education Program (NCEP), only about half of the variability in coronary heart disease risk can be attributed to conventional risk factors (i.e. LDL, HDL and triglyceride levels). Other, more specific risk factors, enhance predictive power of cardiovascular disease in individuals. Lp(a) is one of these specific risk factors that may be independent of other lipid-related risk factors.

NCEP Specific Risk Factors:

- **Lp(a)**
- RLP
- HDL2b
- Small-dense LDL

Why is Lp(a) so harmful?

Evidence suggests that Lp(a) may serve as the link between thrombosis and atherosclerosis. The surface of many genetic variations of Lp(a) is very similar to the surface of plasminogen, an anti-thrombotic molecule. Due to their similar structure, Lp(a) blocks the receptor site for plasminogen, thus inhibiting the formation of plasmin, the fibrinolytic enzyme that would normally bind to a clot and dissolve it. Recent clinical studies have implicated Lp(a) as a risk factor for blood clots whether or not atherosclerosis is present. Because Lp(a) is a small, very dense LDL, it can easily penetrate the arterial lining, become oxidized and build plaque, thus contributing to atherosclerosis independent of its thrombotic potential.

How is high Lp(a) treated?

Although heredity plays a large role in the levels of Lp(a), treatment with niacin can lower levels of Lp(a).

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Additional references at http://www.spectracell.com/online-library-lpp-lpa-abstract

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RLP (Remnant Lipoprotein)

What is RLP?

RLP is a very atherogenic lipoprotein composed primarily of very low density lipoproteins (VLDL) and intermediate density lipoproteins (IDL). Considered one of the most harmful lipoproteins, RLP (also called remnant-like particles) is very highly correlated with cardiovascular disease. In fact, studies show that the composition of arterial plaque closely resembles composition and density of RLP.

Why measure RLP?

According to the National Cholesterol Education Program (NCEP), only about half of the variability in coronary heart disease risk can be attributed to conventional risk factors (i.e. LDL, HDL and triglyceride levels). Other, more specific risk factors, enhance predictive power of cardiovascular disease in individuals. RLP is one of these specific risk factors that may be independent of other lipid-related risk factors.

NCEP Specific Risk Factors:
- Lp(a)
- **RLP**
- HDL2b
- Small-dense LDL

Why is RLP so harmful?

Although RLP is relatively large compared to most LDL particles, it is particularly harmful because unlike LDL particles, which have to undergo oxidation before they can be taken into the arterial intima by macrophage cells, RLP can be readily scavenged by macrophage cells even when they are not oxidized. Once scavenged by a macrophage, RLP is transformed into foam cells which are the building blocks of arterial plaque. In fact, elevated RLP has been found in survivors of myocardial infarction and persons with significant coronary atherosclerosis.

Additionally, RLP contributes to endothelial dysfunction by impairing the vascular relaxation process as well as enhancing platelet aggregation.

How is high RLP treated?

Although heredity plays a large role in the levels of RLP, consumption of omega-3 fatty acids can significantly lower levels of RLP. Therapies that normally lower triglycerides are also effective at lowering RLP.

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Small-dense LDL

What is small-dense LDL?

There are five major subgroups of Low Density Lipoproteins (LDL): IDL (intermediate density lipoprotein), I, II, III and IV. IDL is the largest, least dense and most buoyant, while LDLIV is the smallest and most dense. LDL particles that are small are also dense and these terms are often used interchangeably. The smaller the LDL particle, the more dangerous it is. In fact, small-dense LDL (LDLIII and LDLIV) is three times more atherogenic than buoyant LDL.

Why measure LDL subgroups?

According to the National Cholesterol Education Program (NCEP), only about half of the variability in coronary heart disease risk can be attributed to conventional risk factors (i.e. LDL, HDL and triglyceride levels). Other, more specific risk factors, enhance predictive power of cardiovascular disease in individuals. Small - dense LDL is one of these specific risk factors that may be independent of other lipid-related risk factors.

