HDL3-P Activation

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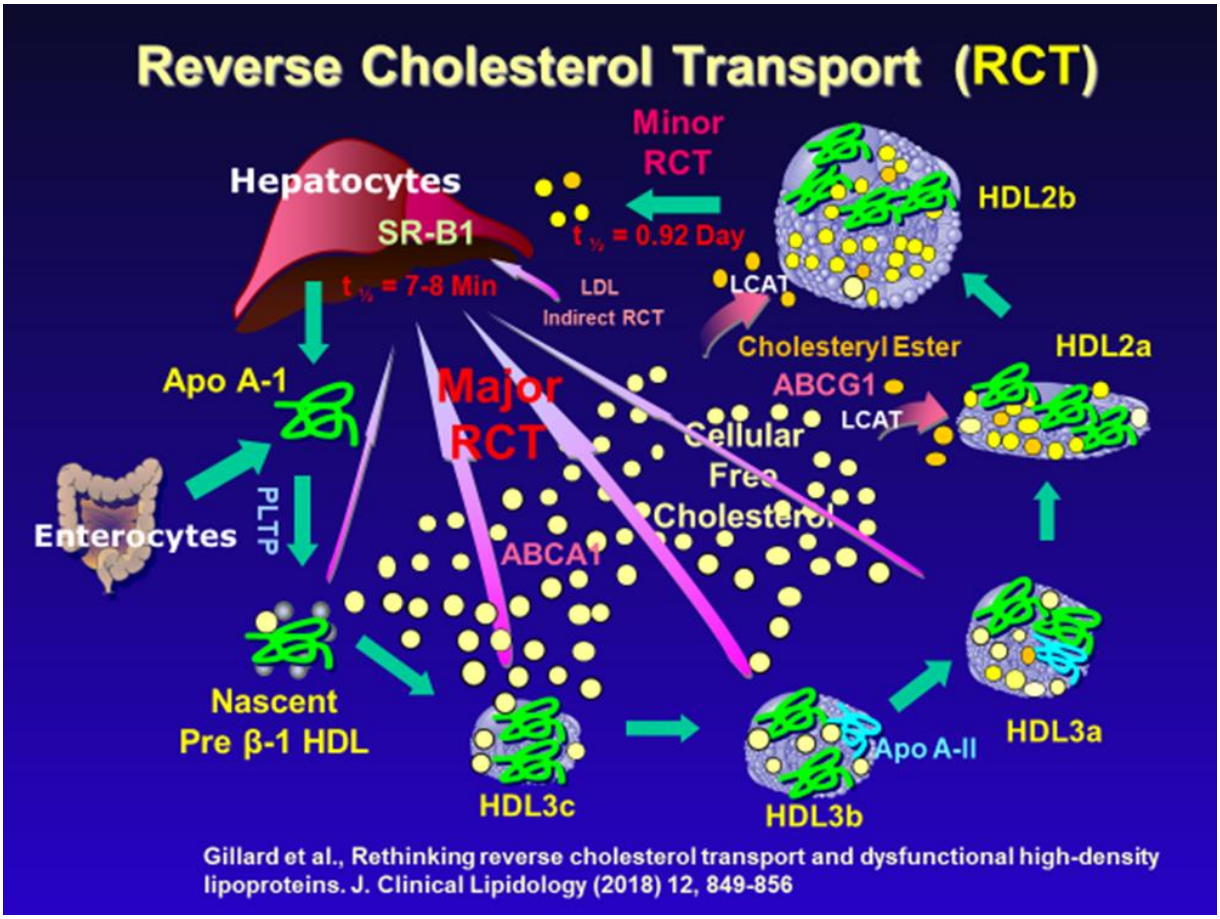
HDL3 particles (HDL3-P) are the smallest fully formed HDL particles. Hepatocytes and enterocytes produce the most important protein of HDL, Apo A-1. Apo-A1 collects phospholipids and a small amount of unesterified cholesterol to form a nascent Pre β-1 HDL. The Pre β-1 particles rapidly gather free cholesterol to become fully formed HDL3 particles. HDL3 particles scavenge macrophage and free cellular cholesterol to increase in size from the smallest HDL3c to the larger HDL3b and HDL3a particles. If the process continues the HDL collects cholesterol ester through the action of lecithin cholesterol acyltransferase (LCAT) to become HDL2a and finally HDL2b particles.

