**Inflammatory Biomarkers and their Association with Atherosclerosis**

Atherosclerosis is associated with specific inflammatory biomarkers, which can be measured to help evaluate a patient’s risk for heart disease and cardiac events.
Looking Beyond Lipids to Identify Cardiovascular Risk

The risk of developing heart disease has traditionally been assessed by measuring LDL-C (low-density lipoprotein cholesterol; the carrier of “bad” cholesterol) and HDL-C (high-density lipoprotein cholesterol; the carrier of “good” cholesterol). Recent studies demonstrate that approximately 50% of heart attacks and strokes occur in patients with ‘normal’ cholesterol levels. This suggests that many individuals at risk are presumed low-risk because they have ‘normal’ or controlled cholesterol levels. Therefore, routine cholesterol testing may fail to fully identify patients at risk for heart attack and stroke.

Although it is essential to assess cholesterol levels, adverse events (such as heart attack, stroke or death) have been associated with inflammation, specifically vulnerable plaque related to increased white blood cell activation. The role of inflammation in the development of cardiovascular disease and subsequent adverse cardiac events was proposed in 1976 by Dr. Russell Ross, a world-renowned vascular biologist, in his “Response to Injury Hypothesis”.

Inflammation and the “Response to Injury Hypothesis”

Dr. Ross’s “Response to Injury Hypothesis” provided insight into the initiation and subsequent progression of cardiovascular disease. Briefly, cardiovascular disease is initiated through increased cholesterol and its subsequent oxidation leading to injury of the artery wall. The body responds to the injury with an inflammatory response designed to remove cholesterol from the artery wall. This process becomes dysregulated and ultimately potentiates the progression of cholesterol deposition and vulnerable plaque formation, placing an individual at increased risk of plaque rupture and subsequent heart attack or stroke.

Inflammatory Biomarkers

Cleveland HeartLab, Inc. offers inflammatory biomarker testing to help practitioners evaluate cardiovascular risk in patients. This group of tests covers a patient’s biomarker profile which may result from lifestyle concerns (F₂-Isoprostanes, OxLDL) to the development of cardiovascular disease (ADMA, Microalbumin, hsCRP) and formation of vulnerable plaque and increased risk for an adverse event (Lp-PLA₂, MPO).

F₂-Isoprostanes (F₂-IsoPs) are the ‘gold standard’ for measuring oxidative stress in the body. Elevated levels may be the result of excessive red meat intake, reduced activity levels, and smoking, and identify risk for atherosclerosis and cancer.

Oxidized LDL (OxLDL) is formed when the ApoB protein on LDL particles becomes oxidized. Elevated levels may be the result of poor lifestyle choices and identify risk of metabolic syndrome.

ADMA is a metabolite of L-arginine and can inhibit NO production. Elevated levels of ADMA are associated with endothelial dysfunction, insulin resistance, hypertension and subclinical atherosclerosis.

Microalbumin is the quantification of small amounts of albumin, a serum protein, in the urine to assess function and integrity of the kidneys. Elevated levels are associated with endothelial dysfunction and risk of cardiovascular morbidity and mortality.

High-sensitivity C-reactive protein (hsCRP) is an acute-phase protein released into the blood by the liver during inflammation. Elevated levels are associated with the risk of future adverse cardiovascular events in apparently healthy individuals and individuals with stable coronary artery disease.

Lp-PLA₂ is a vascular-specific inflammatory enzyme that increases with the activation of macrophages in the atherosclerosis lesions of the artery wall under the collagen cap. Increased Lp-PLA₂ Activity is associated with risk of coronary heart disease (CHD) or a CHD event.

Myeloperoxidase (MPO) is a vascular-specific inflammatory enzyme released by white blood cells into the bloodstream in response to vulnerable plaque, erosions, or fissures in the artery wall. Elevated MPO levels are associated with risk of cardiac events in subgroups otherwise characterized as low risk, and may assist cardiovascular risk prediction when used independently or alongside standard biomarker testing such as hsCRP.

References: