

METAMETRIX CARDIOVASCULAR HEALTH PROFILE

The development of cardiovascular disease is a complex and multi-factorial process, so why would you trust your health to the measurement of just cholesterol and triglycerides? The **Metamatrix Cardiovascular Health Profile** offers a more in-depth look at the risk factors for cardiovascular disease than the typical lipid assessment. It combines conventional and innovative testing, including markers of nutrition, oxidative damage, inflammation, and hormone imbalances. The Metamatrix Cardiovascular Health Profile offers you and your patient valuable information to individualize integrative therapies that can reduce or eliminate the multiple risk factors for cardiovascular disease. Included in each report is a summary of results and the calculated “Cardiovascular Index” that helps you identify the strongest abnormalities and recommendations for supplement therapy.

Read on to learn more about Cardio related analytes and how they can affect you and your patient’s health!

LIPOPROTEIN FACTORS:

CHOLESTEROL

Cholesterol is a lipid found in the cell membranes of all tissues, it regulates membrane fluidity over a wide range of temperatures, and it is transported in blood. It also aids in the manufacture of bile and is important for the metabolism of fat soluble vitamins (A, D, E, and K). It is the major precursor for the synthesis of vitamin D and of the various steroid hormones.

HDL CHOLESTEROL

HDLs carry fatty acids and cholesterol from the body’s tissues to the liver. Epidemiologic evidence has shown a powerful inverse relationship between HDL and cardiovascular disease. In the Framingham Heart Study the risk of major Coronary Heart Disease (CHD) events increased by nearly 25% for every 5-mg/dl decrease in HDL below the median values and CHD events correlated more strongly with HDL than with either total or LDL.¹ In a meta-analysis of 4 large population-based studies, every 1% increase in HDL corresponded to a nearly 3% reduction in CHD risk.² HDL-C levels above 75 mg/dl have been associated with prolonged life.³ Although much of the antiatherosclerotic properties of HDL is considered to be mediated by reverse cholesterol transport (RCT), HDL-C has other beneficial effects, including reducing endothelial dysfunction, as well as anti-inflammatory, antioxidant, and antithrombotic effects.^{4,5}

LDL CHOLESTEROL

LDL transports cholesterol and triglycerides from the liver to peripheral tissues. LDL also regulates cholesterol synthesis at these sites. Lipid abnormalities are associated with the presence of Cardiovascular Disease (CVD). Low HDL and/or abnormal Triglyceride levels, when added to abnormal LDL, are associated with a higher prevalence of CVD.

TRIGLYCERIDES

Triglycerides are major components of very low density lipoprotein (VLDL) and chylomicrons, and play an important role in metabolism as energy sources and transporters of dietary fat.

LIPOPROTEIN(a) (Lp(a))

Lipoprotein(a) is assembled in the blood from LDL molecules and glycoproteins called apolipoprotein-a (apo-a). High Lp(a) is a risk factor for coronary heart disease, cerebrovascular disease, atherosclerosis, thrombosis, and stroke. Lp-(a) concentrations may be affected by disease states, but are only slightly affected by diet, exercise, environmental factors and lipid-reducing drugs. Niacin and aspirin are known to significantly reduce the levels of Lp(a) in some individuals.



TOTAL/HDL

The total cholesterol to HDL cholesterol ratio is a number that is helpful in predicting an individual's risk of developing atherosclerosis. High total cholesterol and low HDL cholesterol increases the ratio, and is undesirable. Conversely, high HDL cholesterol and low total cholesterol lowers the ratio, and is desirable.

LDL/HDL

The HDL/LDL ratio looks at the ratio of good cholesterol (HDL) to bad cholesterol (LDL). Changing the proportions of dietary fatty acids may be more important than restricting the percentage of total or saturated fat energy, at least when derived mainly from lauric and myristic acids, both of which increase HDL cholesterol.⁶

CHRONIC INFLAMMATORY MARKERS

FERRITIN

Excessive iron is sequestered by ferritin in a non-toxic and readily available form in the cell. The expression of ferritin is regulated at both the transcriptional and post-transcriptional levels by iron, cytokines, hormones, and oxidative stress. Hyperferritinemia is associated with liver disease; alcohol excess; chronic inflammatory conditions, and malignancy. Patients with autoimmune inflammatory diseases, such as rheumatoid arthritis commonly have an elevated serum ferritin which more likely reflects disease activity.

