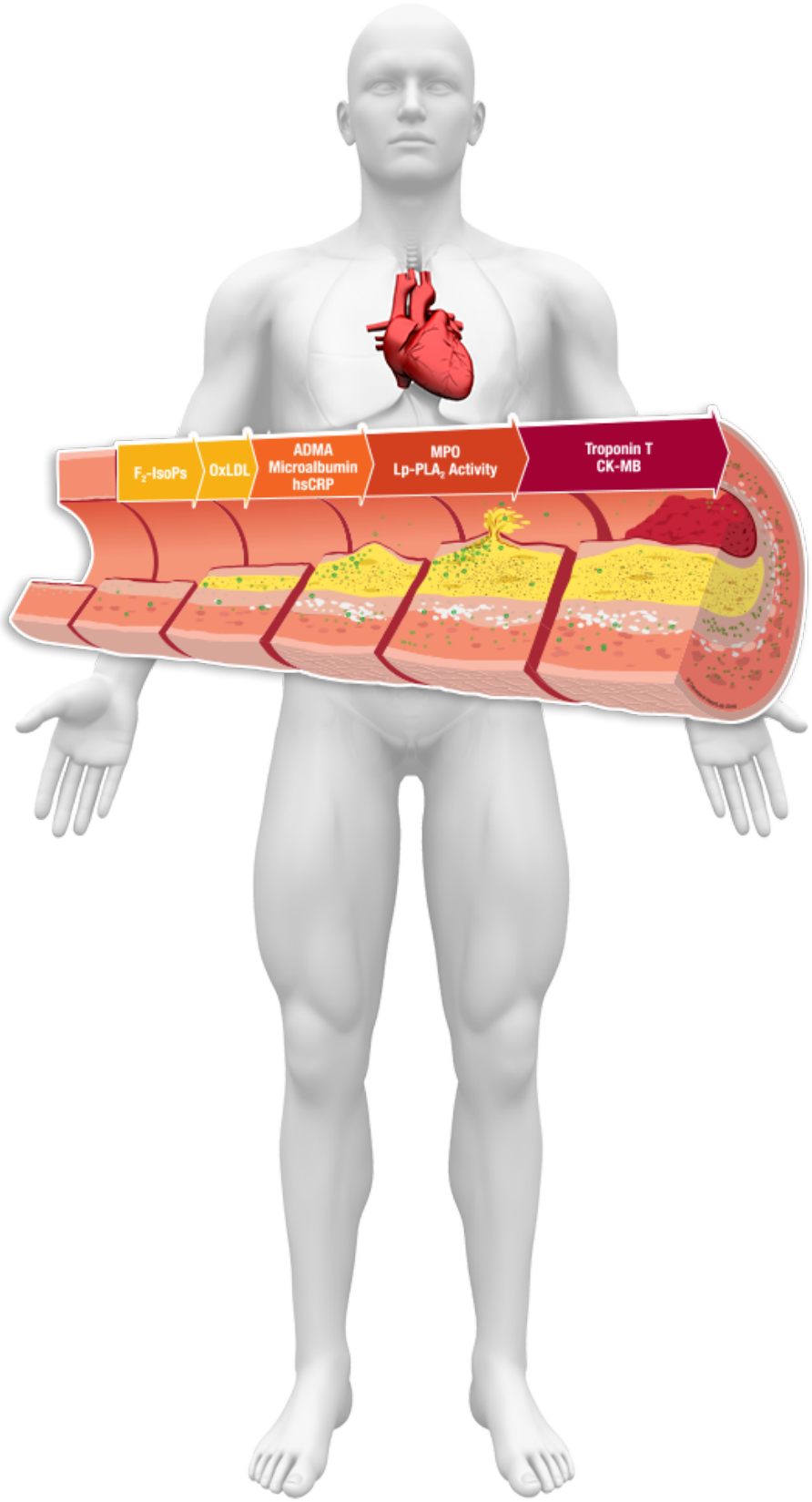
Read about our **response to the 2019 Novel Coronavirus outbreak.**

(https://www.questdiagnostics.com/home/Covid-19/)

ClevelandHeartLab®
Know your risk.

(HTTPS://WWW.CLEVELANDHEARTLAB.COM/)



(/wp-content/uploads/2018/11/CHL-D003-JUL2018-Artery-Wall-OnePager.pdf)

The Science

While routine lipid screening plays an important role in cardiovascular risk assessment it does not provide a complete picture of your health. In fact, nearly 50% of all heart attacks and strokes occur in patients with 'normal' cholesterol levels. Recent evidence goes beyond lipids to suggest that inflammation within the artery wall is the primary contributor to this residual risk for heart attack and stroke. Inflammation contributes to both vulnerable plaque formation and to plaque rupture.

inflammation testing™ from ClevelandHeartLab

Inflammation can be easily measured with advanced testing that assesses a patient's inflammatory state and cardiovascular risk. Monitoring their inflammatory status may allow you to catch the beginning, or even treat advanced stages of inflammation, in an effort to reduce their cardiovascular risk.

