Is HDL cholesterol always good for you? Surprises, overturns and promises

According to the World Health Organization, coronary heart disease is a major cause of death worldwide. In 2008, 17.3 million people died from heart disease, and this number is expected to rise further, reaching an estimated of 23.6 million deaths in the year 2030. In the USA alone, in 2009, one out of every six deaths was due to coronary heart disease. Coronary heart disease, is the occlusion of coronary arteries of the heart that occurs due to buildup of fat in the arterial wall, also called atherosclerosis. The more severe the atherosclerosis, the smaller the lumen of the artery and the harder the free flow of blood and nutrients to the heart. A number of clinical studies established that people with high levels (>40mg/dl for men and >50mg/dl for women) of HDL cholesterol in blood are less likely to develop coronary heart disease. This observation suggested that HDL cholesterol is a good cholesterol in the fight against this disease.

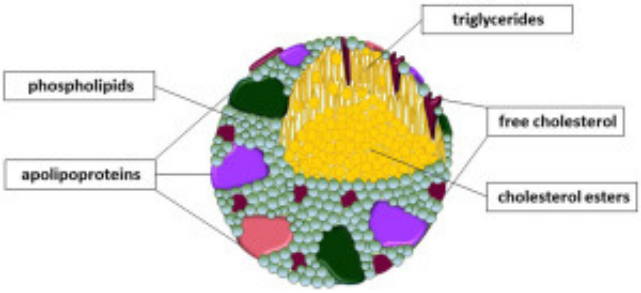

Fig. 1. Schematic representation of a typical spherical HDL particle. This particle is made of apolipoproteins and phospholipids, mainly present on their surface, and esterified cholesterol and some triglycerides in their inner lipid core.

In a recent paper published in the American Journal of Physiology Endocrinology and Metabolism Prof. Kyriakos E. Kypreos group from the University of Patras in Greece provided a critical historic overview of all current knowledge on HDL, focusing on the most recent and novel findings correlating HDL properties and functionality with various pathophysiological processes and disease states.

According to the authors, HDL cholesterol may not always correlate with a protective effect against coronary heart disease. Cholesterol is a form of fat and it has very limited solubility in water or blood. As a result, in blood cholesterol is transported in small spherical particles called lipoproteins (Fig. 1). In particular HDL cholesterol is transported in small lipoprotein particles called HDL (High Density Lipoprotein). These HDL particles are made of proteins and phospholipids, mainly present on their surface, and esterified cholesterol and some triglycerides in their inner lipid core (Fig. 1.). Under physiological conditions, properly functioning HDL lipoproteins receive excess cholesterol from the arterial walls of the heart and transfer it to the liver for degradation, a process known as

reverse cholesterol transport (Fig. 2.). This results in a substantial reduction of atherosclerosis in coronary arteries. At the same time HDL lipoproteins inhibit inflammation and lipid oxidation, two additional contributing factors to coronary heart disease development. Conditions that cancel these protective functions of HDL render HDL lipoproteins dysfunctional. In that case it does not matter anymore how much of HDL cholesterol one carries in blood, since it can no longer be protective against heart disease. Therefore, in addition to the amount of HDL cholesterol one has in blood, the quality of HDL lipoprotein is also very important for protection from lipid buildup in the arterial wall.

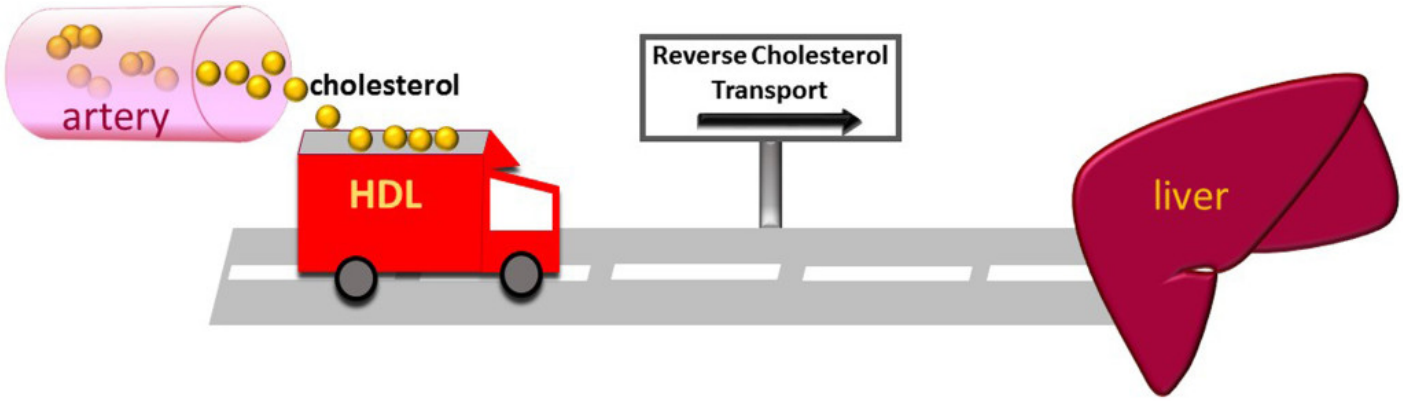

Fig. 2. A simplified depiction of reverse cholesterol transport. Properly functioning HDL particle is the vehicle that collects excess cholesterol from the arteries of the heart and transfers it to the liver for degradation.

Emerging evidence from studies in people and experimental animals strongly supports that the beneficial properties of HDL are also very important in a number of other diseases, such as obesity, type 2 diabetes mellitus, nonalcoholic fatty liver disease, sepsis, osteoarthritis and osteoporosis, obstructive pulmonary diseases, and brain disorders. The better understanding of the parameters influencing HDL lipoprotein properties will be invaluable for the development of new drugs for the treatment of all these medical conditions.

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Publication

Advances in high-density lipoprotein physiology: surprises, overturns, and promises.

Constantinou C, Karavia EA, Xepapadaki E, Petropoulou PI, Papakosta E, Karavyraki M, Zvintzou E, Theodoropoulos V, Filou S, Hatziri A, Kalogeropoulou C, Panayiotakopoulos G, Kypreos KE. *Am J Physiol Endocrinol Metab. 2016 Jan 1*