FIBRINOGEN

Fibrinogen is a sticky, fibrous coagulant in the blood that appears to significantly increase the risk of experiencing a stroke or cardiovascular disease. Analysis of the large-scale EUROSTROKE project showed fibrinogen to be a powerful predictor of stroke.⁷ The study found fibrinogen to predict fatal and nonfatal strokes, first time strokes, and hemorrhagic and ischemic strokes. Recent research has shown that fibrin plays a key role in the inflammatory response and development of rheumatoid arthritis. It may be elevated in any form of inflammation, as it is an acute phase protein.

C-REACTIVE PROTEIN (CRP)

CRP is an acute phase reactant and its levels rise dramatically during inflammation. Measuring and charting C-reactive protein values can prove useful in determining disease progress or the effectiveness of treatments. Recent research suggests that patients with elevated levels of CRP are at an increased risk for diabetes, hypertension and cardiovascular disease.^{8,9} A study of over 700 nurses showed that those in the highest quartile of trans fat consumption had blood levels of C-reactive protein that were 73% higher than those in the lowest quartile.¹⁰

OTHER IMPORTANT INDICATORS

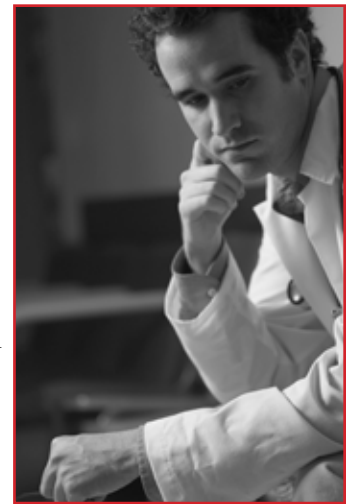
Insulin: Insulin resistance is considered a core component in the pathophysiology of metabolic syndrome. A fasting serum insulin level of greater than the upper limit of normal is considered evidence of insulin resistance.

TESTOSTERONE

Testosterone has stimulatory effects on bones, muscles, erythropoietin, libido, mood and cognition. It is reduced in metabolic syndrome and diabetes. and therapy with testosterone in these conditions may lower LDL cholesterol, blood sugar, glycated hemoglobin and insulin resistance. The best measure is bio-available testosterone which is the fraction of testosterone not bound to sex hormone binding globulin. Several forms of testosterone administration are available making compliance much less of an issue with testosterone replacement therapy.¹¹

SEX HORMONE BINDING GLOBULIN (SHBG)

SHBG is a glycoprotein that binds to sex hormones, specifically testosterone and estradiol. Its' level is decreased by high levels of insulin and insulin-like growth factor 1 (IGF-1) and high androgens, while high estrogen and thyroxine levels increase it. SHBG





concentrations are thought to be regulated primarily through opposing actions.¹² Low SHBG may serve as a predictive marker of insulin resistance in women with polycystic ovary syndrome (PCOS), particularly in those who are obese.¹³ Erectile dysfunction is associated with low bioavailable and free testosterone levels, as well as age, visceral adiposity and hypertension in type 2 diabetic men.¹⁴ Conditions with low SHBG include, PCOS, diabetes, and hypothyroidism. Conditions with high SHBG include pregnancy, hyperthyroidism, and anorexia nervosa. Low SHBG may be an important independent factor for cardiometabolic risk, particularly in women.¹⁵

FREE ANDROGEN INDEX

Circulating testosterone is primarily bound to SHBG, or albumin, only a small percentage is unbound. The sum of the free- and albumin-bound testosterone is often referred to as bioavailable testosterone. Low levels may indicate testosterone deficiency, which may contribute to fatigue, erectile dysfunction, weight gain, osteoporosis and loss of secondary sex characteristics. In women, androgens are most often measured when there is concern that they may be raised (as in hirsutism or the polycystic ovary syndrome). SHBG increases with aging and is associated with Alzheimer's disease.

OXIDANT STRESS FACTORS

HOMOCYSTEINE

Hyperhomocysteinemia is a well-established risk factor for cardiovascular disease. Various factors, both modifiable and non-modifiable, determine the plasma homocysteine concentrations, these include genetic abnormalities, age, sex and various nutritional and hormonal determinants, all of which play a role in atherosclerosis and accelerated peripheral and cardiovascular disease. Several hormones modulate homocysteine metabolism and hence may play a role in the pathogenesis of cardiovascular disease. Much conflicting data exists in the literature on the role of insulin on homocysteine metabolism.¹⁶