Cleveland HeartLab offers unique inflammation testing which provides additional and complementary insight into cardiovascular risk beyond cholesterol testing alone. Our inflammation testing consists of simple blood and urine biomarkers that identify inflammatory risk across a risk spectrum. This additional information allows for targeted treatment to reduce risk over one's lifetime.

This group of tests covers a patient's biomarker profile which may result from lifestyle concerns (F_2-IsoPs, OxLDL) to the development of metabolic or cardiovascular disease (ADMA/SDMA, Microalbumin, hsCRP) and formation of vulnerable plaque and increased risk for an adverse event (Lp-PLA_2 Activity, MPO).

+ F_2-Isoprostanes
+ Oxidized LDL (OxLDL)
+ ADMA/SDMA
+ Microalbumin
+ hsCRP
+ Lp-PLA_2 Activity
+ Myeloperoxidase (MPO)

Artery Wall One-Pager (/wp-content/uploads/2018/11/CHL-D003-JUL2018-Artery-Wall-OnePager.pdf)

*For more information and detailed references, please refer to our **Clinical References (/providers/clinical-references/)** page. For a complete list of all tests offered, please reference our **test menu (/test-menu/)**.*

+ A Multimarker Approach Can Aid in Stratifying Cardiovascular Risk

ADVANCED LIPID TESTING

Cleveland HeartLab offers advanced lipid testing to aid in determining cardiovascular risk in patients, alongside a Standard Lipid Panel which is commonly performed at least once a year in most medical practices. While a Standard Lipid Panel provides cholesterol and triglyceride measurements, other measurements readily available can address additional risk factors for disease including the number of atherogenic particles, the size of these particles and the inherent risk of developing CVD.

HDL Function Panel with HDLfx pCAD Score (HDLfx Test)

HDL cholesterol particles are considered to be cardioprotective because of their anti-atherogenic properties, which include increasing reverse cholesterol transport, promoting endothelial nitric oxide production, and anti-inflammatory and antithrombotic effects. Low HDL-C, a component of metabolic syndrome, is predictive of cardiovascular risk, but clinical trials have shown therapeutically increased HDL-C levels do not reduce rates of cardiovascular events. These findings led to an understanding that the physiological impact of HDL may be dependent on its functionality, more so than low or high HDL-C levels. The importance of HDL function to CVD is highlighted by findings that patients who have the highest cholesterol efflux capacity (CEC), a marker of HDL function, have a 67% reduction in cardiovascular risk compared to the lowest quartile CEC.

Provider Information (/wp-content/uploads/2020/05/CHL-MI8623-HDLfx-Practitioner-One-Pager-0520.pdf)

LipoFraction NMR (and LipoFraction NMR with Lipids)

Evaluation of lipoprotein particles has been used to support management of cardiovascular disease (CVD) risk for over 15 years, and lipoprotein subclass analysis has become a valuable tool to help clinicians better stratify patients at risk. In situations where LDL-C or HDL-C levels determined as part of a conventional lipid panel are optimal, additional LDL-C and HDL-C subclass analysis may identify patients with increased CVD risk. Enhanced identification of these previously unidentified at-risk patients can help physicians incorporate treatment that can help reduce atherosclerotic CVD and significantly reduce cardiovascular events.

Provider Information (/wp-content/uploads/2020/04/CHL-D040-SEPT2019-NMR-Practitioner-One-Pager.pdf)

Apolipoprotein B (ApoB) and A1 (ApoA1)

ApoB is the primary apolipoprotein found on the surface of LDL (the carrier of "bad" cholesterol), IDL (intermediate-density lipoprotein), VLDL (very low-density lipoprotein) and Lp(a) (lipoprotein (a)). ApoB acts as a ligand for LDL receptors on various cells throughout the body thereby regulating cholesterol influx into tissues. ApoA1 is the major apolipoprotein of HDL (the carrier of "good" cholesterol) and promotes cholesterol efflux from the artery wall to the liver for excretion.

Small-Dense LDL (sdLDL)

LDL, which carries "bad" cholesterol, exists either as large, more buoyant particles or as smaller, more dense particles (sdLDL). sdLDL is more easily oxidized, has a higher affinity for vessel walls, and remains in the circulation longer because it is less likely to be cleared by the liver, making it more atherogenic than larger LDL particles.

Provider Information (/wp-content/uploads/2020/11/CHL-D125-SEPT2019-sd-LDL-Practitioner-One-Pager.pdf)

Lipoprotein (a) (Lp(a))

Lp(a) is a plasma lipoprotein consisting of a cholesterol-rich LDL particle attached to an additional apolipoprotein called apo(a). Lp(a) levels are genetically determined and not affected by changes in lifestyle.

METABOLIC TESTING

Metabolic syndrome has become increasingly common in the United States. It's estimated that about 34% of adults in the United States have metabolic risk. Some factors contributing to metabolic syndrome are genetic while others can be modified with lifestyle changes. Cleveland HeartLab offers metabolic testing options. Some of these tests are highlighted below.

TMAO

Gut microbes live symbiotically within the human digestive tract and play important roles in host defense, immunity, and nutrient processing and absorption. This diverse community is unique to each person and influenced by both acute and chronic dietary exposures to various food sources. Nutrients such as phosphatidylcholine (also known as lecithin), choline, and L-carnitine are abundant in animal-derived products such as red meat, egg yolk and full-fat dairy products. When consumed, these nutrients are processed by gut

bacteria resulting in the release of various metabolites including TMA (trimethylamine) into the blood. TMA is then transported to the liver where it is converted into TMAO which has been shown to regulate various physiological processes involved in the development of atherosclerosis.

Provider Information (/wp-content/uploads/2018/11/CHL-D074-AUG2018-TMAO-Practitioner-One-Pager.pdf)

GlycoMark®

The GlycoMark® test provides a 2-week measure of average daily maximum blood glucose by measuring blood levels of 1,5-anhydroglucitol (1,5-AG), a glucose-like sugar found in food. When blood glucose levels are well controlled, most circulating 1,5-AG is reabsorbed in the kidneys instead of being excreted in the urine. In healthy individuals, circulating levels of 1,5-AG are high, with median values exceeding 20 µg/mL. However, when blood glucose levels are high, 1,5-AG reabsorption is blocked and a majority is excreted in the urine. Blood glucose spikes of greater than 180 mg/dL result in 1,5-AG loss in the urine. Individuals with type 2 diabetes have low circulating levels of 1,5-AG2,4. Unlike HbA1c testing, which measures an individual's average glucose over a 2-3 month period, the GlycoMark® test reveals more recent deteriorations in glucose control.

Adiponectin

Adiponectin is an abundant hormone released by adipocytes (or fat cells), commonly referred to as an adipokine. Adiponectin plays a large metabolic role in the body, participating in the regulation of glucose levels, insulin sensitivity and lipid catabolism. Adiponectin also helps support proper endothelial functioning and has multiple anti-inflammatory properties, including inhibiting the transformation of macrophages to foam cells, one of the first steps of atherosclerosis. Unlike other adipokines, adiponectin levels are lower in obese individuals. As adipocytes become larger with weight gain, they release less adiponectin. Among healthy individuals, women typically have higher adiponectin levels than men, and adiponectin levels tend to decrease as a person ages.

Provider Information (/wp-content/uploads/2018/12/CHL-D024-DEC2018-Adiponectin-Practitioner-One-Pager.pdf)

VITAMINS AND SUPPLEMENTS

Testing levels of certain vitamins, fatty acids or metabolites can provide insight into your patient's risk for metabolic and cardiovascular risk. Cleveland HeartLab offers vitamin and supplement tests that are additive and complementary to our inflammatory and advanced lipid testing options. Some of these tests are highlighted below.

OmegaCheck™

Omega-3 and omega-6 fatty acids are polyunsaturated long chain fatty acids (PUFA) required by the body for proper functioning, normal growth and the formation of neural synapses and cellular membranes. Omega-3 and -6 fatty acids are considered "essential" and obtained primarily from dietary sources. Three of the most important omega-3 fatty acids are eicosapentaenoic acid (EPA), docosapentaenoic acid (DPA) and docosahexaenoic acid (DHA). Omega-3 fatty acids are primarily obtained from food sources, such as oily fish. They have antioxidant, anti-

inflammatory and anti-thrombotic effects, and can help to reduce triglyceride levels. Two of the most important omega-6 fatty acids are arachidonic acid (AA) and linoleic acid (LA). Omega-6 fatty acids are obtained from animal sources and plant oils, and have pro-inflammatory and pro-thrombotic properties at high levels.

Provider Information (/wp-content/uploads/2018/12/CHL-D052-DEC2018-OmegaCheck-Practitioner-One-Pager.pdf)

CoQ10

Coenzyme Q10 (CoQ10) is a fat-soluble, vitamin-like substance present in most cells, primarily in mitochondria. CoQ10 has two major roles within the human body: it participates in aerobic cellular respiration generating energy (i.e., ATP) and is a powerful antioxidant. CoQ10 exists as two forms in the body: ubiquinone and ubiquinol (the active form of CoQ10, which is made from ubiquinone). Endogenous synthesis of CoQ10 is a very complex process requiring an adequate supply of numerous precursors and cofactors, and deficiencies in one or more of these components can adversely affect the production of adequate amounts of CoQ10. CoQ10 deficiency may also be caused by one or more of the following: insufficient dietary intake, impairment of CoQ10 biosynthesis, poor gastrointestinal absorption, and/or excessive utilization of CoQ10 by the body.

