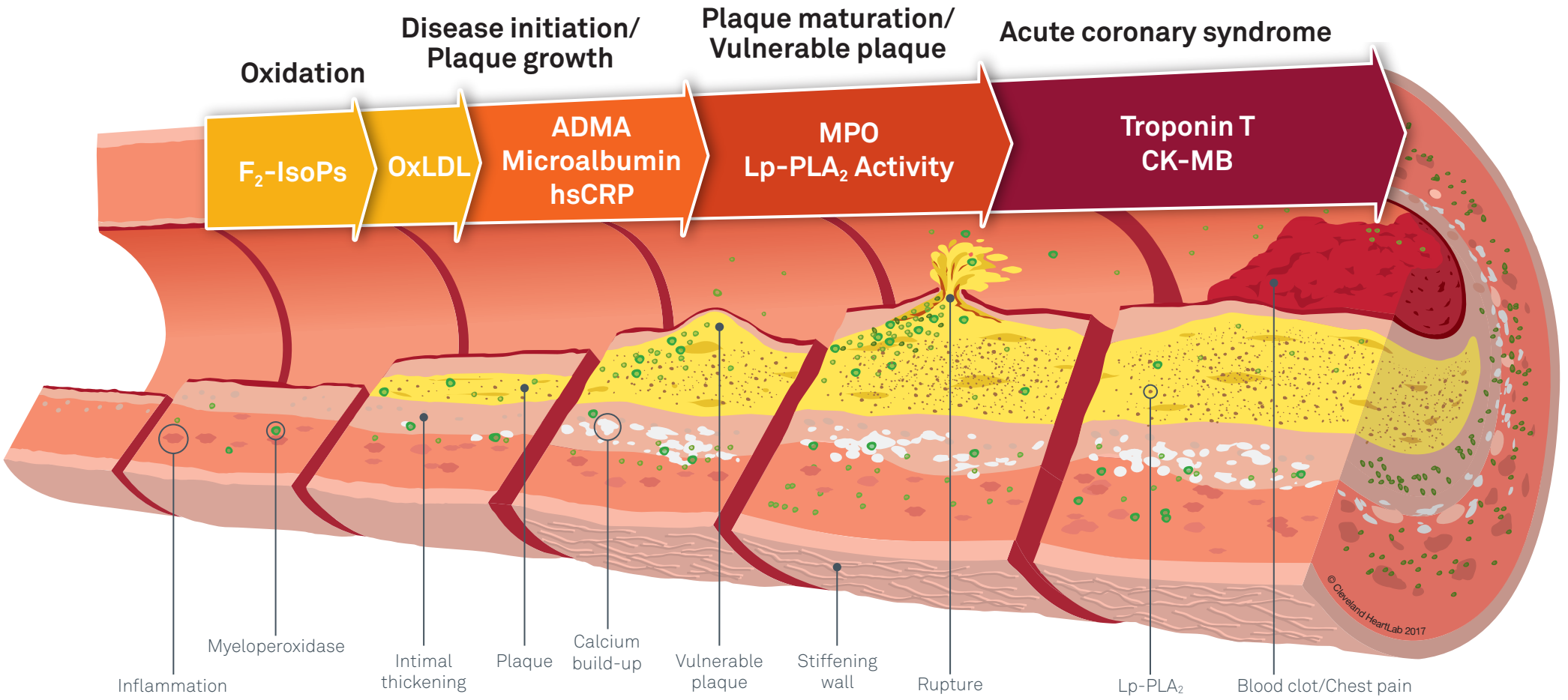
inflammation testing from ClevelandHeartLab™

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 cardiovascular events.



“Approximately 50% of heart attacks and strokes occur in patients with ‘normal’ cholesterol levels[1].”

PAIRING ADVANCED LIPID ASSESSMENT WITH INFLAMMATION TO IDENTIFY CARDIOVASCULAR RISK

The risk of developing cardiovascular disease has traditionally been assessed by measuring low-density lipoprotein cholesterol (LDL-C) and high-density lipoprotein cholesterol (HDL-C). Recent studies demonstrate that approximately 50% of heart attacks and strokes occur in patients with ‘normal’ cholesterol levels.[1] An advanced lipid assessment, or measuring the number of apolipoproteins or lipoprotein particles present, has been shown to better predict cardiovascular disease (CVD) risk than traditional lipid tests.[2,3] Atherogenic particles can infiltrate the vessel wall contributing to macrophage activity, foam cell production, atherosclerotic plaque formation, and CVD events.

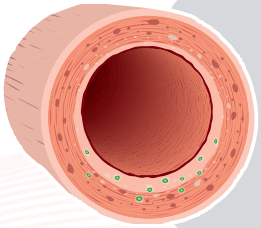
Although it is essential to assess cholesterol levels, adverse events (such as a heart attack, stroke, or death) have been associated with inflammation,[4] specifically vulnerable plaque related to increased white blood cell activation. The prominent clinical trials, JUPITER (2009) and CANTOS (2017), characterize inflammation as a critical component of atherosclerotic disease and cardiovascular risk, independent of lipids.[5,6]

INFLAMMATION AND THE “RESPONSE TO INJURY HYPOTHESIS”

In 1976, world-renowned vascular biologist, Dr. Russell Ross, proposed the “Response to Injury Hypothesis”, providing insight into the initiation and subsequent progression of cardiovascular disease.[4] Risk factors such as smoking, hypertension, and diabetes can damage the vessel wall, making it more susceptible to penetration and accumulation of atherogenic cholesterol. 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.

