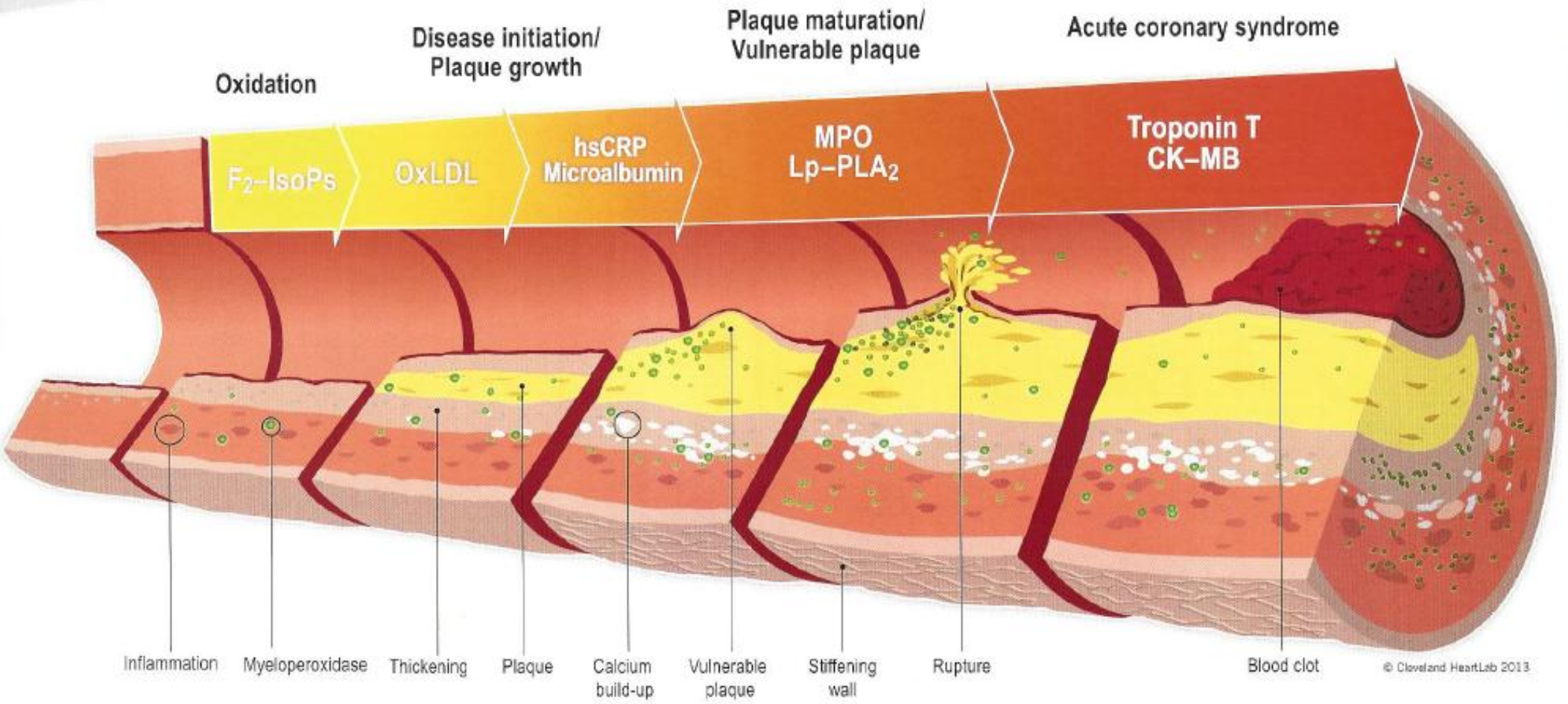
ClevelandHeartLab®

Know your risk.

Inflammatory Biomarkers and the Progression of Atherosclerosis

The progression of atherosclerosis is marked by specific inflammatory biomarkers, and their levels can be measured to determine a patient's risk for heart disease and cardiac events.



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Approximately **50%** of heart attacks and strokes occur in patients with ***'normal'*** cholesterol levels[1].

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[1]. This suggests that many individuals at risk are presumed low-risk because they have 'normal' or controlled cholesterol levels. Therefore, routine cholesterol testing is failing to fully identify patients at risk for heart attack and stroke.

Although it is essential to know your cholesterol levels, what actually causes adverse events (heart attack, stroke or death) is inflammation[2], 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 formalized in 1976 by Dr. Russell Ross, a world-renowned vascular biologist, in his "Response to Injury Hypothesis"[2].

INFLAMMATION AND THE "RESPONSE TO INJURY HYPOTHESIS"

The "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.

References

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THE CVD INFLAMMATION PROFILE™

Cleveland HeartLab, Inc. designed the CVD Inflammation Profile™ to more accurately estimate cardiovascular risk for patients who may warrant more aggressive and comprehensive therapy. This group of tests covers an individual's full spectrum of risk from lifestyle concerns (long-term risk; F_2-IsoPs) to the development of cardiovascular disease (early to mid-term risk; OxLDL, hsCRP, Urinary Microalbumin) and initiation of vulnerable plaque and increased risk for adverse cardiac event (near-term risk; Lp-PLA_2 and MPO). In short, an individual's risk for heart disease progression and mortality coincide with biomarker elevations along the inflammation continuum.

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 predict the risk of cardiac events in subgroups otherwise associated with low risk[3,4], and enhances cardiovascular risk prediction when used independently or alongside standard biomarker testing such as hsCRP[5].

Lp-PLA_2 (The PLAC® Test) 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. Elevated levels of Lp-PLA_2 predicts the risk of future adverse cardiac[6] and cerebrovascular events[7].

High-Sensitivity CRP (hsCRP) is a highly-sensitive quantification of CRP, an acute-phase protein released into the blood by the liver during inflammation. Elevated hsCRP levels are associated with the risk of future adverse cardiovascular events in apparently healthy individuals[8] and individuals with stable coronary artery disease[9]. Reductions of hsCRP and LDL cholesterol are associated with a reduction in the rate of atherosclerotic progression[10] and improved clinical outcomes[11].

Urinary Microalbumin (MACR) is the quantification of small amounts of albumin, a serum protein, in the urine which assesses the functioning and integrity of the kidneys. Elevated urinary microalbumin levels are associated with endothelial dysfunction and increased risk in cardiovascular morbidity and mortality[12].

Oxidized LDL (OxLDL) is formed when the ApoB protein on LDL particles becomes oxidized. Elevated OxLDL levels are associated with an increased risk of metabolic syndrome[13] and coronary heart disease[14] in healthy individuals due to lifestyle risks.

F_2-Isoprostanes (F_2-IsoPs) are the 'gold standard' for measuring oxidative stress in the body. Increased oxidative stress may be the result of excessive red meat intake[15] or reduced activity levels[16]. Elevated F_2-IsoPs levels are present in individuals with lifestyle-related risk for atherosclerosis[17] and cancer[18,19], including smoking, deconditioning and poor diet.

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