COENZYME Q10

CoQ10 is the most common type of Coenzyme Q, which is present in the mitochondria of human beings. It has been widely used for the treatment of various types of ailments which affect the heart, and is used in the treatment of diseases of the gums and some cancers. It is an antioxidant, and is related in structure to both vitamin K and vitamin E. Research studies using CoQ10 supplementation were found to delay the formation of 8-OHdG, an effect that was observed up to 12 weeks after stopping supplementation.¹⁷ Statins have been found to decrease plasma CoQ10 levels, while supplementation with CoQ10 increased their levels.¹⁸ CoQ10 supplementation is often utilized with statins and research has found it to decrease muscle pain associated with statin treatment.¹⁹

ALPHA-TOCOPHEROL

Decreased chronic disease incidence is associated with dietary vitamin E intakes, but more than 90% of Americans do not consume the recommended dietary amounts (15 mg/day). Vitamin E status in the Alpha-Tocopherol, Beta-Carotene Cancer Prevention study showed that men in the highest quintile compared with the lowest quintile, of serum alpha-tocopherol had significantly lower incidences of total and cause-specific mortality. Findings from the Women's Health Study support a role for vitamin E in decreasing the risk cardiovascular disease and thromboembolism. Additionally a reduction of cardiovascular events was found in individuals with diabetes mellitus.^{20,21}

LIPID PEROXIDES (TBARS)

TBARS reflects the formation of lipid oxidation products. Lipid peroxides are the product of free radical damage. Reactive oxygen species (ROS) play a major role in the pathogenesis of different chronic and degenerative diseases, including atherosclerosis. Evidences indicate that lipid peroxidation plays a vital role in the pathogenesis of cardiovascular disease.^{22, 23}

MAGNESIUM

Low serum and dietary Magnesium may be related to the etiologies of cardiovascular disease, hypertension, diabetes, and atherosclerosis.²⁴

ANALYTE	INTERVENTION	METABOLIC ASSOCIATION
TOTAL CHOLESTEROL	Garlic	Inhibits HMG-CoA reductase
	Niacin	Decrease synthesis in the liver, favorably alters sub fractions of LDL
	Vitamin C	Anti-inflammatory, antioxidant, clinical trials show a decrease in cholesterol
	Vitamin E and C	Paraoxonase inhibits atherogenic LDL and HDL oxidation. Vitamin E and C scavenges free radical products that may depress paraoxonase activity.
	Fish oil	Inhibits transcription for lipogenesis enzymes
LDL	Fish oil	Over expression of endothelial lipase caused by pro-inflammatory cytokines decreases HDL cholesterol
	Niacin	Lowers LDL levels, and VLDL synthesis
	Vitamin E and C	Paraoxonase inhibits atherogenic LDL and HDL oxidation. Vitamin E and C scavenges free radical products that may depress paraoxonase activity.
	Garlic	Decreases 3-hydroxy-3-methyl glutaryl coenzyme A reductase activity and increases bile acid excretion
HDL	Garlic	Decreases HMG-CoA reductase and increases bile excretion
	Niacin	Increases HDL levels by inhibiting the HDL apo AI catabolic pathway
	Vitamin C and E	Inhibition of paraoxonase activity
TRIGLYCERIDES	Carnitine	Increases utilization of triglycerides
	Chromium	Improves insulin activity which inhibits production of triglycerides
	Fish oil	Activation of PPAR
	Garlic	Decreases the synthesis of triglycerides in liver
	Vitamin C	Increases uptake into cells
	Niacin	Lowers triglyceride levels by inhibiting diacylglycerol acyltransferase 2.
LIPOPROTEINS	Niacin	Decreases the rate of Lp(a) synthesis
FERRITIN	Black tea, green tea	Decreased Fe+ absorption
FIBRINOGEN	Fish oil	Reduced thrombin generation
	Garlic	Anticoagulation activity, inhibits platelet aggregation
C-REACTIVE PROTEIN	Fish oil	Anti-inflammatory
	B-complex	Antioxidant and anti-inflammatory via homocysteine-lowering effect
INSULIN	Chromium, vanadium	Increases insulin sensitivity
TESTOSTERONE	DHEA	Precursor to testosterone
	Boron	Decreases elimination
	Zinc	Inhibits conversion of testosterone to DHT
SHBG	Diet and exercise	Decreases SHBG
	Nettles	Blocks testosterone binding to SHBG
HOMOCYSTEINE	Folic acid, Vitamin B12, Vitamin B6, Betaine	Re-methylation of homocysteine
COENZYME Q10	CoQ10	Increases serum and tissue levels
VITAMIN E	Mixed tocopherols and tocotrienols	Increases vitamin E tissue and serum levels
RBC MAGNESIUM	Magnesium	Increases magnesium serum and tissue levels
LIPID PEROXIDES	Antioxidants	Decreases oxidized lipids
ADMA	Arginine, folic acid	Competes with ADMA increasing production of NO2

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