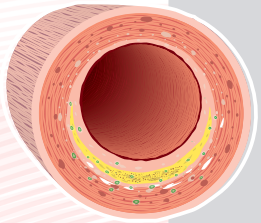
INFLAMMATORY BIOMARKERS

Quest’s Cleveland HeartLab Center of Excellence, 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 (F_2-IsoPs, OxLDL) to the development of cardiovascular disease (ADMA, Microalbumin, hsCRP) and formation of vulnerable plaque and increased risk for an adverse event (Lp-PLA_2, MPO).



F_2-Isoprostanes (F_2-IsoPs) are prostaglandin-like compounds used for measuring oxidative stress in the body. Elevated levels may be the result of excessive red meat intake,[8] reduced activity levels,[9] and smoking, and identify risk for atherosclerosis[10] and cancer.[11,12]

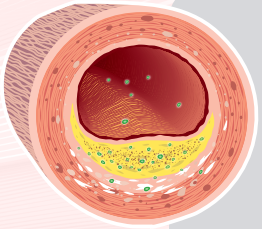
Oxidized LDL (OxLDL) is formed when the apolipoprotein B subunit on LDL particles becomes oxidized. Elevated levels may be the result of poor lifestyle choices and identify risk of metabolic syndrome.[13]



Asymmetric Dimethylarginine (ADMA) is a metabolite of L-arginine and can inhibit nitric oxide (NO) production. Elevated levels of ADMA are associated with endothelial dysfunction,[14] insulin resistance,[15] hypertension,[15] and subclinical atherosclerosis.[16]

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 of microalbumin/creatinine are associated with endothelial dysfunction and risk of cardiovascular morbidity and mortality.[17]

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[18] and individuals with stable coronary artery disease.[19]



Lp-PLA_2 is a vascular-specific inflammatory enzyme that increases with the activation of macrophages in atherosclerotic lesions of the artery wall under the collagen cap. Increased Lp-PLA_2 Activity is associated with risk of coronary heart disease (CHD)[20] or a CHD event.[21]

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,[22,23] and may assist cardiovascular risk prediction when used independently or alongside standard biomarker testing, such as hsCRP.[24]

References 1. Sachdeva A et al. Lipid levels in patients hospitalized with coronary artery disease: An analysis of 136,905 hospitalizations in Get With The Guidelines. *Am Heart J*. 2009; 157: 111-117. 2. Pischon T, Girman CJ, Sacks FM, Rifai N, Stampfer MJ, Rimm EB. Non-high-density lipoprotein cholesterol and apolipoprotein B in the prediction of coronary heart disease in men. *Circulation*. 2005;112(22):3375-83. 3. Cole TG, Contois JH, Csako G, et al. Association of apolipoprotein B and nuclear magnetic resonance spectroscopy-derived LDL particle number with outcomes in 25 clinical studies: assessment by the AACC Lipoprotein and Vascular Diseases Division Working Group on Best Practices. *Clin Chem*. 2013;59(5):752-70. 4. Ross R and Glomset JA. *N Engl J Med*. 1976; 295: 369-377. 5. Ridker PM, Danielson E, Fonseca FA, et al. Rosuvastatin to prevent vascular events in men and women with elevated C-reactive protein. *N Engl J Med*. 2008;359(21):2195-207. 6. Ridker PM, Macfadyen JG, Everett BM, et al. Relationship of C-reactive protein reduction to cardiovascular event reduction following treatment with canakinumab: a secondary analysis from the CANTOS randomised controlled trial. *Lancet*. 2018;391(10118):319-328. 7. Morrow JD. Quantification of isoprostanes as indices of oxidant stress and the risk of atherosclerosis in humans. *Arterioscler Thromb Vasc Biol*. 2005;25(2):279-86. 8. Tappel A. *Med Hypotheses*. 2007; 68: 562-564. 9. Shi M et al. *Environ Health Prev Med*. 2007; 12: 202-208. 10. Schwedhelm E et al. *Circulation*. 2004; 109: 843-848. 11. Rossner P et al. *Cancer Epidemiol Biomarkers Prev*. 2006; 15: 639-644. 12. Epplein M et al. *Cancer Epidemiol Biomarkers Prev*. 2009; 18: 1962-1970. 13. Holvoet P et al. *JAMA*. 2008; 299: 2287-2293. 14. Böger RH et al. Asymmetric dimethylarginine (ADMA): A novel risk factor for endothelial dysfunction: its role in hypercholesterolemia. *Circulation*. 1998; 98: 1842-1847. 15. Stühlinger MC et al. Relationship between insulin resistance and an endogenous nitric oxide synthase inhibitor. *JAMA*. 2002; 287: 1420-1426. 16. Maas R et al. Association of the endogenous nitric oxide synthase inhibitor ADMA with carotid artery intimal media thickness in the Framingham Heart Study offspring cohort. *Stroke*. 2009; 40: 2715-2719. 17. Gerstein HC et al. *JAMA*. 2001; 286: 421-426. 18. Ridker PM et al. *N Engl J Med*. 1997; 336: 973-979. 19. Ndrepepa G et al. *Am J Med*. 2006; 119: 355.e1-355.e8. 20. Oei HS et al. Lipoprotein-associated phospholipase A2 activity is associated with risk of coronary heart disease and ischemic stroke: The Rotterdam Study. *Circulation*. 2005; 111: 570-575. 21. Cushman M et al. Lipoprotein-associated phospholipase A_2 ($Lp\text{-}PLA_2$) activity and coronary heart disease risk in a biracial cohort: The reasons for geographic and racial differences in stroke (REGARDS) Cohort. *Atherosclerosis*. 2015; 241: e1-e31. 22. Meuwese MC et al. *J Am Coll Cardiol*. 2007; 50: 159-165. 23. Karakas M et al. *J Intern Med*. 2012; 271: 43-50. 24. Heslop CL et al. *J Am Coll Cardiol*. 2010; 55: 1102-1109.

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