

# Desialylated Atherogenic Low-Density Lipoprotein in Atherosclerosis

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## Abstract

Pathogenesis of atherosclerosis and the search for novel therapies and diagnostic markers remain major problems of modern medicine. Currently available therapeutic approaches are often not sufficiently effective, probably due to the complexity of the disease mechanisms. This review focuses on the evaluation of low-density lipoprotein (LDL) as risk factors of atherosclerosis. We summarize the current paradigm of LDL involvement in atherogenesis. We question the currently widely accepted hypothesis of the central role of oxidized LDL in atherogenesis and present an alternative concept of multiple modification of LDL that confers its pro-atherogenic properties. According to a series of studies conducted with blood serum and LDL from atherosclerotic patients, desialylation is one of the earliest if not the first atherogenic modification of LDL. Desialylation occurs in the bloodstream and is followed by a cascade of other modifications, including the reduction of LDL particle size and increase of its density, acquisition of negative electrical charge, oxidation and formation of highly atherogenic complexes.

Cardiovascular diseases (CVDs) are responsible for the high mortality and morbidity rates among adults worldwide posing a major socioeconomic burden not only on the health care system of a country but also on the whole national economic growth. The WHO World Heart Day (2017) has declared that the death toll in 2016 due to CVDs was an estimated 17.9 million people representing 31% of all causes of deaths in the world. The global cost of CVD management was \$863 billion in 2010 alone, with an expected increase of 22% by 2030.

Atherosclerosis is the main underlying cause of life-threatening CVDs. Relying on the population-based observational studies, it was established that the high incidence of atherosclerosis is prevalent among older adults in societies that adopt the Western pattern of diet and lifestyle. In that regards, various risk factors contributing to the development of atherosclerosis were identified, including tobacco smoking, hypertension, dyslipidaemia, hyperglycaemia/insulin resistance, overweight/obesity, and genetic predisposition. According to the current understanding, these conditions trigger vascular damage and lipid penetration into the vascular wall. In particular, atherogenic dyslipidaemia plays an important role in the development of atherosclerotic lesions. Hypercholesterolemia was reported as the highest attributable risk factor for atherosclerosis and subsequent coronary heart disease in a given population. Moreover, it was shown that persistently elevated levels of LDL were directly associated with the progression from early stage fatty streaks to advanced-stage, lipid-rich lesions. In addition, ethnicity also may determine the

incidence, severity, and age/sex distribution of atherosclerosis. A cohort study demonstrated that these parameters were higher among white American older men than in other ethnic groups, even after the adjustment of modifiable risk factors.

Furthermore, there is strong evidence that atherosclerosis affects young people and its prevalence and extent increase with age. Numerous studies reported that the subclinical form of atherosclerosis is frequently present in a large population of young adults in association with the presence of atherosclerosis risk factors. In fact, the incidence of clinically silent atherosclerotic lesions may reach up to 100% in this cohort of subjects. Young patients exhibit variations in etiologies and risk-factor profiles compared to older patients, resulting in differences in disease progression, prognosis, and treatment. The development of atherosclerotic lesions in young people can be attributed to the assumption that compared to older people, they are more likely to be smokers, male, obese, drug users, and have a positive family history. In particular, cocaine and other illegal drug use have been increasingly linked to accelerated atherosclerosis and acute myocardial infarction in teenagers. Asymptomatic atherosclerosis can have a prolonged latent period lasting for many years, even decades, prior to the first onset of clinical symptoms. In many cases, the acute ischemia of organs is its first clinical manifestation and is often fatal.