NCEP Specific Risk Factors:

- Lp(a)
- RLP
- HDL2b
- **Small-dense LDL**

Lipoproteins transport cholesterol throughout the body. But it is the actual lipoprotein particle, not the cholesterol within them, that penetrates the arterial wall and causes heart disease. That is why it is necessary to know the number of small LDL particles.

Why is small-dense LDL so harmful?

Smaller particles of LDL can more easily penetrate the arterial wall than large LDL particles simply due to their size. Therefore, the smaller the LDL particle, the more likely it is to enter the arterial endothelium, where it becomes oxidized, is taken up by a macrophage cell which then becomes a foam cell, which eventually stick together to build plaque within the arteries. Evidence also suggests that small-dense LDL is associated with vascular dementia.

It is also important to know *how many* LDL particles are present, in addition to their size. Just as small LDL particles can fit through the arterial lining more easily than large LDL particles, the more LDL particles there are, the more likely they will enter the arterial intima, regardless of size. It is therefore imperative to measure both the size (density) *and* number of LDL particles.

How is small-dense LDL treated?

Therapeutic treatment for small-dense LDL includes the use of niacin and fibrates. Lifestyle changes (diet and exercise) show beneficial effects as well.

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Apolipoprotein B100

What is apolipoprotein B100?

Apolipoprotein B is a protein that is attached to the surface of all low density lipoproteins (LDL). ApoB attaches to cells, acting like a "key" that unlocks a pathway to which cholesterol that is carried within the LDL can be delivered into the cells that need it. The protein occurs in two main forms: ApoB100 (produced by the liver) and a shortened version ApoB48 (produced in the small intestine). Specifically, every molecule of VLDL, IDL, Lp(a) and LDL has exactly one, and only one apoB100 molecule attached to it.

Why measure apolipoprotein B?

It is now understood that the number of lipoprotein particles versus cholesterol levels within those particles is a superior indicator of cardiovascular risk. Since a single molecule of apoB is present on all non-HDL lipoproteins, apoB indicates the number of atherogenic lipoprotein particles in blood.

Even when LDL levels are not in the high-risk range, high levels of ApoB100 are associated with increased risk of cardiovascular disease. This is especially true in patients with elevated triglycerides or low HDL. Although the terms apoB, non-HDL and LDL are often used interchangeably, LDL and non-HDL are often calculated, but apolipoproteinB is measured directly. Apolipoprotein B levels should be under 100 mg/dL.

Why are high levels of apolipoprotein B harmful?

Apolipoprotein B levels reflect the number of atherogenic lipoprotein particles in plasma. Atherosclerosis (hardening of the arteries) occurs as the result of several contributing factors including inflammation and an unhealthy lipoprotein profile. The higher the number of LDL particles that are present in the circulatory system, the higher the probability these LDL particles will penetrate the arterial lining, become oxidized and cause vascular damage, particularly if they are the atherogenic type. Once vascular damage occurs, atherosclerotic lesions form foam cells that become arterial plaque and heart disease risk increases.

How is apolipoprotein B treated?

It is treated in the same way high LDL is treated, which includes pharmaceuticals such as statins, bile acid sequestrants, niacin or fibrates, depending on the specific type of LDL that is elevated.

References

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hs-CRP (HighSensitivity C-Reactive Protein)

What is hs-CRP?

hs-CRP is a protein that is manufactured in response to inflammation in the body. Since it is an acute phase protein, levels of hs-CRP will rise dramatically when a specific injury or infection exists, regardless of where in the body the damage occurs. Levels of hs-CRP increase simultaneously when inflammatory enzymes such as IL-6 (interleukin-6) are present.

Why measure hs-CRP?

Elevated CRP is indicative of systemic (whole body) inflammation, which includes vascular inflammation, a known cause of heart disease. Extensive literature shows that elevated CRP is very predictive of cardiovascular risk. In fact, in the large Physician's Health Study, CRP was one of only two risk factors that demonstrated statistically significant trends with sudden cardiac death after controlling for age and smoking. (The other was the omega 3 index.)

It should be noted that although CRP is very predictive of heart disease risk, it is not specific to vascular inflammation. In other words, if acute inflammation exists from injury or infection, for example, CRP values will rise, even when cardiovascular inflammation is not present. However, when CRP remains chronically high in the absence of acute causes, cardiovascular disease should be considered.

Interestingly, evidence suggests that CRP is particularly relevant in predicting cardiovascular events in asymptomatic people with no known heart disease. Therefore, in the absence of more traditional cardiovascular risk factors such as smoking and hypertension, it can be used to re-classify "intermediate risk" people into more appropriate risk categories – either higher or lower depending on hs-CRP levels.

Only the high sensitivity CRP assay will detect low levels of chronic inflammation associated with heart disease. Hs-CRP levels should be less than 3.0 mg/L.

Why is hs-CRP harmful?

hs-CRP is a marker, not necessarily a cause, of inflammation, so the protein itself is not directly harmful. Rather CRP is indicative that low-grade inflammation exists and should be treated. Since cardiovascular disease is considered a disease of inflammation – vascular injury, damage from oxidative stress and abnormalities in lipoprotein metabolism – chronically elevated levels of hs-CRP are dangerous. In addition, abdominal obesity and insulin resistance are strong predictors of hs-CRP. Elevated CRP is also linked with peripheral arterial disease, stroke and endothelial dysfunction (blood vessels do not respond appropriately to signals for dilation and constriction).

How is hs-CRP treated?

Reducing whole-body inflammation is the key to hs-CRP. Lifestyle changes can effectively lower hs-CRP (smoking cessation, weight loss and exercise). Pharmacological intervention includes the use of statins, which reduce hs-CRP levels independent of their low-density lipoprotein lowering effects.

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Additional references at http://www.spectracell.com/online-library-lpp-crp-abstract

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Homocysteine

What is homocysteine?

Homocysteine is a sulphur containing amino acid that is synthesized by the body rather than ingested via diet. It is created from a process called demethylation of another amino acid, methionine and can be recycled back into methionine (a benign amino acid) or converted into cysteine (a benign amino acid with antioxidant properties) in the presence of adequate B-vitamins.

Why measure homocysteine?

High homocysteine levels are linked to such vascular disorders as heart disease, stroke and peripheral artery disease as well as dementia and Alzheimer's disease. Specifically, elevated homocysteine is associated with thrombosis (blood clots) causing a 2-3 fold increase in risk of cardiovascular events. It is considered as strong of an indicator of vascular disease as smoking or hypertension. Evidence also suggests a link between elevated homocsysteine and migraines, erectile dysfunction, shortened telomeres (a marker for aging) and even age-related hearing loss. Homocysteine levels should be less than 11 umol/mL.

Why is homocysteine harmful?

Some research suggests that high levels of homocysteine may act as an arterial abrasive and physically damage arteries. This arterial trauma affects the endothelial lining of the arteries, which normally responds to enzymatic or hormonal cues to dilate or contract. When the endothelial lining of the blood vessels becomes dysfunctional, vascular health is seriously compromised. High homocysteine can also stem from renal disease since homocysteine is partially cleared through the kidneys. Patients with kidney disease often have very high levels of homocysteine, which some consider the primary reason that vascular disease so often coincides with renal failure.

How is homocysteine treated?

In many cases, high levels of homocysteine can be lowered by low-cost, non-invasive therapy with little side effects. Correcting a deficiency in folate, vitamin B6 or vitamin B12 can reduce homocysteine levels significantly. Each of these vitamins is necessary for the proper conversion of homocysteine into methionine and a deficiency in any one of them can cause homocysteine levels to rise. Similarly, supplementation with the amino acid betaine or cysteine may lower homocysteine levels, especially in the absence of B vitamin deficiencies. Other modifiable contributors to elevated homocysteine include smoking and high meat diets.

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Insulin

What is insulin?

Insulin is a hormone that allows blood sugar to be utilized by muscle, liver and fat cells throughout the body. It is produced by specialized cells called β-cells in the in the pancreas and secreted in response to elevated blood sugar levels. Its main function is to regulate plasma glucose levels within a narrow range. Insulin binds to cellular insulin receptors, which signals glucose to be taken up into various types of cells (such as skeletal muscle or liver tissue) thus removing it the bloodstream. Ingested carbohydrates stimulate insulin production as well as some stimulatory hormones such as adrenaline.