Vitamin D

Vitamin D is a fat-soluble vitamin naturally present in some foods, but the main source is synthesis within the body after exposure to sunlight. Vitamin D has various roles within the body, but primarily regulates the absorption of calcium in the gut, maintaining adequate serum calcium and phosphate concentrations thatcontribute to mineralization of bone. Vitamin D is available in two forms. Vitamin D3 (cholecalciferol) is mainly made in the skin upon exposure to UV light, and is also found in fish. The main source of Vitamin D2 (ergoalciferol) is fortified foods and supplements. Although commonly considered bioequivalent, Vitamin D2 may not be as bioavailable to the body as Vitamin D3. Vitamin D is metabolized in the liver to the prohormone Vitamin D25, OH.

GENETIC TESTING

Cleveland HeartLab also offers the following genetic tests.

Apolipoprotein E

ApoE is an apolipoprotein found in blood that, in association with lipids, forms lipoproteins including very low-density lipoproteins (VLDL). ApoE plays multiple roles in the regulation of lipid and lipoprotein levels in the blood. ApoE serves as a ligand for members of the low-density lipoprotein (LDL) receptor family, and is involved in the removal of lipoproteins from the circulation for excretion in the liver. ApoE is also involved in the formation of chylomicrons and VLDL, and affects the activity of other proteins and enzymes that are involved in lipid metabolism, such as hepatic lipase and lipoprotein lipase. Polymorphisms in the ApoE gene result in three separate

alleles encoding three distinct protein isoforms: e2, e3, and e4. There are 6 possible genotypes: e2/e2, e2/e3, e2/e4, e3/e3, e4/e3, and e4/e4. The allelic frequencies differ between ethnic groups, but in general the e3/e3 genotype is the most common, while e2/e4 is the least common.

× CYP2C19

CYP2C19 is a member of the cytochrome P450 family of enzymes involved in the metabolism and bioactivation of drugs. In particular, CYP2C19 is integral for the generation of the active form of clopidogrel (Plavix®), which is prescribed in a prodrug form. This prodrug is converted by CYP2C19 to the active form in the liver. Several variants of CYP2C19 have been identified which have an impact on its ability to metabolize drugs.

OTHER ADVANCED CARDIOVASCULAR TESTS

Cleveland HeartLab, Inc. also offers other advanced cardiovascular testing that are additive and complementary to our inflammatory and advanced lipid testing.

AspirinWorks®

AspirinWorks® is an enzyme-linked immunoassay (ELISA) to for the quantitative measurement of 11-dehydrothromboxane B2 (11-dhTXB2) levels in urine which aids in the qualitative detection of aspirin effect in apparently healthy individuals post-ingestion.

Galectin-3

Galectin-3 is one of the most widely studied galectins, a family of soluble B-galactoside-binding lectins that play a regulatory role in inflammation. Galectin-3 affects the synthesis of matrix compounds, such as type I collagen. When cardiac tissue is injured, macrophages infiltrate the tissue and secrete galectin-3, which promotes collagen synthesis and ultimately leads to cardiac fibrosis and adverse cardiac remodeling. Galectin-3 is independent of, and complementary to, natriuretic peptides as they identify separate and distinct biological processes. Galectin-3 is a mediator of cardiac fibrosis and adverse cardiac remodeling, whereas natriuretic peptides such as NT-proBNP or BNP identify myocardial stretch.

Provider Information (/wp-content/uploads/2018/11/CHL-D013-AUG2018-Galectin-3-Practitioner-One-Pager.pdf)

Troponin T, High Sensitivity

The troponin protein complex plays a key role in the regulation of cardiac muscle contractions. Prolonged ischemia of the myocardium can lead to death of cardiomyocytes and release of intracellular proteins, such as troponins, into circulation. For this reason, Troponin T levels exceeding the 99th percentile of a normal reference population are designated as the decision level for the diagnosis of an MI in conjunction with that patient's clinical

presentation. The development of high-sensitivity assays allows for lower levels of cardiac troponins to be assessed for other etiologies. Literature shows that even minimal increases of troponin levels are associated with unfavorable cardiovascular and all-cause mortality outcomes. This association is also independent of conventional risk factors.

Provider Information (/wp-content/uploads/2020/01/CHL-Troponin-T-High-Sensitivity-clinical.pdf)

AWARDS AND RECOGNITION

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