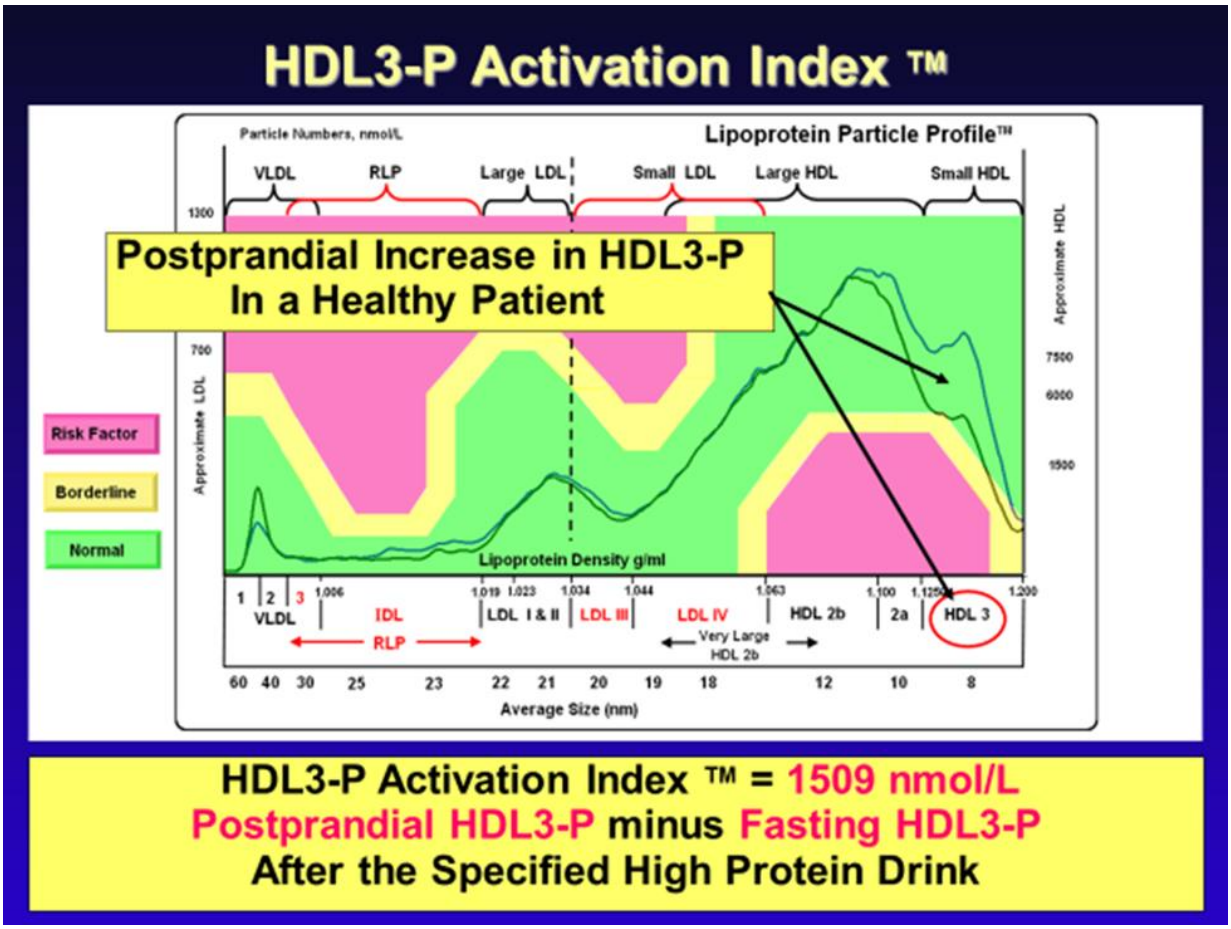
The action of HDL is complex with the primary function being that of reverse cholesterol transport (RCT) where the particles transport unesterified and esterified cholesterol back to the liver to be removed from the body. Recently new information has been published showing that HDL3-P is the major player in the RCT process and completes the cycle with a half-life of 7–8 minutes. Previously it was thought that HDL2b was the final step in RCT however it is now understood that HDL2b-P has a slower path of RCT with a half-life of 0.92 days.



An additional action of HDL is to provide anti-inflammatory and antioxidant protection to LDL most likely from paraoxonase-1. In this process HDL3 was found to be a more powerful antioxidant than HDL2 and the protector of LDL.

Clearly HDL3-P is an important player in cardiovascular health since it not only protects LDL from oxidation but provides the main path for excess cholesterol removal from both peripheral cells and macrophages building plaque in the arterial intima. The mechanism by which HDL3-P metabolism was thought to proceed, was an on-going process of the generation of the HDL3 particles growing to HDL2 particles then leading to RCT. Since most cholesterol testing is done on fasting patients and most testing measures cholesterol, not lipoprotein particles, the true metabolic process has gone un-detected. I observed that a non-fasting Lipoprotein Particle Profile (LPP), when compared to a fasting LPP for a patient, showed an increase in the small HDL-P's along with the previously known increases in triacylglycerols and insulin. This response was interpreted by others as a less favorable result following the guidance by many researchers that large HDL was the important HDL for RCT. However, since small HDL's (HDL3's) are needed to build large HDL's this observation appeared to be mis-interpreted.

After limited testing it was determined that the HDL3-P response was primarily due to protein, not carbohydrates or fat and that most people responded well in 90 minutes with shorter and longer times not showing significant differences. Based on this data, I proposed the HDL3-P Activation assay where the patient should give a fasting specimen and then drink a high protein drink, wait approximately 90 minutes and then give a second postprandial specimen. The HDL3-P Activation is the increase in HDL3-P in the postprandial specimen over the fasting specimen.



The lipoprotein response was only in the small HDL region and only in the particle numbers, not the HDL cholesterol results. This result makes it clear why this activation has not been previously reported since most testing is done with fasting specimens and usually not measuring lipoprotein particle numbers.

HDL3-P Activation results show increases in HDL3-P between 0% and 100% with an increase in total HDL-P of over 30%. This is clearly not a minor response with patients having diagnosed cardiovascular disease and diabetes mellitus giving poor responses and healthy individuals giving the best responses. Additionally, the initial value of fasting HDL3-P appears to be unrelated to the postprandial response so measuring fasting HDL3-P or HDL3-C is not useful.

HDL3-P is primarily responsible for reverse cholesterol transport and this process is very significant in the development of cardiovascular disease. The stimulated production of these particles is critical to cardiovascular health and believed to be a major risk factor. It is also significant that protein appears to be necessary for the response and that protein is necessary to make the main protein of HDL3, Apo A-1.