Why measure insulin?

Insulin levels tell a lot about the efficiency with which a person can metabolize carbohydrates. Fasting insulin levels are inversely correlated to insulin sensitivity. That is, the higher the insulin level, the less sensitive a person is to the glucose- clearing effect of insulin. Especially in persons without diabetes, elevated fasting insulin can facilitate diagnosis of insulin resistance, which predisposes a person to cardiovascular disease. Insulin resistance is also linked to higher rates of stroke.

When a diagnosis of metabolic syndrome is made, clinicians will often look at the possibility of insulin resistance. Of the metabolic syndrome clinical factors, elevated fasting blood sugar (a possible indicator of insulin resistance) is often thought to be the most dangerous factor. (Three of five warrant diagnosis of metabolic syndrome – (1) obesity, (2) low HDL, (3) high triglycerides, (4) hypertension or (5) elevated fasting blood glucose).

Why are high levels of insulin harmful?

Insulin levels can be elevated for two reasons: the body is de-sensitized to the action of insulin (insulin resistance), or blood sugar levels are high enough to warrant excess release of insulin in order process the glucose in the bloodstream. Since elevated blood sugar levels can act as an arterial abrasive and contribute significantly to atherosclerosis, high levels of insulin generally mean excess blood sugar is present.

How is high insulin treated?

In the absence of full-blown diabetes, to which high insulin is a precursor, the primary line of therapy is lifestyle changes – specifically weight loss, when visceral adiposity (fat in the midsection) is present, and exercise. Even modest amounts of weight loss can reverse or retard some of the effects of insulin resistance, thus altering metabolism in such a way that promotes efficient energy production over fat storage. Moderate exercise also helps to lower insulin levels, even in the absence of weight loss.

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Triglycerides

What are triglycerides?

Triglycerides (also known as triacylglycerol or TAG) are the major transporters of dietary fats throughout the bloodstream. Specifically, it is composed of one glycerol molecule that is attached to three fatty acids, hence the term triglyceride. VLDL (very low density lipoproteins) and chylomicrons are made up largely of triglycerides. Besides transporting fat throughout the bloodstream so that it can be used for fuel, triglycerides also store fat in adipose tissue (fat cells) when the body's demand for fuel is less than what is ingested from diet.

Why measure triglycerides?

Elevated triglycerides are a major risk factor for heart disease and diabetes because high serum levels of triglycerides are indicative of abnormal lipoprotein metabolism. Extremely high triglyceride levels (over 500 mg/dL) can cause pancreatitis. Triglyceride levels should fall below 150 mg/dL. Since triglycerides go up after a meal, they are typically measured after 12 hours of fasting.

Why are high triglycerides harmful?

High triglycerides negatively affect LDL particle size. Through a complex metabolic interaction, triglycerides promote the formation of small, dense LDL particles, which are particularly atherogenic. Even in the presence of normal LDL cholesterol, patients with high triglycerides typically have endothelial dysfunction, where their blood vessels do not dilate and constrict properly. In addition, excess triglycerides lower nitric oxide levels and increase many inflammatory compounds further contributing to vascular injury and endothelial dysfunction.

Elevated triglycerides set off a cascade of events that negatively alters a patient's lipoprotein profile. For example, elevated triglycerides cause higher excretion rates of apolipoprotein A1 through the kidneys, thus leading to low HDL levels. This explains the strong inverse relationship between triglycerides and HDL.

How are triglycerides treated?

Diets high in carbohydrates increase triglyceride levels, particularly in those with insulin resistance or obesity. Specifically, decreasing the amount of ingested simple sugars will usually lower triglyceride levels. An increase in the consumption of omega 3 fatty acids, whether from food or supplements can reduce triglyceride levels substantially in a dose-dependent manner. Regular exercise also reduces triglyceride levels leading to better energy metabolism overall. Pharmaceuticals commonly used to lower triglycerides include fenofibrates (such as Tricor or Trilipix) and omega 3 fatty acids.

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